

## Authority Paper

<b>Paper Title</b>	<b>Mitochondria replacement consultation: advice to Government</b>
<b>Agenda Item</b>	<b>2</b>
<b>Paper Number</b>	[HFEA (20/03/13) 665]
<b>Meeting Date</b>	20 March 2013
<b>Author</b>	Hannah Darby, Senior Policy Manager
<b>For information or decision?</b>	Decision
<b>Recommendation</b>	For the Authority to consider the draft report regarding mitochondria replacement and agree the advice it wishes to provide to the Government, as proposed in the Executive Summary.
<b>Resource Implications</b>	In budget
<b>Implementation</b>	Final report to Government as soon as possible
<b>Communication</b>	For immediate publication
<b>Organisational Risk</b>	High
<b>Annexes</b>	Annex i: Summary of evidence Annex ii: Deliberative public workshops Annex iii: Public representative survey Annex iv: Open consultation questionnaire Annex v: Open consultation meetings Annex vi: Patient focus group Annex vii: Regulatory considerations Annex viii: Scientific review: update

## **1 Summary of advice to Government**

- 1.1 The Secretary of State for Health and the Secretary of State for Business, Innovation and Skills asked the Human Fertilisation and Embryology Authority (HFEA) in January 2012, to seek public views on emerging IVF-based techniques to prevent the transmission of mitochondrial disease, with support from Sciencewise Expert Resource Centre<sup>1</sup>. These techniques, which are referred to as mitochondria replacement, are currently illegal in treatment in the UK.
- 1.2 Mitochondria are present in almost all human cells. They generate the majority of a cell's energy supply. For any cell to work properly, the mitochondria need to be healthy. Unhealthy mitochondria can cause genetic disorders known as mitochondrial disease.
- 1.3 There are many different conditions that are linked to mitochondrial disease. They can range from mild to severe or life threatening, and can have devastating effects on the families that carry them. Currently there is no known cure and treatment options are limited. For many patients with mitochondrial disease, preventing the transmission of the disease to their children is a key concern.
- 1.4 The evidence presented here is drawn from a multi-method research and engagement project conducted between July and December 2012 which looked at the social and ethical issues raised by mitochondrial replacement. The evidence also addresses a range of practical regulatory issues.
- 1.5 In considering this evidence, and developing the analysis presented in this report, the HFEA has also brought to bear its experience of regulating IVF and research involving human embryos over the past 20 years.
- 1.6 It is not the task of the HFEA to advise the Government as to whether it should permit mitochondrial replacement in treatment. That decision would require a change in the law and is, quite properly, one which only Parliament can take. If the Government does wish to take steps

---

<sup>1</sup> The Sciencewise Expert Resource Centre (Sciencewise-ERC) is funded by the Department for Business, Innovation and Skills (BIS). Sciencewise-ERC aims to improve policy making involving science and technology across Government by increasing the effectiveness with which public dialogue is used, and encouraging its wider use where appropriate to ensure public views are considered as part of the evidence base. It provides a wide range of information, advice, guidance and support services aimed at policy makers and all the different stakeholders involved in science and technology policy making, including the public. The Sciencewise-ERC also provides co-funding to Government departments and agencies to develop and commission public dialogue activities. [www.sciencewise-erc.org.uk](http://www.sciencewise-erc.org.uk)

to change the law, it must draft Regulations as provided by the Human Fertilisation and Embryology Act 1990 (as amended) ('the Act').

1.7 Our advice to Government, set out in this report, is that there is general support for permitting mitochondria replacement in the UK, so long as it is safe enough to offer in a treatment setting and is done so within a regulatory framework. Despite the strong ethical concerns that some respondents to the consultation expressed, the overall view is that ethical concerns are outweighed by the arguments in favour of permitting mitochondria replacement.

1.8 We have therefore framed our advice so as to inform the Government's thinking, should it be minded to put Regulations forward to Parliament to make this possible. The advice we give below addresses the policies and safeguards that might guide those Regulations.

1.9 We set out our advice to Government in section 6, organised under the following themes:

- Modification of embryos and changing the germ line
- Implications for identity and the status of the mitochondria donor
- General views on the permissibility of the techniques
- Licensing models and further regulatory issues

1.10 Each theme discusses the issues and provides advice, in bold, at the end. That advice is reproduced here.

#### **Modification of embryos and changing the germ line**

1.11 In order to address concerns that permitting these techniques might open the door to other less desirable ones, the Authority advises that any Regulations allow for the specific germ line modifications proposed and consulted on (ie, the replacement of mitochondria) only. They should be drafted in such a way as to mirror the prohibition on modifying nuclear DNA in the Act and preclude in a treatment setting techniques which alter nuclear DNA, permit somatic cell nuclear transfer, or allow use of the techniques for anything other than avoiding serious disease.

1.12 In order to address concerns about the safety implications of changing the germ line, the Authority advises that mechanisms are put in place to allow for further recommended research (as outlined by the expert scientific panel in its report at Annex viii). The Authority also advises that licensed centres carrying out mitochondria replacement are

encouraged to conduct follow-up studies on any children born as a result.

### **Implications for identity and the status of the mitochondria donor**

- 1.13 The Authority advises that mitochondria donors should have a similar status to that of tissue donors. Children born of mitochondria replacement should not have a right to access identifying information about the donor when they reach the age of 18.
- 1.14 Existing systems for ensuring the traceability of gametes and embryos used in fertility treatment should be used in mitochondrial donation:
- licensed clinics should keep records to ensure they are able to trace all mitochondria donations from procurement to use and storage, including being able to identify the donor
  - the HFEA should keep a register of treatment cycles involving mitochondria replacement, resulting children and medical information about mitochondria donors.
- 1.15 The Authority advises that any Regulations should facilitate arrangements for disclosure of non-identifying information to mitochondria donors and children born as a result of their donation:
- parents and children conceived of mitochondria replacement should be entitled to find out non-identifying medical information about mitochondria donors once they reach the age of 16 (either from a licensed centre or the HFEA)
  - mitochondria donors should be entitled to find out basic non-identifying information about children resulting from their donation eg, the number, sex and year of birth (either from a licensed centre or the HFEA).
- 1.16 Local systems, based on mutual consent, should be put in place (eg, by clinics, in collaboration with appropriate charities or professional bodies) to facilitate voluntary exchange of information and contact between mitochondria donors and children resulting from their donation. These systems could reflect the voluntary systems in place for exchange of information following tissue donation.

### **General views on the permissibility of the techniques**

- 1.17 The Authority advises that mechanisms be put in place to allow for further consideration of the safety and efficacy of the techniques, in light of further research suggested by the expert scientific panel (outlined in its report at Annex viii), in conjunction with HFEA consideration of a licence application. The techniques should only be

carried out in clinical practice once experts advise the HFEA that these results are reassuring.

### **Licensing models and further regulatory issues**

- 1.18 The Authority advises that any Regulations permitting mitochondria replacement, should:
- ensure the techniques are only used to avoid serious mitochondrial diseases in cases where clinical specialists have deemed it to be appropriate
  - require the HFEA to approve each licensed centre wishing to offer mitochondria replacement as a clinical treatment
- 1.19 In order to future-proof the Regulations, they should provide flexibility for the HFEA to design a process for approving the use of mitochondria replacement in individual cases. Given the novel nature of these treatments, we recommend that the HFEA approves the use of mitochondria replacement on a case-by-case basis. It may be appropriate in the future to move to a more localised, clinic-based approval process.

## 2 Introduction and background

- 2.1 The Secretary of State for Health and the Secretary of State for Business, Innovation and Skills asked the Human Fertilisation and Embryology Authority (HFEA) in January 2012 to seek public views on emerging IVF-based techniques to prevent the transmission of mitochondrial disease, with support from Sciencewise Expert Resource Centre. These techniques are referred to as mitochondria replacement.
- 2.2 The HFEA is the UK's independent regulator for IVF treatment and embryo research. Our role is to protect patients and the public interest, to drive improvement in the treatment and research sectors and to provide information to the public and policymakers about treatment and research. The HFEA is a public body with substantial expertise in public dialogue and consultation often on contentious ethical and scientific issues, recent examples being the licensing of human-animal hybrid embryos for research and policies regarding sperm, egg and embryo donation. The HFEA has long experience of regulation and policy in such difficult areas.
- 2.3 On considering advice from the HFEA, the Government will decide whether to seek Parliamentary approval to permit one or both of the procedures for treatment.
- 2.4 The HFEA, with support from Sciencewise Expert Resource Centre, commissioned OPM (in partnership with Forster and Dialogue by Design) to conduct a multi-method research and engagement project looking at the possible social and ethical issues and arguments relating to mitochondria replacement. The project consisted of five strands (the findings of which are summarised at Annex i):
- Deliberative public workshops (Annex ii)
  - Public representative survey (Annex iii)
  - Open consultation questionnaire (Annex iv)
  - Open consultation meetings (Annex v)
  - Patient focus group (Annex vi)
- 2.5 At the request of Government, the HFEA has also considered the practical implications of allowing these techniques within the existing regulatory regime. The report at Annex vii highlights some of the regulatory issues associated with permitting mitochondria replacement.
- 2.6 As outlined in section 5 below, in anticipation of the outcomes of the public dialogue work, the Secretary of State for Health asked the

HFEA, in December 2012, to provide an updated view of the science to support the assessment of the efficacy and safety of the two mitochondria replacement techniques: pro-nuclear transfer and maternal spindle transfer. The HFEA reconvened a small panel of experts to advise on this; their conclusions are outlined in the report at Annex viii.

### **The mitochondria replacement techniques**

- 2.7 Mitochondria are present in almost all human cells. They generate the majority of a cell's energy supply. For any cell to work properly, the mitochondria need to be healthy. Unhealthy mitochondria can cause genetic disorders known as mitochondrial disease.
- 2.8 There are many different conditions that are linked to mitochondrial disease. They can range from mild to severe or life threatening, and can have devastating effects on the families that carry them. Currently there is no known cure and treatment options are limited. For many patients with mitochondrial disease, preventing the transmission of the disease to their children is a key concern.
- 2.9 Mitochondrial disease can be caused by faults in the genes within a cell's nucleus that are required for mitochondrial function or by faults within the small amount of DNA that exists within the mitochondria themselves, which is inherited from the mother. It is the latter form of mitochondrial disease that could be avoided using two new medical techniques, termed pro-nuclear transfer (PNT) and maternal spindle transfer (MST). These are currently at the laboratory stage, with active research programmes going on in the UK and the United States.
- 2.10 Mitochondria replacement holds great promise for women with mitochondrial disease who wish to have children who are genetically related to them. They are at the cutting edge, both of science and ethics and are currently only permitted in research. They involve removing the nuclear DNA from an egg or embryo with unhealthy mitochondria, and transferring it into an enucleated donor egg or embryo with healthy mitochondria.
- 2.11 If mitochondria replacement were to be made available for treatment in the UK, it would be the first time that modified embryos were used to make a child. The resulting child will have inherited nuclear DNA from its parents and mitochondrial DNA from a donor. These changes to a person's mitochondria will be passed down the maternal line through the mitochondrial DNA to the next generation.

## The legislation and regulatory context

- 2.12 The Human Fertilisation and Embryology Act (1990) (as amended) ('the Act') governs research and treatment involving human embryos and related clinical practices in the UK. The Act only permits eggs and embryos that have not had their nuclear or mitochondrial DNA altered to be used for treatment. However, in 2008 the Act was amended, introducing new powers which allow for Regulations to be passed by Parliament that will allow techniques that alter the DNA of an egg or embryo to be used in assisted conception, to prevent the transmission of serious mitochondrial disease.

## 3 Timeline

- 3.1 The table below sets out the key milestones regarding mitochondria replacement, relating both to the HFEA's considerations and other related developments:

2005	Research licence for pronuclear transfer granted
May 2010	The Authority's Scientific and Clinical Advances Advisory Committee considers research developments
June 2011	The Authority's Ethics and Law Committee considers ethical issues
April 2011	Core panel of experts, co-ordinated by the HFEA, reports to the Secretary of State for Health on the safety and efficacy of methods to avoid mitochondrial disease
January 2012	The Secretary of State for Health and the Secretary of State for Business, Innovation and Skills asks the HFEA to carry out public dialogue work
January 2012 – June 2012	Public dialogue and consultation work planning and preparation
July – August 2012	Public dialogue work takes place (deliberative public workshops and public representative survey)
September – December 2012	Open consultation runs (open consultation questionnaire, open consultation meetings and patient focus group)
December 2012	The Secretary of State for Health asks the HFEA to provide an updated view of the science to support the assessment of the efficacy and safety of MST and PNT
January 2013	Core panel of experts reconvened and call for evidence issued



- 3.2 In 2012, the Nuffield Council on Bioethics conducted a six-month inquiry into the ethical issues raised by “new techniques that aim to prevent the transmission of maternally-inherited mitochondrial DNA disorders” and concluded that “if these novel techniques are adequately proven to be acceptably safe and effective as treatments, it would be ethical for families to use them”<sup>2</sup>.

## 4 Public dialogue and consultation

- 4.1 The overall aim of the public dialogue and consultation work was to identify:
- The process of deliberation people use to form views on mitochondria replacement
  - The differences between informed and uninformed public views on these techniques
  - Interested stakeholders’ arguments for and against the use of the techniques
  - Analysis of the ethical and regulatory issues involved
- 4.2 The public dialogue work was designed to gain an insight into the views of members of the public on the ethical and social issues associated with the techniques. The public representative survey provides an indication of the views of the UK population by the sampling of a representative group. The deliberative work focuses on how people’s views change over time and develop when introduced to different information. The outcomes of the open consultation questionnaire and open meetings provide an insight into those with a specific interest in the issues, as the participants were self-selecting the findings from these strands of the consultation are not necessarily representative. Each strand is summarised below:

**Deliberative public workshops:** Workshops were held in Newcastle, Cardiff and London in July 2012 and participants met twice in each location. Participants were recruited to represent a broad spectrum of age, gender, socio-economic status and family circumstances. Thirty people were recruited for each location. The aim of this strand of the consultation was to explore public attitudes in depth, and to understand participant viewpoints as they become increasingly engaged with, and knowledgeable about, mitochondrial disease and mitochondria replacement techniques. The first meetings focused on helping participants to understand the techniques – PNT and MST –

---

<sup>2</sup> ‘Novel techniques for the prevention of mitochondrial DNA disorders: an ethical view’ Nuffield Council on Bioethics, June 2012

while the second events focused on the social and ethical issues relating to the techniques.

**Public representative survey:** In August 2012, just under 1000 face-to-face interviews were carried out with members of the public across 175 random locations. For each location, demographic quotas were set to ensure the sample was representative. The aim of the survey was to benchmark public opinion on: general attitudes towards medical research and genetic treatments; awareness of IVF and mitochondrial disease; views on the genetic treatment of mitochondrial disease; and attitudes to the regulation of genetic treatments.

**Open consultation meetings:** Two public meetings were held in November 2012. The first of these was in London (53 self-selecting attendees) and the second in Manchester (39 self-selecting attendees). The meetings were open to anyone wishing to attend and were advertised on the HFEA consultation website, through HFEA networks, and promoted to stakeholders and the public in a number of ways. At each meeting, a panel of speakers shared their knowledge and views with audience members. Panellists were selected to reflect a range of different perspectives and areas of expertise, and to provoke discussion amongst participants. The events involved a combination of small group discussions around particular issues, whole group debates, and discussion between and across the panel and the floor.

**Open consultation questionnaire:** A public consultation was held between September and December 2012. Self-selecting respondents were invited to consider a range of information presented on the consultation website, and to respond to seven questions using the online questionnaire. Responses made via email or post were also accepted while the consultation was open. A total of 1,836 responses were received, the majority of which via the consultation website. Respondents included stakeholder organisations, individuals with personal experience of mitochondrial disease as well as a large number of members of the public.

**Patient focus group:** One focus group was held with six participants. The aim of the focus group was to create a forum where people affected by mitochondrial disease, either directly or indirectly, could give their in-depth views on mitochondria replacement techniques. The group was comprised mainly of parents who had children affected by mitochondrial disease and someone who had been diagnosed with MELAS<sup>3</sup>. A telephone interview was also carried out with someone unable to attend the focus group.

---

<sup>3</sup> Mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes – abbreviated to MELAS.

- 4.3 In addition to HFEA-led events, there were also a number of other relevant conferences and meetings which coincided with the consultation period, which included the following:
- Progress Educational Trust debate, 25 September 2012: 'Freeing Us from Our Cells: Avoiding Inherited Mitochondrial Disease'
  - The Cheltenham Literature Festival, 14 October 2012: 'The Modern Family'
  - Science London debate, 19 November 2012: 'The great mitochondria transfer debate'
  - 'Sixth form conference 2012: Decoding DNA', organised by Wales Gene Park and Techniquet, 21 November: HFEA presentation on 'Medical Frontiers: Debating Mitochondria Replacement'
  - The Wales Gene Park in association with Techniquet offered a free session to schools/colleges that allowed more than 80 post-16 students the opportunity to respond to the open consultation questionnaire.
- 4.4 An Independent Oversight Group was set up to ensure the consultation was balanced and accessible. The Group was made up of a diverse range of experts who each brought a different perspective to the project. The role of the Group was to help ensure the dialogue material was comprehensive, balanced and accessible to a lay audience. It also ensured that the engagement process was far reaching, accessible and targeted all relevant stakeholder groups. The terms of reference and membership of the Group are available on the consultation website<sup>4</sup>.
- 4.5 The HFEA also considered the practical implications of allowing these techniques within the existing regulatory regime. The report at Annex vii highlights some of the regulatory issues associated with permitting mitochondria replacement. In order to inform this report, following discussion of issues with the Authority's Ethics and Law Committee and Scientific and Clinical Advances Advisory Committee, we consulted with fertility sector staff and other professionals who have direct experience of working with patients and donors in the clinic environment, rather than the general public.

---

<sup>4</sup> <http://mitochondria.hfea.gov.uk/mitochondria/about-the-consultation/independent-consultation-oversight-group/>.

## **5 Safety and efficacy of the techniques**

- 5.1 The Secretary of State for Health asked the HFEA, in February 2011, to carry out a scientific review to scope “expert views on the effectiveness and safety of mitochondrial transfer”. In order to carry out this task, the HFEA established a small panel, with broad-ranging scientific and clinical expertise, to collate and summarise the current state of expert understanding on the safety and efficacy of methods to avoid mitochondrial disease through assisted conception. The HFEA submitted a report<sup>5</sup> of the panel’s findings to the Department of Health on 18 April 2011.
- 5.2 The panel concluded that evidence available at that time did not suggest that the techniques are unsafe. Nevertheless, the report stated that these techniques are relatively novel, especially when applied to human embryos, and there is relatively little data to provide robust evidence on safety. The panel therefore urged that additional research be undertaken to provide further safety information and knowledge about the biology of human mitochondria. The panel proposed a (minimum) set of experiments that it felt were critical.
- 5.3 The report concluded that PNT and MST are potentially useful for a specific and defined group of patients whose offspring may have severe or lethal genetic disease, and who have no other option of having their own genetic child. These techniques may be preferable for patients with high levels of abnormal mitochondria for whom PGD is not suitable and more broadly, given that PGD can only reduce, not eliminate, the risk of transmitting mitochondrial disease.
- 5.4 Following these recommendations, a new mitochondrial research centre<sup>6</sup> was been set up in Newcastle, funded by the Wellcome Trust, which is carrying out the research as set out by the panel.
- 5.5 Subsequently, and in anticipation of the outcomes of the public dialogue work, the Secretary of State for Health asked the HFEA, in December 2012, to provide an updated view of the science to support the assessment of the efficacy and safety of pro-nuclear transfer and maternal spindle transfer techniques, including any recently published findings and the extent to which the panel’s recommendations of April 2011 have been addressed. This latest report can be found at Annex viii. The panel concluded that although the results with the two techniques are promising, further experiments need to be done before introducing either into clinical practice to provide further reassurance

---

<sup>5</sup> <http://www.hfea.gov.uk/6372.html>

<sup>6</sup> <http://www.ncl.ac.uk/iah/research/centres/wellcome/>

with respect to efficiency and safety. The panel updated its advice regarding critical and recommended experiments.

## **6 Analysis and advice**

- 6.1 As outlined in section 4, a number of different methods were used to gauge public opinion in order to identify the differences between informed and uninformed views and to carry out a qualitative analysis of the key themes and views. General attitudes towards assisted reproductive technologies have not been explored; the conclusions reached and the advice offered start from the basis of regulated IVF and associated techniques being acceptable.
- 6.2 The analysis outlined below points out where views relate either to that of self-selected or randomly selected participants. Table 1 in Annex i outlines the selection methods and the number, type and knowledge level of participants for each strand of the public dialogue and consultation.
- 6.3 The questions put to respondents throughout the different strands of the public dialogue focussed around the following themes:
- Modification of embryos
  - Changing the germline
  - Implications for identity
  - The status of the mitochondria donor
  - Permissibility of the two mitochondria replacement techniques
  - Models for regulation
- 6.4 In all the strands, participants were given the opportunity to express thoughts and views which did not necessarily fit into these themes.

### **General comments**

- 6.5 Our advice to Government, based on the evidence collected through the public dialogue and consultation, is that there is general support for permitting mitochondria replacement in the UK, so long as it is safe enough to offer in a treatment setting and is done so within a regulatory framework. Despite the strong ethical concerns that some respondents to the consultation expressed, the overall view is that ethical concerns are outweighed by the arguments in favour of mitochondria replacement.
- 6.6 We have therefore framed our advice in order to inform the Government's thinking, should it be minded to put Regulations forward to Parliament to make this possible. The advice we give below

addresses the policies and safeguards that might guide those Regulations.

- 6.7 It is worth noting that there are also ethical issues associated with deciding not to seek Parliament's approval to permit mitochondria replacement. Such a move would restrict the reproductive options of people with serious mitochondrial disease, denying them access to a treatment which has clinical promise.
- 6.8 The public dialogue and consultation work we undertook was focused on gathering and understanding public views on the social and ethical issues associated with mitochondria replacement. We wanted to explore their views independent of any questions of safety and efficacy. In practice, however, people's views on these issues tended to be linked to questions of safety; this was a strong theme through all the responses. Sometimes, safety concerns become a proxy for concerns about ethical and social issues, which are often hard to express. On other occasions, support for mitochondria replacement dipped when the scientific evidence was less clear.
- 6.9 The public expects questions of safety to be settled by the experts and that new treatments will not be made available until there is a consensus that it is safe to move from the laboratory to the clinic. The vast majority of people trust that someone will have the expertise to decide when the techniques are safe enough to use in humans and that mechanisms for robust follow-up research will be put in place.
- 6.10 However, safety is not a black and white issue. In reproductive medicine particularly, it is not possible to be absolutely certain about the consequences of a new treatment until children are born. Although such uncertainties are often difficult to accept, the evidence we have collected suggests that the public do understand this in the context of mitochondria replacement. For them, provided that there is further assessment of the safety of mitochondria replacement before it is offered in the clinic, and that it is properly regulated, it would be reasonable to proceed.

### **Modification of embryos and changing the germ line**

- 6.11 We sought views - through all of the public dialogue and consultation strands - about the fact that mitochondria replacement techniques result in changes to a person's mitochondria which will be passed down the maternal line through the mitochondrial DNA to the next generation. If the child is female, that change will be passed to their child and so on.
- 6.12 This passing down of a change from one generation to the next makes mitochondria replacement a form of germline modification. Given that

this has never been permitted on human embryos in a treatment setting before, it would clearly be a significant step and may raise important social and ethical questions. Does modifying the germ line affect a child's right to an open future? Is germline modification a step too far into a natural biological process?

- 6.13 It should be noted that some respondents did not accept the idea that mitochondria replacement is germline modification in the sense that it is commonly understood. Given that the two techniques involve replacing a woman's mitochondria with that of a donor, her mitochondrial DNA is not being modified, but rather substituted. Although this procedure might not be without its consequences for the embryo created, it is not the same as altering the genes with a person's mitochondria.

*Positive attitudes towards germline modification*

- 6.14 The public was largely relaxed about changing the germ line. When randomly selected members of the public were presented with information about what is currently known about the risks and uncertainty of changing the germ line, the majority felt that the benefits would outweigh those risks. Their views were largely shaped by the importance they placed on individual and personal choice for parents. When asked for their initial reaction, just over half of the public said they were 'very' or 'fairly' positive about changing the germ line, assuming the technique was shown to be safe.

- 6.15 Self-selected respondents expressing their views through the open consultation questionnaire and meetings held a broader range of views of this issue. Those in favour of the techniques felt either that the only implication of changing the germ line is the removal of terrible disease from a family, that the germ line would be changed for the better, or that any negative implications would be outweighed by the positive ones. Some felt that the germ line would not be changed significantly and parents could 'ideally' choose a mitochondria donor with a mitochondrial DNA sequence very similar to that of the mother.

*Concerns around safety*

- 6.16 However, the main theme running through responses to the open consultation questionnaire was the uncertainty and risk involved with introducing a new technique and the extent to which any consequences can be predicted. Others argued that if negative implications are identified, the consequences (once introduced to the germ line) would be so severe and far reaching that even a small risk should be considered carefully.
- 6.17 Some measures can be taken to address, as far as possible, these safety concerns. The panel of experts commissioned by the HFEA to

examine the safety and efficacy of the mitochondria replacement techniques recommended a set of experiments (critical and recommended) to be undertaken before the techniques can be deemed safe enough for use in human treatment. These include experiments which focus on the possible impact of changing the germ line, in particular the derivation and examination of human embryonic stem cell lines (then primordial germ cells) from embryos created from the techniques. The panel also thought that there is no evidence for any mismatch between the nucleus and any mtDNA haplogroup<sup>7</sup>, at least within a species ie, the nucleus from one person should be compatible with the mitochondria of another person.

- 6.18 The scientific panel (in the 2011 report and the 2013 update – see Annex viii) and respondents feeding into the regulatory considerations report (Annex vii) also recommended that families using these techniques be encouraged to take part in long-term follow-up studies in order to monitor any possible effects on children born and future generations. This was also a recommendation made by the Nuffield Council on Bioethics<sup>8</sup>, in its examination of the ethical issues arising from mitochondria replacement. There are arguments for both this being recommended as best practice and it being a formal condition of use of the technique. Commitment would be needed from patients and their children for a number of years and, although it's thought they would probably want to take part, there could be no obligation. Practical suggestions for how this follow-up research could take place and what data might be held by the HFEA are outlined in section 5 of Annex vii.

*Societal attitudes towards those born*

- 6.19 One concern raised by a small number of respondents related to the way in which society would view those born using the proposed techniques, or indeed those born to parents who decide not to use them. A small number of respondents felt that if the techniques are made available there will be pressure on parents to use them and discrimination against those who chose not to. They also raised a possible knock-on effect on attitudes towards disabled people more generally. Others were concerned that those born as a result of the techniques might be treated differently because of it or that it might be difficult for the child to come to terms with how they came into being. This question is explored in the 'Implications for identity' section below.

---

<sup>7</sup> A population group who share a common ancestor on the maternal line.

<sup>8</sup> 'Novel techniques for the prevention of mitochondrial DNA disorders: an ethical view' Nuffield Council on Bioethics, June 2012



- 6.20 These arguments could be – and have been - made in relation to other methods for avoiding the transmission of genetic diseases, be that prenatal diagnosis or PGD. It is beyond the scope of this piece of work to explore in detail the extent to which these techniques have served to devalue people with genetic diseases, but it is not a concern which has been significant enough for society to decide to deny people access to prenatal diagnosis or PGD.

*Slippery slopes?*

- 6.21 The predominant ethical issue raised by those with concerns about mitochondria replacement was that making changes to the germline for this purpose could lead to other germline modifications or, at least, to those modifications becoming more acceptable.
- 6.22 There are two dimensions to the idea of what is commonly called the slippery slope argument. The first is technical: is it possible that a change in legislation to permit one technique could inadvertently open the door to other, less desirable, techniques? The second is more conceptual: does social acceptance of one technique make it harder to argue against a further, more controversial, development? More specifically, will there be a demand, in future, for modification of nuclear DNA (germline gene therapy) and, if yes, will it be more difficult to resist this because modification of mitochondrial DNA is permitted?
- 6.23 The technical dimension of the slippery slope argument can be addressed through careful regulation and monitoring. The Act already prohibits the use in treatment of eggs, sperm or embryos which have had their nuclear or mitochondrial DNA modified<sup>9</sup>. It also prohibits the use in treatment of eggs and sperm which have been created *in vitro* and embryos which have been created through somatic cell nuclear transfer (SCNT) ie, cloning. If Regulations permitting mitochondria replacement were enacted, they would need to reflect these prohibitions in the parent legislation.
- 6.24 The conceptual dimension is more difficult to address because it relies upon a future possibility. We do not know whether there will be a demand in the future for nuclear DNA modification. It may be unlikely, particularly as PGD is an existing, viable option for the avoidance of genetic diseases which arise from mutations in the nuclear DNA. If a method of replacing nuclear DNA were developed, it is possible that the existence of mitochondria replacement would weaken any arguments against it. After all, when considering a novel technique, it

---

<sup>9</sup> Human Fertilisation and Embryology Act 1990 (as amended), section 3ZA, paragraphs (2)(b), (3)(b) and (4)(b)

is often helpful to look to existing, comparable techniques to guide our thinking about its acceptability.

- 6.25 However, the prospect of modifying the nuclear DNA would be a distinct development requiring a change to the law and, therefore, public and parliamentary debate. It would entail different risks and might be of interest to families who already have reproductive options available to them. Similar concerns were raised when SCNT was permitted for research purposes in 2001, with some arguing that this would lead to reproductive cloning. More than a decade on, however, opposition to reproductive cloning has not softened. Whilst concerns about slippery slopes should not be ignored, we can take comfort from the fact that the UK has a sufficiently developed system of regulation and tradition of public debate to minimise the risk of such concerns materialising.

*Is this a form of cloning?*

- 6.26 Many of the respondents to the public consultation questionnaire who expressed concerns about germline modification did so because they associated it with eugenics and cloning. One of the panellists in the London open consultation meeting argued that PNT is in fact cloning, because it involves the creation of an embryo which is then destroyed when its nuclear material is transferred to an embryo with healthy mitochondria.

- 6.27 However, the overwhelming majority of the audience challenged this view, arguing that although a similar methodology is used in PNT (the nuclear material is transferred from one embryo to another), it is not equivalent to SCNT. Any children resulting from PNT would have arisen from fertilisation and be genetically unique, not a genetic copy of an existing person. They would be the genetic child of the woman receiving treatment and her partner. Furthermore, PNT does not involve reprogramming cells or nuclei, as SCNT does, which is a relatively inefficient process and associated with significant risks of abnormal development.

*Future generations*

- 6.28 Some respondents to the public consultation questionnaire argued that any change to the germ line is inappropriate because there is no way for those affected to give consent. This view is contradicted by a few respondents, who regard making choices for subsequent generations as a very ordinary part of being a parent.

- 6.29 The few patients we spoke to expressed very little concern about this issue, mostly commenting that a change to the germ line would be 'preventing the disease' and that this is, in essence, a good thing.

- 6.30 Although some respondents, particularly those responding to the public consultation questionnaire, expressed concerns about modifying the germ line, the prevailing view of the majority of participants across all strands of the consultation was that the positive outcome of both mitochondria replacement techniques – a healthy child, free of faulty mitochondria – outweighs the possible negative consequences of changing the germ line.

***Advice***

- 6.31 **In order to address concerns that permitting these techniques might open the door to other less desirable ones, the Authority advises that any Regulations allow for the specific germ line modifications proposed and consulted on (ie, the replacement of mitochondria) only. They should be drafted in such a way as to mirror the prohibition on modifying nuclear DNA in the Act and preclude in a treatment setting techniques which alter nuclear DNA, permit somatic cell nuclear transfer, or allow use of the techniques for anything other than avoiding serious disease.**
- 6.32 **In order to address concerns about the safety implications of changing the germ line, the Authority advises that mechanisms are put in place to allow for further recommended research (as outlined by the expert scientific panel in its report at Annex viii). The Authority also advises that licensed centres carrying out mitochondria replacement are encouraged to conduct follow-up studies on any children born as a result.**

**Implications for identity and the status of the mitochondria donor**

- 6.33 Children born following mitochondria replacement will have inherited nuclear DNA from their parents and mitochondrial DNA from a donor. This would be a first for medical science and it raises the question of whether the contribution of mitochondrial DNA from a third person will impact on the future child's sense of identity or on our concepts of parenthood.

***Three parent IVF?***

- 6.34 Some media reports have referred to mitochondria replacement as 'three parent IVF', based on the fact that three individuals would be contributing DNA to create a child. Views on this issue amongst randomly selected members of the public, gleaned through the deliberative public workshops, were relatively balanced, although a slight majority were not concerned about this issue.
- 6.35 Most rejected the 'three parent IVF' idea, arguing that mitochondrial DNA contributes little or nothing to a child's personal characteristics and the donor should not therefore be regarded as a parent. A few

participants felt that the donation of healthy mitochondria would have helped a child to exist free from mitochondrial disease and that this should be recognised by giving the donor some sort of parental status. Views were shaped by using a range of comparisons and analogies, such as to adoption, organ donation, sperm donation, blood transfusion and bone marrow donation and by information on the amount and role of mitochondrial DNA in a person's genetic makeup.

- 6.36 Views of the public gleaned through the public representative survey tended to be more positive than negative about the idea of DNA from three people. When asked for their initial reaction to the fact that eggs or embryos resulting from new treatments would contain small amounts of genetic information from a third person, 44% said they were 'very' or 'fairly' positive, whilst 15% were 'very' or 'fairly' negative.

*What status should mitochondria donors have?*

- 6.37 Views on how mitochondria contribute to a person's identity, or sense of identity, are closely linked to how people think about the status of the donor and what, if any, information (eg, personal, medical or contact details) should be available to the future child. The public hold varied views on whether a child born from mitochondria replacement should be able to access information about the mitochondria donor involved. About a third of the deliberative public workshops participants held to the view that a child should have the right to know about their donor. By contrast, the number of participants that did not, increased during this process, from 31% at the start to 45% at the end.

- 6.38 The outcomes of the open consultation questionnaire and meetings demonstrate that self-selected respondents' views on the social and ethical implications relating to a person's sense of identity are also closely linked to their view on the status of the mitochondria donor. Respondents who referred to the donor as a third parent usually expressed concern about implications for identity. The concerns expressed about identity can be broadly grouped together as follows:

- Children being confused by knowing that they carry DNA from three people (some drawing comparisons to adopted or donor-conceived children, arguing they suffer from identity issues)
- Children born from PNT feeling unhappy about the creation and destruction of embryos
- General concerns about the potential emotional and psychological damage which children could experience

- 6.39 Those who regarded the social and/or genetic connection between donor and child as less significant mostly said they were not worried about the implications for identity, giving the following reasons:

- There is no connection between mitochondrial DNA and identity
- The genetic information important for identity is held in the nuclear DNA
- Identity is determined by more than genetic factors
- Mitochondria donation is comparable to organ, bone marrow or blood donation, which are not seen as influencing the recipient's sense of identity
- The impact on the child will be similar to or less significant than in sperm or egg donation (participants at the open consultation meetings felt that children born from mitochondria replacement might be 'happier' in the knowledge that they are genetically related to both their parents)

6.40 Views expressed through the open consultation questionnaire and meetings showed a roughly equally split between those who felt that mitochondria donation is similar to gamete donation and those who see it as different. Those who felt it is similar commonly took this view because mitochondria replacement involves procreation or genetic transfer. Those that saw it as different from gamete donation often said "it won't determine the characteristics of individuals; it will simply prevent them from inheriting a genetic disease".

6.41 It is clear that people's views on the importance and role of mitochondrial DNA determines their views on the status of the mitochondria donor and how they conceptualise the relationship between the donor and the child.

6.42 It is noteworthy that where respondents see the donation as making a genetic contribution of mitochondrial DNA, which has significance over and above the avoidance of mitochondrial disease (and therefore affecting personal characteristics), they tended to infer a role for the donor in the child's life (suggesting disclosure of identifying information). In contrast those who see the donation as having a minimal impact, tended to infer no role for the donor.

*Views specifically relating to PNT*

6.43 Many respondents suggested that mitochondrial donation for PNT differs from other donations, and is unacceptable because it involves the creation of an embryo with no intention of it being carried to term or born.

6.44 Embryos are often disposed of in fertility clinics, either because they are no longer needed for a patient's treatment, they are found to be affected by a genetic condition following PGD or they are found to be the wrong tissue type following pre-implantation tissue typing. From

this point of view, the creation and subsequent destruction of an embryo for PNT is nothing new. Embryos are also created during licensed research and are destroyed during or after the study.

- 6.45 However, PNT would represent the first time embryos were created, in a treatment situation, with no intention of being used (albeit that either their nuclear material or everything other than their nuclear material will go on to be used in treatment).

*What information should be available?*

- 6.46 When asked about different models for the disclosure of information about the mitochondria donor to the child, a substantial number of respondents to the open consultation questionnaire felt that no information, or only non-identifying information, should be disclosed. These respondents often saw MST and PNT as more like blood or tissue donation than egg or sperm donation, and so concluded that the donor's identity need not be disclosed.

- 6.47 Respondents who favoured a model allowing the donor's information to be disclosed along with their identity once the child reaches 18 years of age, tended to feel more strongly about the consequences and significance of mitochondria replacement. Their main concern was the medical, emotional or legal rights of children born through the procedure, which are sometimes explained as potential conditions determining what information should be disclosed. Several respondents felt it was important that donor consent should be sought to clarify which information would be disclosed if a donor's identity were to be disclosed to the child.

- 6.48 Patients felt that, as no nuclear DNA would be used from a third party, the techniques are more akin to blood or tissue donation. On this view, the child's sense of self would be inherited from their parents. They felt strongly that donors should remain anonymous and, moreover, that donors should want to, because no nuclear DNA is being donated.

*What do stakeholders think?*

- 6.49 Fertility sector staff and other professionals who attended a workshop to discuss regulatory considerations relating to mitochondria replacement came to a greater consensus. The majority view was that mitochondria donors are akin to tissue donors and should not be identifiable, as their genetic contribution is less likely to affect a person's identity than gamete donation.

- 6.50 Some stakeholders referred to the basis for removing gamete donor anonymity in 2005 as a useful starting point. This change was based on the idea that a donor-conceived child had a right to know who made them who they are. The main policy objective was to enable

donor-conceived children to have access to information about their genetic origins, similar to the right that adopted people have, for both health and personal history reasons.

- 6.51 In contrast, some stakeholders argued that current scientific evidence suggested that the role of mitochondria is limited to energy production and therefore, in their view, does not impact on a person's physical characteristics. They felt that if mitochondria donors were treated on a par with gamete donors then this could have the perverse effect of de-valuing the status of gamete donation. And they felt that children born through mitochondria replacement may be curious to find out details of their donor - just as the recipient of a tissue donation might - but that curiosity is not enough to warrant providing identifying donor information.
- 6.52 The majority agreed that there may be benefit for some donor information being held as the science surrounding the role of mitochondria could change, and that there is a possibility that it may later come to light that a donor suffers from a previously unidentified heritable disorder. This point was echoed at one of the open consultation meetings. As outlined in Annex vii, the European Union Tissue and Cells Directive already requires HFEA-licensed centres to ensure they are able to trace all tissues and cells from procurement to use and storage, including being able to identify the donor.
- 6.53 There was also a consensus at the workshop to discuss regulatory considerations that mitochondria donors should be able to find out the same type of information about their donation as is currently available to gamete donors (ie, the number, sex, and year of birth of any child). However, it is worth noting that when gamete donors were anonymous, they were initially unable to find out this type of information about their donation.

*Analogies with other types of donation*

- 6.54 In summary, views regarding the implications for identity and the status of the donor are shaped by using a range of comparisons and analogies to other types of donation and by views on information regarding the amount and role of mitochondrial DNA in a person's genetic makeup. Irrespective of the views on these issues, people generally think that mitochondria donors would play an important role – whether just to help ensure a child is free from disease or further – which should be recognised. The most common view was that a child should not have the right to know about their donor; therefore mitochondria donors should be anonymous.
- 6.55 There is a wide spectrum of information provision relating to different types of donation in the UK and the basis for this varies – some

involve the donor making a genetic contribution to a child, some involve the saving of a life. For example, legislation entitles children born following gamete donation to find out non-identifying information about their donor when they reach the age of 16, and then identifying information once they reach the age of 18. The non-identifying information can include a goodwill message and personal description of the donor (pen portrait)<sup>10</sup>. Although not based in statute, it is established practice for bone marrow donors to be provided with the recipient's gender and general age group, and there are systems in place for information exchange (eg, messages of luck or thanks) and contact between the donor and recipient, if mutual consent is in place<sup>11</sup>. These systems are managed by transplant centres and donor registries.

- 6.56 The balance of public views suggests that mitochondria donors should not be treated in the same way as gamete donors. Instead, they should be given a status similar to tissue donors. As mitochondria are thought not to be responsible for a person's characteristics (beyond their health)<sup>12</sup>, information about a mitochondria donor's personal details and identity should only be disclosed on a basis of mutual consent through a system without a statutory standing.
- 6.57 As the techniques involve the creation of embryos *in vitro*, and transfer to a woman, information about treatment cycles involving mitochondria replacement will be kept on the HFEA Register. As the state of mitochondrial DNA can have significant health consequences, children born following mitochondria replacement and their parents should be able to access medical information about the mitochondria donor.

### **Advice**

- 6.58 The Authority advises that mitochondria donors should have a similar status to that of tissue donors. Children born of mitochondria replacement should not have a right to access identifying information about the donor when they reach the age of 18.**

<sup>10</sup> 'For donor conceived people – What can you find out if you were conceived after 1 April 2005': <http://www.hfea.gov.uk/5526.html>

<sup>11</sup> Information from The Anthony Nolan Trust <http://www.anthonynolan.org/>

<sup>12</sup> "The small mtDNA genome encodes 13 genes essential for the ETC [energy production], the remaining components being encoded by about 67 genes residing on chromosomes in the nucleus. The mtDNA also carries transfer RNA (tRNA) genes required for mitochondrial protein synthesis. Mitochondria have other important roles in cellular physiology, notably in programmed cell death (apoptosis) and steroid synthesis, although these depend on genes encoded entirely within the nucleus." [http://www.hfea.gov.uk/docs/2011-04-18\\_Mitochondria\\_review\\_-\\_final\\_report.PDF](http://www.hfea.gov.uk/docs/2011-04-18_Mitochondria_review_-_final_report.PDF)



- 6.59 Existing systems for ensuring the traceability of gametes and embryos used in fertility treatment should be used in mitochondrial donation:**
- licensed clinics should keep records to ensure they are able to trace all mitochondria donations from procurement to use and storage, including being able to identify the donor
  - the HFEA should keep a register of treatment cycles involving mitochondria replacement, resulting children and medical information about mitochondria donors.
- 6.60 The Authority advises that any Regulations should facilitate arrangements for disclosure of non-identifying information to mitochondria donors and children born as a result of their donation:**
- parents and children conceived of mitochondria replacement should be entitled to find out non-identifying medical information about mitochondria donors once they reach the age of 16 (either from a licensed centre or the HFEA)
  - mitochondria donors should be entitled to find out basic non-identifying information about children resulting from their donation eg, the number, sex and year of birth (either from a licensed centre or the HFEA).
- 6.61 Local systems, based on mutual consent, should be put in place (eg, by clinics, in collaboration with appropriate charities or professional bodies) to facilitate voluntary exchange of information and contact between mitochondria donors and children resulting from their donation. These systems could reflect the voluntary systems in place for exchange of information following tissue donation.**
- General views on the permissibility of the techniques**
- 6.62** General views on the permissibility or acceptability of the techniques were sought through all of the public dialogue and consultation strands. Randomly selected members of the public remain broadly in favour of the two new techniques during the process of finding out about them and the possible ethical and social issues. The principal reason given for this was because the techniques give parents the opportunity to have healthy children who are genetically their own, which is not possible using current lawful techniques.
- 6.63** Views are shaped by information on the amount and role of mitochondrial DNA in a person's genetic makeup and great

importance is placed on individual and personal choice for patients. Views are also largely dependent on the safety of the techniques - the risks involved, long term safety and success rates. This was demonstrated by the fact that when, during one of the deliberative public workshops, support for the techniques dipped following questioning of the robustness of information regarding the scientific basis. Where opposition was expressed it was mainly because PNT involves manipulating and disposing embryos; the latter concern is applicable to all assisted reproduction techniques.

- 6.64 We know, from the representative survey of the public, that people are generally positive about the benefits of medical research. Almost nine out of 10 are in favour of providing people with serious genetic diseases with 'healthcare and treatment to manage their condition' and the majority are positive about embryo testing during IVF. Over half are 'very' or 'fairly' positive about mitochondria replacement when asked for an initial reaction, even though about half feel that 'the application of medical research leads to unforeseen negative side effects'.
- 6.65 It is important to bear in mind that the majority of the general public are unlikely to be aware of mitochondria replacement, as only just over a quarter of people know what mitochondrial disease is – awareness being strongly correlated to levels of education.
- 6.66 The open consultation questionnaire, the result of which represents views from a self-selected sample, was unique in terms of slightly more people opposing than supporting the techniques, often arguing that their use would amount to inappropriate interference with the natural or spiritual aspect of reproduction, or that any artificial or in vitro manipulation of embryos is unethical.
- 6.67 Proponents again focused on the benefits they could offer to parents, children or society more broadly, particularly the potential to avoid disease and allow parents the opportunity to have a healthy child. Some felt that, if the techniques were possible, there is a clear ethical obligation to implement them. Such views were echoed strongly at one of the open consultation meetings and the patient focus group. Patients also stressed the importance of individual parents and families having the choice about whether or not to use these techniques, whilst also being aware that use of these techniques would be a medical first and there may be a degree of risk involved.
- 6.68 In conclusion, there is considerable public support for mitochondria replacement and the majority of concerns relate to the safety rather than ethical issues associated with the techniques. As outlined in section 5, a panel of scientific experts has advised on the safety of the

efficacy of the techniques and concluded that there is no evidence to suggest that the techniques are unsafe. The panel has recommended further experiments which need to be done before introducing either into clinical practice.

### **Advice**

- 6.69 The Authority advises that mechanisms be put in place to allow for further consideration of the safety and efficacy of the techniques, in light of further research suggested by the expert scientific panel (outlined in its report at Annex viii), in conjunction with HFEA consideration of a licence application. The techniques should only be carried out in clinical practice once experts advise the HFEA that these results are reassuring.**

### **Licensing models and further regulatory issues**

- 6.70 If the Government was minded to draft Regulations permitting mitochondria replacement, it is likely that there will need to be some criteria to specify when these techniques can be used, bearing in mind how comparable activities are regulated.
- 6.71 Under the existing regulatory regime, clinics have to demonstrate competence before they can provide particular treatments. This is particularly important in the case of specialist services like pre-implantation genetic diagnosis (PGD). It is difficult to see why the same principles should not apply to MST and PNT.
- 6.72 Taking this model, the HFEA would only allow specialist clinics to offer these treatments if they had the relevant expertise and equipment to do so. We asked the public and stakeholders for their views on regulatory models, ie, when and how should patients be able to access mitochondria replacement and who should decide when the techniques are used. In all the consultation strands participants argued that strong regulation is essential if the techniques are licensed for clinical use.
- 6.73 The following possible options for accessing treatment were discussed:
- Clinics and their patients to decide when mitochondria replacement is appropriate in individual cases.
  - The regulator to decide which mitochondrial diseases are serious enough to require mitochondria replacement and, just for these diseases, permit clinics and patients to decide when it is appropriate in individual cases.
  - The regulator to decide which mitochondrial diseases are

serious enough to require mitochondria replacement and also decide, just for these diseases, when it is appropriate in individual cases.

- 6.74 Of the self-selected respondents to the open consultation questionnaire who expressed a preference for a particular regulatory model, close to half opted for the first system. This would involve clinics and individual patients being free to make a decision about whether or not to use mitochondria replacement in a particular case, without any regulatory stipulations regarding which conditions or cases it may be suitable for. This preference was often associated with a view that a central regulatory body may lack sensitivity to individual circumstances and a feeling that individual patients should be empowered to choose the best option for their own families. This was a view echoed strongly at the open consultation meeting in Manchester.
- 6.75 However, a similar number preferred an option that includes a role for the regulator. The majority of these respondents expressed a preference for a broad regulatory framework outlining those diseases that are deemed serious enough to warrant mitochondria replacement but which provides flexibility for patients and clinicians to reach individual decisions within this framework. This is currently how the HFEA authorises the availability of PGD for certain genetic conditions.
- 6.76 A minority of respondents expressed a preference regulatory a model in which a central regulator would maintain responsibility for making decisions about particular cases. This is currently how the HFEA regulates use of pre-implantation tissue typing (PTT). Reasons given in support of a regulatory framework, which were also echoed at the open consultation meeting in London, include:
- it would provide a buffer against abusive profiteering and a wide range of 'slippery slope effects' or illegal use, which might otherwise ensue
  - a central regulator would promote fairness by making sure that all applications for treatment would be judged according to the same criteria
  - it could ensure that priority is given to those at risk of passing on the most severe forms of mitochondrial disease
- 6.77 The views of those who object to mitochondria replacement being offered as a treatment, under any circumstances, have not been outlined here.
- 6.78 Views of randomly selected members of the public, gleaned from the deliberative public workshops and the public representative survey,

were mixed. Over a third of respondents (36%) favoured the option of couples being allowed to decide for themselves. A further 39% favoured some kind of involvement from a regulator, whilst one fifth (20%) favouring an expert regulator deciding on case-by-case basis (20%). A similar proportion (19%) favoured an expert regulator approving clinics, with medical specialists deciding who to offer it to (19%).

6.79 Deliberative workshop participants who supported regulation tended to do so because of the uncertainty of the risks associated with the techniques and the possibility of techniques becoming available in other countries with less stringent regulatory regimes (ie, where the techniques could be misused). Almost half of participants favoured some kind of regulation (43% at the start of the day to 48% by the end of their discussions). Although a large proportion of participants felt that couples themselves should make the decision about treatment (in consultation with their doctor), without the involvement of a regulator, reflecting the view that individual and personal choice for parents is paramount. This view rose from 35% at the start of the day to 40% by the end.

6.80 As outlined in section 3 of Annex vii, it is useful to make comparisons to other comparable techniques that have a basis in the HFE Act 1990 (as amended), in particular, the testing of embryos cannot take place unless the Authority is satisfied:

“...that there is a significant risk that a person with the abnormality will have or develop a serious physical or mental disability, a serious illness or any other serious medical condition”

6.81 To ensure that the Authority is satisfied, authorisation processes are in place for PGD and PTT:

- In the case of PGD, embryo testing clinics apply to the HFEA for permission to test for a particular genetic condition which they believe meets the relevant criteria in the Act (as noted above). If approved, any clinic with the appropriate licence can test for this condition in the embryos of patients who they deem appropriate. PGD has already been approved for a number of specific and named mitochondrial diseases (mostly caused by nuclear DNA defects) and it is a reproductive option for some patients at risk of passing on mitochondrial disease. The HFEA processes the majority of applications for PGD within approximately four months; this process includes seeking views of a peer reviewer.
- In the case of PTT, the HFEA approves embryo testing on a case by case basis. Only conditions that have already been

approved under the authorisation process for PGD can be considered for PTT. In making its decision, the HFEA will consider a referral from the child's treating clinician to ensure that the treatment is necessary and all other options have been considered. Applications are processed within 30 working days (approximately six weeks).

- 6.82 Some stakeholders, who expressed their views at a workshop, favoured mirroring the PGD approach, suggesting that the HFEA should approve conditions, and leave the judgement as to which patients receive the treatment with clinical staff.
- 6.83 However, the majority of workshop delegates agreed that the complexity and variable basis of mitochondrial disease, as outlined further in section 3 of Annex vii, would suggest an approach in which licensed clinics decided who should receive this treatment, according to criteria in the Regulations. This would determine if the disease was likely to develop into a serious condition, and whether mitochondria replacement is suitable for the patient. Fertility clinics would need to liaise with genetics teams and mitochondria specialists, to investigate how a disease may manifest (taking into account the level of unhealthy mitochondria and a patient's family history), before deciding the most appropriate treatment.
- 6.84 The majority agreed that the decision on who should receive the treatment should be made by clinicians, rather than the HFEA, and that patient referral from mitochondria expert centres (of which there are currently three<sup>13</sup>), could be worked into any new authorisation process.
- 6.85 In conclusion, a large proportion of the public favour some kind of regulatory oversight of access to mitochondria replacement. Bearing in mind past experience regarding the introduction of new comparable techniques into clinical practice, it seems unlikely that Parliament would allow mitochondria replacement techniques to be permitted without a degree of oversight of access to these services.
- 6.86 The complex and variable nature of mitochondrial disease suggests a case-by-case approach to decision making. However, given the assurances of regulatory oversight that Parliament is likely to want, we suggest that mitochondria replacement techniques be authorised in a similar way to PTT. However, in order to future-proof any Regulations, such oversight might be better expressed in HFEA guidance and processes, rather than on the face of the Regulations themselves.

---

<sup>13</sup> <http://www.mitochondrialncg.nhs.uk/>

Further detail regarding possible mechanisms for this is outlined at Annex vii.

***Advice***

- 6.87 The Authority advises that any Regulations permitting mitochondria replacement, should:**
- ensure the techniques are only used to avoid serious mitochondrial diseases in cases where clinical specialists have deemed it to be appropriate
  - require the HFEA to approve each licensed centre wishing to offer mitochondria replacement as a clinical treatment
- 6.88 In order to future-proof the Regulations, they should provide flexibility for the HFEA to design a process for approving the use of mitochondria replacement in individual cases. Given the novel nature of these treatments, we recommend that the HFEA approves the use of mitochondria replacement on a case-by-case basis. It may be appropriate in the future to move to a more localised, clinic-based approval process.**
- 6.89 A number of other regulatory issues were considered, some of which may require further consideration should mitochondria replacement be permitted in clinical practice, which are outlined in section 7 of Annex vii.**



# Medical frontiers: Debating mitochondria replacement

## Annex I: Summary of evidence

Report to HFEA

February 2013

OPM  
252B Gray's Inn Road,  
London WC1X 8XG

tel: 0845 055 3900  
fax: 0845 055 1700  
email: [info@opm.co.uk](mailto:info@opm.co.uk)  
web: [www.opm.co.uk](http://www.opm.co.uk)



Client	HFEA
Document title	Medical frontiers: Debating mitochondria replacement summary of evidence
Date modified	12 March 2013
Status	Final
OPM project code	8984
Author	Robin Clarke, Remco van der Stoep
Quality assurance by	Diane Beddoes
<b>Contact details</b>	
Main point of contact	Tim Vanson
Telephone	020 7239 7806
Email	<a href="mailto:tvanson@opm.co.uk">tvanson@opm.co.uk</a>

If you would like a large text version of this document, please contact us.



## Contents

1. Introduction .....	1
1.2 Methodological statement .....	2
2. Public dialogue and consultation findings .....	5
2.1 Permissibility of new techniques .....	5
2.2 Changing the germline .....	9
2.3 Implications for identity .....	11
2.4 The status of the mitochondria donor .....	14
2.5 Regulation of mitochondria replacement .....	17
2.6 Attitudes to legislation change .....	19

# 1. Introduction

Mitochondria are present in almost all human cells. They are often referred to as the cell's 'batteries' as they generate the majority of a cell's energy supply. For any cell to work properly, the mitochondria need to be healthy. Unhealthy mitochondria can cause genetic disorders known as mitochondrial disease.

There are many different conditions that are linked to mitochondrial disease. They can range from mild to severe or life threatening, and can have devastating effects on the families that carry them. Currently there is no known cure and treatment options are limited. For many patients with mitochondrial disease preventing the transmission of the disease to their children is a key concern.

Mitochondrial disease can be caused by faults in the genes within a cell's nucleus that are required for mitochondrial function or by faults within the small amount of DNA that exists within the mitochondria themselves. It is the latter form of mitochondrial disease that could be avoided using two new medical techniques, termed pro-nuclear transfer (PNT)<sup>1</sup> and maternal spindle transfer (MST)<sup>2</sup> which UK researchers are working on.

These techniques are at the cutting edge, both of science and ethics and are currently only permitted in research. They involve removing the nuclear DNA from an egg or embryo with unhealthy mitochondria, and transferring it into an enucleated donor egg or embryo with healthy mitochondria.

The Human Fertilisation and Embryology Act (1990) (as amended) ('the Act') governs research and treatment involving human embryos and related clinical practices in the UK. The Act currently prevents the clinical use of these techniques (or any other technique that involves genetic modification of gametes and embryos to treat patients). However, in 2008 the Act was amended, introducing new powers which enable the Secretary of State for Health to permit techniques which prevent the transmission of serious mitochondrial disease. The Secretary of State for Health and the Secretary of State for Business, Innovation and Skills asked the Human Fertilisation and Embryology Authority (HFEA) to seek public views on these emerging techniques. On considering advice from the HFEA the Government will decide whether to propose regulations legalising one or both of the procedures for treatment.

The HFEA, together with the Sciencewise Expert Resource Centre<sup>3</sup>, therefore commissioned OPM (in partnership with Forster and Dialogue by Design) to conduct a multi-method research and engagement project looking at the possible social and ethical issues and arguments relating to the techniques. The project consisted of five strands:

---

<sup>1</sup> Pronuclear transfer involves transferring the pronuclei from an embryo with unhealthy mitochondria and placing them into a donor embryo, which contains healthy mitochondria and has had its pronuclei removed. A pronucleus is a small round structure containing nuclear DNA seen within an embryo following fertilisation. A normal embryo should contain two pronuclei, one from the egg (maternal pronucleus) and one from the sperm (paternal pronucleus).

<sup>2</sup> The maternal spindle is a structure within the egg containing the mother's nuclear DNA. Maternal spindle transfer involves transferring the spindle from the intending mother's egg, with unhealthy mitochondria, and placing it into a donor egg with healthy mitochondria.

<sup>3</sup> The Sciencewise Expert Resource Centre (Sciencewise-ERC) is the UK's national centre for public dialogue in policy making involving science and technology issues

1. Deliberative public workshops
2. Public representative survey
3. Patient focus group
4. Open consultation meetings
5. Open consultation questionnaire

This research provides the evidence base that will inform the HFEA's advice to the Secretary of State.

This report provides an overall summary of the evidence from the five different consultation strands and, where possible, highlights areas of agreement and disagreement. It sits alongside the five separate strand reports.

## 1.2 Methodological statement

The five separate strands summarised in this report were:

- **Deliberative public workshops:** Workshops were held in Newcastle, Cardiff and London in July 2012 and participants met twice in each location. Participants were recruited to represent a broad spectrum of age, gender, socio-economic status and family circumstances. Thirty people were recruited for each location. The aim of this strand of the consultation was to explore public attitudes in-depth, and to understand participant viewpoints as they become increasingly engaged with, and knowledgeable about, mitochondrial disease and mitochondria replacement techniques. The first meetings focused on helping participants to understand the potential treatment techniques – pronuclear transfer (PNT) and maternal spindle transfer (MST) – while the second events focused on the potential social and ethical issues relating to the techniques.
- **Public representative survey:** In August, just under 1,000 face-to-face interviews were carried out with members of the public across 175 random locations. For each location, demographic quotas were set to ensure the sample was representative. The aim of the survey was to benchmark public opinion on: general attitudes towards medical research and genetic treatments; awareness of IVF and mitochondrial disease; views on the genetic treatment of mitochondrial disease; and attitudes to the regulation of genetic treatments.
- **Open consultation meetings:** Two public meetings were held in November 2012. The first of these was in London (53 attendees) and the second in Manchester (39 attendees). The meetings were open to anyone wishing to attend and were advertised on the HFEA consultation website, through HFEA networks, and promoted to stakeholders and the public in a number of ways. At each meeting, a panel of speakers shared their knowledge and views with audience members. Panellists were selected to reflect a range of different perspectives and areas of expertise, and to provoke discussion amongst participants. The events involved a combination of small group discussions around particular issues, whole group debates, and discussion between and across the panel and the floor.
- **Patient focus group:** One focus group was held with six participants. The aim of the focus group was to create a forum where people affected by mitochondrial disease, either directly or indirectly, could give their in-depth views on mitochondria replacement techniques. The group was comprised mainly of parents who had children affected by

mitochondrial disease and someone who had been diagnosed with MELAS<sup>4</sup>. One telephone interview was also carried out with someone unable to attend the focus group.

- **Open consultation questionnaire:** A public consultation was held between 17th September and 7th December 2012. Respondents were invited to consider a range of information presented on the consultation website, and to respond to seven questions using the online questionnaire. Responses made via email or post were also accepted while the consultation was open. A total of 1,836 responses were received, the majority of which were received via the consultation website. Respondents include stakeholder organisations, individuals with personal experience of mitochondrial disease as well as a large number of members of the public.

When reading this report the reader should keep in mind that the participants involved in each strand of the public dialogue had varying levels of knowledge about mitochondrial diseases and the associated concepts that were discussed. Some had little prior knowledge whilst others were well informed. The findings from the public representative survey should be treated as a snapshot of current public awareness of the issues and their views on them. People who completed the open consultation questionnaire formed a self-selected sample, rather than being recruited to a quota sample specification. This tends to mean that their levels of awareness and knowledge of the issues consulted on were higher than those of the population as a whole, though this cannot be assumed to be the case for all consultation respondents. The same point can be made about those attending the open consultation meetings. Patient focus group participants were directly or indirectly affected by mitochondrial disease and hence were likely to have higher levels of awareness and knowledge. Participants in the deliberative public workshops went on a journey from initially low levels of awareness and knowledge to develop a deeper understanding of the science and social and ethical issues. Deliberative public dialogue aims in part to explore whether and how information and deliberation impacts on participants' views. They were provided with information about the subject by experts, videos and information sheets.

A further point to bear in mind when reading this report is that many of those with higher levels of knowledge and awareness of the science and wider debate surrounding it have well considered and firmly held views about the issues.

---

<sup>4</sup> Mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes – abbreviated to MELAS.

The table below provides a summary of the types of people that took part in the consultation, how many participated, how they were selected and what their level of knowledge about the subject matter is.

**Table 1: Summary of participants in the consultation**

	<b>Participants</b>	<b>Selection method</b>	<b>Knowledge level of consultation issues</b>	<b>Number of participants</b>
<b>Deliberative public workshops</b>	Members of the public	Recruited to a quota sample	Low at start of the workshops, much higher by the end	Approx 30 participants at each workshop
<b>Public representative survey</b>	Members of the public	Random quota sample	Most people likely to have had low knowledge of the consultation issues	979 participants
<b>Open consultation meetings</b>	Interested stakeholders and members of the public	Self-selected sample through open invitation	Interested and knowledgeable about the consultation issues, but levels of knowledge were likely to be variable	53 participants (London meeting) and 39 participants (Manchester meeting)
<b>Patient focus group</b>	People directly or indirectly affected by mitochondrial disease	Invited to attend through patient contacts and patient groups	Interested and knowledgeable about the consultation issues, but levels of knowledge were variable	7 participants (including 1 telephone interview)
<b>Open consultation questionnaire</b>	Interested stakeholder and members of the public	Self-selected sample	Varied - relevant information was available via the consultation website which respondents were encouraged but not obliged to consult	1,836 participants responded to the consultation

## 2. Public dialogue and consultation findings

The headline findings of all five strands of the public dialogue and consultation fall under six main themes:

1. Permissibility of new techniques
2. Changing the germline
3. Implications for identity
4. The status of the mitochondria donor
5. Regulation of mitochondria replacement
6. Attitudes towards legislation

Under each of these headings we set out the main findings from each consultation strand, highlighting areas of agreement and disagreement. Where possible, findings were analysed across the different strands to identify areas of consensus and difference.

This report does not comment on the accuracy of people's views about the issues covered by the consultation. It does not seek to endorse or reject people's views; it presents them in an objective manner for the reader to consider.

### 2.1 Permissibility of new techniques

#### Deliberative public workshops

At the first deliberative public workshop meetings in Newcastle, Cardiff and London the focus was on providing participants with information on the science behind the new mitochondria replacement techniques. Overall, participants were fairly positive about the techniques, seeing them as a way of offering parents the chance to have a healthy child that is genetically their own. A minority argued against the use of pronuclear transfer (PNT) because it involves manipulating and disposing embryos. This argument tended to be made in terms of 'other people' finding the use of embryos in PNT an issue, they felt that it would be 'religious groups' who were the most likely to object. Some participants suggested that the use of these techniques might be seen as "*playing God*" and could result in a "*slippery slope*" to "*designer babies*" and "*aborting disabled people*." Others raised concerns about the safety of the new techniques, and wanted to know about the risks involved and whether research has been carried out in terms of success rates and long-term safety.

In this first round of deliberative public workshops, participants held largely positive views that were shaped by two main factors. Firstly, comparisons were made between the new techniques and treatments that are currently available, such as pre-implantation genetic diagnosis (PGD)<sup>5</sup> and prenatal diagnosis (PND)<sup>6</sup>. Consequently, participants felt that the new

---

<sup>5</sup> This is a procedure that involves testing an embryo in the laboratory for a genetic disease.

<sup>6</sup> This term describes any technique used to determine whether a developing fetus is affected with a genetic disorder or abnormality. This may involve testing the blood taken from the placenta, using ultrasound scanning or retrieving amniotic fluid for testing.

techniques offered a better outcome because they allow parents to have a healthy child that is genetically *'their own'*. The second factor was the importance they placed on personal and individual choice. Participants did not think it was appropriate to prevent access to these new techniques to individuals and families simply because some people (and groups) are opposed to their clinical use.

## Public representative survey

In the public representative survey, participants were asked for their initial reactions to different aspects of potential treatments for mitochondrial disease. The first question was:

*'Scientists are developing techniques which could remove the chance of these mitochondrial diseases by altering the genetic make-up of an egg or embryo during IVF. What is your initial reaction to this?'*

Over half (56%) were *'very'* or *'fairly'* positive about this and 10% were *'very'* or *'fairly'* negative about this. One third (33%) of respondents were undecided (*'neither positive nor negative'* or *'unsure'*).

To help understand survey respondents' views (in this and later sections of this report) about techniques to avoid mitochondrial diseases participants were asked more general questions about attitudes towards medical research, genetic treatments and existing IVF treatments. The findings showed that people were very positive about the benefits of medical research. Nine out of ten agreed that it *'can do a lot to reduce human suffering'* and it *'creates knowledge and treatments which will benefit the wider healthcare system'*. However, 50% also felt that *'the application of medical research leads to unforeseen negative side effects'* with 15% disagreeing and just over a third (36%) saying they were unsure.

Attitudes towards the treatment of people with genetic diseases were very positive. Almost nine out of ten (88%) members of the public were in favour of providing people with serious genetic diseases with *'healthcare and treatment to help manage their condition'* and nearly three-quarters (74%) felt that *'families at risk of having a child with a serious genetic disease should be able to avoid that risk through genetic testing.'* The question about genetic treatment received slightly more opposition (7%) as well as uncertainty (20%).

Respondents showed a high level of awareness of IVF, with 86% saying they had heard of it compared to 14% who had not. Awareness in London was lower than in other areas (65%), which may have been a result of particularly low awareness among BME groups and some faith communities; for example, 51% amongst Muslims. Awareness of mitochondrial disease was relatively low across all respondents, with just over a quarter (28%) stating that they had heard of the disease. Awareness was strongly correlated to levels of education, which rose from 10% (low levels) to 25% (medium levels) and 46% (high levels)<sup>7</sup>. There were small variations by faith: 34% of those with no religion saying they had heard of mitochondrial disease compared to 26% of Christians and 22% of Muslims.

When people were asked about their attitude to the testing of embryos during IVF, nearly two-thirds (65%) were *'very'* or *'fairly'* positive and 27% were undecided or unsure. There

---

<sup>7</sup> In the representative survey respondents were asked to indicate their highest level of education-related qualification—low levels: no qualifications; medium levels: O-Level, GCSE, A-level, GNVQ or similar; high levels: a degree, postgraduate, NVQ/SVQ level 4 or HNVQ.



was a drop off in positive ratings for some of those who described themselves as Christians and slightly more so for Muslims.

## Open consultation meetings

At the open consultation meetings there was a marked difference in the overall balance of views. Greater support for mitochondria replacement was seen in Manchester than in London where those opposed or concerned about the techniques were more vocal (although they were not the majority). When noting this difference it is important to reflect on the composition of attendees. London was attended by some firm sceptics and stakeholder groups who focussed on the risks and uncertainties attached to the new techniques. As a result, the debate at this meeting focussed on the moral status of the embryo and comparisons were made to cloning. By contrast, the Manchester meeting was represented by students and patients who were distinctly more supportive of the techniques with participants arguing that potential social or ethical issues were not significant enough and should not prevent the clinical use of the techniques to help others.

A few participants at the London event voiced concern about possible unforeseen effects of the new techniques and made comments that included: *“we are playing with something unknown and the full risks need to be understood.”* Another statement of concern was the danger of *“taking human embryos lightly.”* Terms such as *“unnatural”* and *“violating the integrity of nature”* were also used. However, the majority of attendees were more positive about the techniques and less worried about risks.

During the debate session at the event in London, some participants suggested that the HFEA needs to consider the *“important moral differences between the two techniques.”* The implicit suggestion was that PNT, which relies on the creation of embryos that will never be transferred into a woman, is more ethically objectionable than maternal spindle transfer (MST). Participants at the Manchester meeting showed a greater consensus about the permissibility of both techniques.

The issue of safety was discussed for some time in Manchester. When a panel member questioned the safety, an audience member responded by saying, *“of course there are risks...this is what happened with the first organ transplant. This is what happened with the first egg donation. More information should be found, more research should be done, but this doesn’t mean it shouldn’t move forward.”* This quote is reflective of how the vast majority of attendees at the Manchester meeting felt. While at the London public meeting there were some people who were critical of the new techniques, in Manchester it was clear that participants were much more positive about them.

## Patient focus group

The patient focus group participants were extremely positive about the new techniques. In part this was because unlike current options they could prevent the resulting child, and also their children from having mitochondrial disease: *“anything that could eliminate mitochondrial disease is a wonderful thing...”* One person did point out that while the techniques are not a cure, they are the best option currently available. Participants were also generally positive about mitochondria replacement because it could enable parents to have a child which is genetically their own, *“it will still be the genes of the mother and father, the child will still look and sound and act like its parents, that’s really important.”*

Some participants did want clarification on the safety and risks of the techniques. One person had questions about what needed to happen to refine the techniques and how

confident the scientists are that the technique would work. She had concerns that the first babies born from these techniques would be an “*experiment*”: “*Imagine being the parents of that first child born this way...it doesn’t sit right with me.*” Others disagreed with this, saying they would be happy to be the first, “*it is a risk I am willing to take...for me the risk is lower than the risk of the disease.*” Some participants said that there is always a degree of uncertainty with respect to medical innovation and that this is “*a part of medical progress.*” Participants stressed the importance of individual parents and families having the choice about whether or not to use these new techniques, arguing that wider social concerns should not be allowed to prevent them from making this choice.

## Open consultation questionnaire

The first question of the open consultation questionnaire asked respondents for their views on offering MST and PNT to people at risk of passing on mitochondrial disease to their child. A total of 1,235 respondents answered this question, of which slightly more disagreed with the introduction of both techniques. Looking at respondent types, there was a difference between the views expressed by respondents in specified categories, such as ‘student’ and ‘family member or friend affected by mitochondrial disease’, who were more often in support than in opposition, and those by respondents describing themselves as ‘other’, who predominantly stated opposition.

Proponents of the techniques tended to focus on the benefits they could offer to intending parents, children, or society more broadly, particularly the potential to avoid disease and allowing parents the opportunity to have a healthy child: “*If by introducing both these techniques, we can wipe out mitochondrial diseases and the suffering that goes with it, then it can only be a good thing.*” Some felt that if the techniques are possible, there was an ethical obligation to implement them.

In contrast, those opposing the techniques were more likely to discuss ethical issues, often arguing that the use of the techniques would amount to inappropriate interference with the natural or spiritual aspect of reproduction: “*It is not imperative that people have their own biological children, in fact such conditions are nature’s way of preventing weaknesses being passed from generation to generation.*” Others focused on the use of embryos, particularly in relation to PNT, arguing that any artificial or *in vitro* manipulation of embryos is unethical. Where respondents support one technique in particular, they tend to prefer MST because this technique replaces mitochondria in eggs rather than embryos.

Comments about the permissibility of the techniques were also prevalent in responses, received in different formats, which did not respond directly to the questions asked in the online questionnaire. A few of those expressed support, but many more (some 275 in all – most using very similar wording) say they believed the techniques were unacceptable.

## Summary

It is clear that most people believe the two new techniques offer the potential of significant improvements on the reproductive options currently available for women with unhealthy mitochondria. Across the different dialogue strands, most participants seemed to be positive about the techniques with the exception of the open consultation questionnaire where more respondents were opposed than supportive. It was also particularly noticeable that for the majority of people coming to this topic for the first time (mainly people taking part in the deliberative public workshops and the public representative survey), the potential benefits of the new techniques outweighed their concerns about the potential risks. Amongst these

newcomers to the topic, a substantial proportion was undecided and only a few had an initial reaction of disagreeing with the use of these techniques. It is not possible to say whether those who were undecided would become supportive or unsupportive of the techniques if they were given more time to think about and discuss them. It was noticeable that some of them wanted more information about the safety of the techniques before deciding one way or the other.

Those already familiar with the techniques, and the social and ethical debates around them, tended to have set views on whether they should be permitted or not. The majority who took part in the open consultation meetings and the patient focus group were in favour, but at the former there was some very vocal opposition.

## 2.2 Changing the germline

### Deliberative public workshops

*'Changing the germline'* refers to the fact that any changes to a person's mitochondria will be passed down the maternal line through the mitochondrial DNA to the next generation, and if the child is female, to the child after that and so on. People taking part in the deliberative public workshops were presented with information and evidence on what is currently known about the risks and uncertainty of changing the germline. The majority of these people felt that the benefits that would follow from using the new techniques outweigh those risks. Furthermore the risks were not seen as of sufficient magnitude to warrant disallowing techniques that would enable parents to have a healthy child. Some participants pointed out that the introduction of any new treatment will involve some degree of uncertainty. Analysis of the ethics questionnaires show that throughout their discussions about changing the germline, participants' attitudes remained stable, with 64% saying they were *'not at all'* or *'not very'* concerned prior to the discussion and 62% at the end<sup>8</sup>.

Participants' views about the acceptability or not of changing the germline were largely shaped by the importance they placed on individual and personal choice for parents.

### Public representative survey

In the public representative survey participants were asked about their attitude to changing the germ line, assuming this was shown to be safe. Just over half (52%) said they were *'very'* or *'fairly'* positive about it, 12% were *'very'* or *'fairly'* negative about it, and 36% were *'unsure'*.

---

<sup>8</sup> The ethics questionnaire was a brief survey which participants were asked to complete at the start of the meeting, before they received information about an ethical issue and discussed it with other participants. Participants were then asked to complete the questionnaire after receiving the information and having group discussions. The aim was to see if people's views changed as a result of receiving new information and when hearing the opinions of others.

## Open consultation meetings

At the open consultation meetings there were three types of response to this issue. Some people felt that the germline would not be changed significantly. They argued that parents could 'ideally' choose a mitochondria donor with a mitochondrial DNA sequence that was very similar to the mother's. This view was supported by the statement that mitochondrial variation is limited, especially in individuals of the same ancestral origin (e.g. European or sub-Saharan African). A second general response was that the germline effect would be significant and negative. Those responding in this way felt that mitochondria replacement posed *"serious risks to societies and individuals."* The final response highlighted that the techniques would have a significant but positive effect on future generations. People who said this felt that it would be *"more irresponsible"* for society to allow families with a history of the disease *"to have more children and face the risk of more affected children being born."* Comments were made that this would be changing the germline *"for the better"* by creating a *"healthy cell"*, and that *"the child will go on to pass on healthy mitochondria and children will be free from mitochondria disease."*

During the public debate sessions in both London and Manchester, two audience members made a similar point in response to one panellist who argued that changing the germline is morally unacceptable and that it might be difficult for the child to come to terms with how they came into being. In London, the audience member said, *"as parents we are making decisions for our children all the time, some of which they may not agree with...as long as we did it in their best interest, fine. We can do no more than that"*, while in Manchester a participant voiced, *"I have no problem saying to my child 'because I love you'...and why this has this happened to you? So you could live a long, healthy, fulfilling life without the obstacles I've had to deal with."* These two quotes reflect the majority of participant views in London and almost all of those in Manchester.

## Patient focus group

Participants in the patient focus group expressed very limited concern about changes to the female germline following the use of these techniques. They felt that a change in the germline would be 'preventing the disease' and that this is in essence a good thing: *"I have no problem with removing whatever has to be removed and changing the germline...I don't care."*

Focus group participants also said they were comfortable with parents making this decision on behalf of their children because it is about ensuring that their children are healthy. This was felt to be more important than changes to the germline. One participant felt that future generations may resent their parents for not having used a technique that could have saved them much pain and suffering.

## Open consultation questionnaire

In the open consultation questionnaire, respondents were asked whether they thought there were social and ethical implications to changing the germline. Of the 1,115 respondents, those more in favour of the techniques argued that there were no implications, that the only implication was the reduction in instances of a terrible disease, or that any negative implications are out-weighed by the positives. The main theme running through responses was the uncertainty and risk involved in introducing a new technique. Many respondents expressed concern about the extent to which any consequences can be predicted: some respondents commented that *'scientific understanding of genetics is far from*

*comprehensive*'. Others argued that if negative implications are identified, the consequences (once introduced to the germline) would be so severe and far reaching that even a small risk should be considered carefully.

One concern raised relates to the way in which society would view those treated – or not treated – using the proposed techniques. Some respondents felt that if the techniques are made available there will be pressure on parents to use them, discrimination against those who chose not to, and possibly a knock-on effect on attitudes towards disabled people more generally. Others were concerned that those born as a result of the techniques might be treated differently because of it, though some discount this, arguing that *'the new technique(s) will become generally accepted, as new advances always are.'*

The predominant ethical issue raised was that making changes to the germline for this purpose could lead to other changes becoming more acceptable; many respondents identified the idea of germline change with controversial terms like eugenics and cloning. Others argued that any change to the germline is inappropriate because there is no way for all those affected to give consent; a view contradicted by a few who saw making choices for subsequent generations as a very ordinary part of being a parent.

## Summary

The impact of mitochondria replacement techniques on the germline was one of the main ethical debates surrounding their use. Participants' views on whether this issue was deemed acceptable changed little during the deliberative public workshops. The prevailing view of a majority of participants across all five strands of the consultation was that the outcome of the techniques – a healthy child, free of faulty mitochondria and a potentially serious disease – outweighs the possible consequences of changing the germline, even though these might not be apparent until some time in the future.

As we learned in the permissibility discussion, most participants new to this topic felt that the known and unknown effects on the germline are acceptable; however, a substantial number remained undecided, neither for nor against the use of these new techniques.

Those more familiar with the new techniques tended to be familiar with the debate about germline effects and most discussing this issue did not change their existing views.

## 2.3 Implications for identity

### Deliberative public workshops

Participants in the deliberative public workshops held varied views when discussing the potential implications of using DNA from three people on nature and sense of identity. Most participants rejected the 'three parent' label, arguing that mitochondrial DNA contributes little or nothing to a child's personal characteristics. However, a few participants felt that the donation of healthy mitochondria would have helped a child to exist free of mitochondrial disease and that this should be recognised by giving the donor some sort of parental status. Following group discussions, some participants who were at first against using DNA from three people voiced that their opinions had changed and this was not as serious an issue as they had been inclined to believe. Findings from the ethics questionnaires completed by participants showed levels of concern about this dropped slightly throughout the day: at the start of the day 51% said they were *'not very'* or *'not at all'* concerned about this issue whilst 57% said this at the end of the day.



Several factors affected the way in which participants formed and changed their views about mitochondrial donation. In all three deliberative public workshop locations, participants used a range of comparisons and analogies in their discussions, for example, adoption, organ donation and sperm donation. In their presentations, some experts made comparisons between mitochondria donation and blood transfusion or bone marrow donation, and the amount and role of mitochondrial donation in a person's genetic make-up was also highlighted.

## Public representative survey

In the public representative survey, participants were asked about their attitudes to the eggs or embryos resulting from the new treatments containing small amounts of genetic information from a third person. Just over two fifths (44%) said they were 'very' or 'fairly' positive, 15% were 'very' or 'fairly' negative and 40% were 'unsure'.

## Open consultation meetings

At the London open consultation meeting, most attendees were comfortable with the concept of a child having DNA from three people. They felt that mitochondrial DNA has little to do with "identity." One participant said: *"it's just like changing the battery in your laptop."* Another person said *"I don't think of my mitochondrial DNA in the same way as my nuclear DNA."* However, some participants suggested that as knowledge of genetics grows and develops, mitochondria might be found to play a greater role in determining personal characteristics than is currently assumed. During the debate session, views were polarised between those who felt mitochondrial DNA does not play a major role in a person's identity and those for whom the techniques result in an *"artificially constructed identity."*

When contrasting the new techniques with alternatives such as using a donor egg, participants in both London and Manchester felt that children born following mitochondria replacement may be *"happier"* in the knowledge that they are genetically related to both their parents. This comment introduced the possibility that mitochondria replacement techniques might actually resolve some identity issues.

At the Manchester meeting some participants suggested that identity is in part socially constructed and that the media can influence the ways in which people think about a person's identity. For example, *"sensationalised headlines"* surrounding mitochondria replacement techniques might have an impact on how children perceive themselves. Several participants attending the Manchester meeting referred to the position taken by the Nuffield Council of Bioethics on this issue<sup>9</sup>, which says that mitochondria replacement poses *"no ethical problems"* with regards to identity. Some explained their views by drawing comparisons between the new techniques and established medical procedures such as blood transfusions and organ transplants, neither of which are thought to have a significant impact on identity. One person made a counter argument to this by saying that mitochondria are present in every human cell.

One participant in Manchester, whose son is affected by a mitochondrial disorder, suggested that her child's mitochondrial DNA had helped shape his life, but had not affected who he is (e.g. how he looks). The implicit suggestion was that if he had healthy mitochondria, he

---

<sup>9</sup> Nuffield Council on Bioethics, 'Novel techniques for the prevention of mitochondrial disorders: an ethical review' (2012).

would be exactly the same person but without having to cope with the debilitating effects of a disease.

There was more consensus in the public debate session of the Manchester meeting than there was in London. For example, an audience member in Manchester who made the following comment was not challenged by anyone: *"We are not changing characteristics, we are not changing those things that make you, 'you'. What we are changing is energy metabolism."*

### Patient focus group

Participants in the patient focus group were aware that mitochondria replacement techniques mean that a child will have DNA from three people. They drew from their knowledge of the science to say that since no nuclear DNA would be used from a third party, the techniques are more akin to blood or tissue donation, therefore, a child's sense of self would be inherited from their parents: *"everything that makes you 'you' and that makes your child 'your child' is not touched."* Participants felt that some media reports on the issue have been sensationalist, resulting in public debate which is *"misleading"*, *"emotive"* and *"confusing."*

### Open consultation questionnaire

Respondents to the open consultation questionnaire were asked whether they thought mitochondria replacement techniques have social or ethical implications relating to a person's sense of identity. Responses differed widely and were often influenced by a respondents' view on the status of the mitochondria donor; respondents who referred to the donor as a third parent usually expressed concern about implications for identity, whereas those who branded the social and/or genetic connection between donor and child as less significant mostly said they were not worried about implications for identity.

Among respondents who considered that these techniques are likely to have implications for a child's sense of identity, many felt that a child could be confused by knowing that they carry DNA from three people. Respondents believed this may saddle children with questions about who they are, and who their parents are, which they said will have detrimental impacts on their well-being. Some drew comparisons with adopted or donor-conceived children, arguing that they suffer from identity issues and that children resulting from mitochondria replacement could experience similar problems, or worse. A number of respondents felt that children born as a result of using PNT might also feel unhappy about the creation and destruction of embryos: *"Knowing that other people have to die (other embryos are destroyed) to give an individual life is an unfair burden to ask anyone to carry."*

Concerns about potential emotional or psychological damage experienced by children conceived with the help of mitochondria replacement were also expressed, often in similar wording, by many of those who took part without using the consultation website questionnaire - for example in a letter or email.

Respondents who thought these techniques have no implications for a child's sense of identity, or that these implications will be limited, often said that there is no connection between mitochondrial DNA and identity. They emphasised that the genetic information important for identity is held in the nuclear DNA and that this is not affected in MST and PNT, or that identity is determined by other than genetic factors: *"One's sense of identity is conditioned by many influences beyond the chance of genetic inheritance."* Some compared the mitochondria replacement with organ, bone marrow or blood donation, and highlighted that such procedures are not seen as influencing the recipient's sense of identity. Others saw

an analogy with sperm or egg donation, adding that the impact for the child will be similar, or less.

A relatively small number of respondents argued that mitochondria replacement is unlike any existing procedure, emphasising that identity implications are difficult to foresee, and that a cautious approach is important. Many others said that parents will be able to mitigate any identity implications by being open about how the child is conceived: *“I can imagine that if it is not explained clearly to either the parents or the children it could produce issues later in life”*.

## Summary

Those participants who were less familiar with the consultation subject questioned what implications mitochondria replacement might have on a child’s sense of identity. This question raised slightly more concern than a change to the germline. For example, in the public representative survey those who agreed that it is acceptable for a child to carry a small amount of genetic information from a third person dipped just below 50%. The proportion of those who were undecided rose slightly to 40% and the negative figure also rose but remained low at 15%. This issue also raised slightly more concern at the deliberative public workshops, although some participants felt more comfortable about the issue once they had discussed it in further detail. The main reason for this concern was that some participants felt that a *“search for identity”* is something that all young people experience, and that there might also be an emotional impact on the child. Participants drew parallels with adopted children who are keen to find their biological parents as they seek to establish their identity.

Those who were more familiar with the techniques were also more familiar with this ethical issue. While most seemed to be comfortable with the idea of DNA from three people, others felt that this is not acceptable as our understanding of the role of mitochondrial DNA remains limited in some respects and we should be cautious about introducing these techniques into clinical practice.

## 2.4 The status of the mitochondria donor

### Deliberative public workshops

Participants in the deliberative public workshops had varied views on whether a child born through the new techniques should be able to access information about the mitochondria donor involved. Those participants supporting donor anonymity felt quite strongly that the donor’s rights should be protected and that donors themselves should be given a choice about whether or not they want their identity to be revealed to the child. Others felt that a child should have the right to know the identity of their mitochondrial donor and access this information. At the end of the discussion, 45% of participants disagreed that any child born as a result of the new techniques should have the right to access information about the mitochondria donor, compared with 31% at the start of the discussion. The number of participants favouring the child’s right to know about their donor did not largely change – 33% at the start of the day to 31% at the end of the day.

### Public representative survey

This issue was not discussed in the public representative survey.



## Open consultation meetings

At the London open consultation meeting some participants emphasised the importance of keeping records of mitochondria donors, which linked to other comments about the newness of the science. Although there is currently no scientific indication that mitochondrial DNA has an influence on the characteristics of a person, participants noted that this area of genetic science is *“new and could change.”* Some participants argued that those willing to donate their mitochondria are choosing to be part of a child’s life and that we need to be *“upfront about what donor-ship means.”* Others highlighted that access to information about your origins is a fundamental human right. As such, any individual born following mitochondria replacement should be able to find out about their ‘third parent’ and their genetic origins in the same way those children of egg donors can. During the debate session at the meeting some participants called for the establishment of a mitochondria donor register.

In Manchester, participants expressed a range of views about the status of the mitochondria donor. While most were emphatic that there *“is no relationship”* between the child and the donor others maintained that donors are making a *“huge commitment.”* A number of people acknowledged that people may want to know the *“origin of their mitochondria”*, but the general view was that donors should be *“non-traceable.”* Some participants were concerned that the perception of donors as a *‘third parent’* could be strengthened if they could be traced and contacted.

Participants in Manchester described this as *“uncharted territory”* and felt that mitochondria donation could not be satisfactorily compared with either tissue or egg donation, and should be seen in a separate category of its own.

## Patient focus group

People taking part in the patient focus group felt quite strongly that donors should remain anonymous. They also felt that donors should and would want to remain anonymous, because, unlike sperm or egg donation, no nuclear DNA is being donated: *“I’ve donated blood and haven’t given a second thought about where that’s going. There has never been a story in the press that someone wants to know where the blood came from that saved their life.”*

## Open consultation questionnaire

Respondents to the open consultation questionnaire were asked how they view the status of a mitochondria donor compared to other, existing types of donor. A striking point made in responses was that for each type of donation, roughly equal numbers of respondents felt that mitochondrial donation is similar to another type of donation as those who see it as different (i.e. the number of respondents who saw donation of mitochondrial DNA as comparable to gamete donation was virtually equal to the number who saw it as distinctly different).

The most frequently made comparison was with gamete donation. Respondents argued that mitochondrial donation was similar to this because it involves procreation, or genetic transfer. Those who argued that mitochondrial donation is a different proposition often suggested that *“it won’t determine the characteristics of individuals it will simply prevent them from inheriting a genetic disease.”* Those who see mitochondria replacement as less significant than sperm or egg donation tended to support its introduction, whilst those who viewed it as equivalent to these forms of donation tended to be less in favour. There was a similar correlation between views on the contribution of the mitochondria to the resulting child and views on the role of

donor as a 'parent'; where respondents see the donation as affecting personal characteristics they tended to infer a role for the donor in the child's life, in contrast for those who see the donation as having a minimal impact.

Comparisons with tissue, organ and bone marrow donation were also common. Again, arguments typically focused on the genetic contribution, and whether or not the genetic contribution of mitochondrial DNA has significance over and above the avoidance of mitochondrial disease. A few noted that the mitochondrial donation is passed on via the germline, whereas any consequences of tissue donation are limited to the immediate recipient.

Many respondents raised the issue of the rights of the embryo and many of these suggested that mitochondrial donation for pronuclear transfer (PNT) differs from other donations, and is unacceptable because it involves the creation of an embryo with no intention of it being carried to term and born. Others argued that it is a misconception to regard the woman whose eggs are being used as the donor, seeing the mitochondria as being donated by egg or embryo, which they regard as a separate person. As this 'person' is unable to give informed consent to the procedure they concluded that it is unethical.

Respondents to the open consultation questionnaire were also asked, in a separate question, to choose between three models for rules to govern the disclosure of information to the child about the mitochondria donor. They also had the option of calling for another arrangement ('other'), or stating complete opposition to the introduction of the procedures. The largest number of respondents favoured this last option, while other choices divided fairly evenly between the models proposed as part of the question.

A substantial number of respondents expressed a preference for the model, outlining that no information or only information short of the identity of the donor should be disclosed. These respondents often saw maternal spindle transfer (MST) and PNT as more like blood or tissue donation than egg or sperm donation, and so concluded that the donor's identity need not be disclosed. Other arguments included that the child's proper understanding of the procedure is an important element in what information should be disclosed, or that the donation is best understood as an altruistic but impersonal act: *"...The child should have the right to know how they were conceived and why, but have it explained that their genetic characteristics such as physical traits, personality traits, intelligence etc. come from the parents they are growing up with."*

Respondents who favoured a model allowing the donor's information to be disclosed along with their identity once the child reaches 18 years of age, tended to feel more strongly about the consequences and significance of mitochondria replacement: *"If MST is legalised, such children should not be deprived of knowing their egg donor mother."* Their main concern was the medical, emotional or legal rights of children born through the procedure, which are sometimes explained as potential conditions determining what information should be disclosed. A number discussed the age requirement, normally agreeing that some limit is needed.

Several respondents felt it was important that donor consent should be sought to clarify which information is disclosed if a donor's identity would be made available to the child. Others argued that the disclosure of identity is part of the responsibilities of the donor.

A small number of respondents said they opposed the introduction of the techniques but think that if they were to be allowed, children should be able to know the identity of the donor.

Some respondents offered alternatives to the models proposed in the question, including suggestions for more flexible arrangements: *“It should be the choice of each donor as to what information is provided, along with any other conditions of their donation, and the choice of the parents as to whether to accept these conditions.”*

## Summary

Views on this issue were mixed. Discussions at the deliberative public workshops indicated that those participants who supported the anonymity of the mitochondrial donor felt quite strongly that the rights of the donor should be protected and that donors should be given the choice as to whether they want their identity to be revealed to the child. On the other hand, there were also participants who felt that children should have the opportunity to know the identity of the donor, should they request it. At the end of the day, a larger number of participants favoured the anonymity of the donor. The ethics questionnaires revealed that almost half of participants (45% disagreed that any child born after these techniques should have the right to access the individual who donated the mitochondria, compared with 31% at the start of the day. However, the number of participants favouring a child's right to know about their donor did not vary greatly (33% at the start of the day to 31% at the end of the day), which indicates that these participants tended to remain steadfast in their views. Views were similarly varied at the Manchester open consultation meeting, although shifting of views throughout the course of the meeting cannot be assessed.

At the London open consultation meeting and in the patient focus group views appeared less varied. At the former people appeared to agree that mitochondria donors should be on a donor register as is the case with egg donors, but did not specify the level of detailed information to which a child should have access. However, it should be noted that we cannot say whether or not this was a majority view. In the focus group there was a strong view that donors should remain anonymous and that mitochondrial donation is more like blood donation than egg or sperm donation.

## 2.5 Regulation of mitochondria replacement

### Deliberative public workshops

At the deliberative public workshops participants discussing safety and uncertainty about the risks of the new techniques felt that strong regulation would be needed. However, some expressed concern that although regulation and associated activities such as monitoring are important, the demands of the latter may be seen as too much of a burden for some parents and dissuade them from choosing one of the new techniques. Some people questioned how easy it is to track children born by these techniques over time if the parents are against being closely monitored.

A few participants in the deliberative public workshops picked up on concerns raised by a scientist in the video they were shown that even if the techniques are not licensed in the UK they are likely to become available in other countries with less stringent regulation regimes. Participants tended to agree that it would be important for these techniques to be introduced in a regulated environment. This point relates to discussions about the potential misuse of the technology, for example, to select for particular personal characteristics or create ‘designer babies’ rather than reduce the incidence of the disease.

Throughout discussions about the new techniques, participants felt that individual and personal choice for parents is paramount, this was supported by the results of the ethics

questionnaire. Participants were most likely to feel that couples themselves should make the decision about treatment (in consultation with their doctor), without the involvement of an expert regulator. This rose from 35% at the start of the day to 40% by the end of their discussions.

## Public representative survey

Participants in the public representative survey were asked who should decide whether individual couples should have the treatment if the law is changed. Over a third of respondents (36%) favoured the option of couples being allowed to decide for themselves. A further 39% favoured some kind of involvement from a regulator – with one fifth (20%) favouring an expert regulator deciding on case-by-case basis (20%) and a similar proportion (19%) favouring an expert regulator approving clinics, with medical specialist deciding who to offer it to (19%). One quarter of respondents felt unable to express a preference.

## Open consultation meetings

Participants at the open consultation meeting in London saw the need for regulation as highly important and argued that strict controls should be put in place to prevent illegal use of the techniques. Some felt that regulation is also necessary to counteract a potential slippery slope effect by warning that *“once you breach a principle such as allowing hybrids it creates a precedent.”* Some also suggested that those who are most at risk of passing the most severe forms of mitochondrial disease should be prioritised for treatment. In Manchester, participants suggested that the techniques should be regulated in a similar way to egg donation, with licenses being reserved for HFEA approved centres.

In the debate section of the Manchester consultation meeting, participants strongly felt that individual families should have the right to make the choice about whether or not to take advantage of the techniques: *“What we are saying is that there is the potential to have a different choice, and I think that if you don’t agree with it then you don’t have to have it, nobody would force you...If you do, and these techniques exist, well then I think it is unethical not to offer them. In my opinion, that is where there is a real ethical question.”*

## Patient focus group

While this issue was not specifically discussed in the patient focus group, it was clear that most of the group place great importance on personal choice. One person said that if the techniques were licensed for clinical use, treatment should take place in a regulated environment.

## Open consultation questionnaire

Respondents to the open consultation questionnaire were asked to indicate a preference for one of three possible models of regulation if the law were to be changed to allow mitochondria replacement to be carried out in specialist clinics. Almost half of the overall respondents declined to express such a preference, and instead selected a fourth option which allowed them to register an overall objection to mitochondria replacement being offered as a treatment under any circumstances. Respondents who chose this option tended to be of the opinion that no level of regulation could overcome the fundamental ethical objections to mitochondria replacement that they had already expressed in their answers to previous questions. A number of participants were also deeply sceptical about the

robustness of regulatory measures, often believing that their effectiveness would diminish over time.

Of those respondents who indicated a preference for a particular model of decision making, close to half (232 respondents) opt for a system in which clinics and individual patients would be free to make a case-by-case decision about whether or not to use mitochondria replacement, without any regulatory stipulations regarding which conditions or cases it may be suitable for. This preference was often associated with a view that a central regulatory board may lack sensitivity to individual circumstances and a feeling that individual patients should be empowered to choose the best option for their own families.

A similar number (242) of respondents preferred an option that includes a role for the regulator, the majority of which expressed a preference for a broad regulatory framework outlining those diseases that are deemed serious enough to warrant mitochondria replacement but which provided flexibility for patients and clinicians to reach individual decisions within this framework. A minority of respondents expressed a preference for the highest level of regulation: a model in which a central regulator would maintain responsibility for making decisions about particular cases.

Among those advocating a role for the regulator there was a wide feeling that an external regulatory framework would provide a buffer against abusive profiteering and a wide range of *'slippery slope effects'* which could otherwise ensue. It was also suggested that a central regulator would promote fairness by making sure that all applications for treatment would be judged according to the same criteria. Some proposed that the treatment should initially be reserved for those at risk of passing on the most severe forms of mitochondrial disease and ventured that: *"If and when no unexpected issues arise then perhaps it can be considered for other less severe mitochondrial diseases."*

## Summary

In all the consultation strands participants argued that strong regulation is essential if the techniques are licensed for clinical use. Clinics themselves would need to be licensed and access to and use of the techniques should be regulated by a body such as the HFEA.

In discussions about who should make the decision about whether or not to use these techniques, there was a clear preference for individual choice; with parents and clinicians working together to agree what is the best option for them. This view did not appear to be affected by the level of knowledge or awareness people have about the disease or these techniques. The alternative to this would be for wider society to decide whether these treatments are allowed or not, it was felt to be unacceptable that a decision could be taken away from parents on the grounds that some of those within society are against the treatments being licensed.

## 2.6 Attitudes to legislation change

### Deliberative public workshops

At the start of the second meeting of each of the deliberative public workshops participants were asked to record on a scale of 1 to 10 (1 = reject; 10 = support) their response to this question:

*'If the treatment can be shown to be safe, to what extent would you support or reject it being made available to families through HFEA licensed clinics?'*

Over the second day participants revisited this statement twice to help determine the extent to which new information, evidence and discussions have an impact on their support for the treatments. The overall mean score (across all three locations) at the start of the day was 8.2; however, after participants had discussed the ethical issues of using DNA from three people and germline therapy saw the mean figure rise to 8.4. This suggests that this group of participants remained steady in their support for the two techniques after deliberating these ethical issues. By the end of the day the mean score decreased to 7.8 and is likely to have resulted from concerns expressed by a small number of participants about the robustness of the scientific base. These concerns were raised by a scientist's reference in a video about a study on fish models that suggests a potential for mitochondrial DNA in cytoplasm to influence the formation of vertebrae<sup>10</sup>. This suggests that some participants' trust in the safety of these techniques was relatively fragile and easily disrupted by new information.

The deliberative public workshops concluded with participants developing '*messages for the Secretaries of State*' to consider when making their decisions about whether or not to license these techniques:

- Individual choice is important and parents should be able to use these techniques.
- Individuals need to be provided with all the relevant information they need to make an informed choice. This includes information on the potential and long-term risks, any uncertainties and the pros and cons of the two different techniques.
- The techniques must be introduced in a regulated environment.
- Parents who choose to access these techniques should be offered counselling.
- Donors should have confidentiality (although different views remain about whether some information should be available to the child).
- Fairness is an essential criteria and the techniques should be available to all, free of charge.
- The techniques are to be used to produce a healthy child for no other purposes.

Some other participants give more conditional support:

- A more comprehensive scientific assessment of the safety and efficacy must be completed; some participants expected to see human trials stage prior to wider licensing.
- There needs to be more information about how individuals will be able to access the techniques, with an emphasis on the importance of fair, equitable and affordable access.
- There needs to be more information about mitochondrial disease provided to the public, along with information on testing and diagnosis.

## Public representative survey

This issue was not covered in the public representative survey.

---

<sup>10</sup> The reference to this study was dropped from later versions of the video used in the consultation as it was not felt to be relevant because of the lack of transferability of the implications of it to humans and the fact it related to science rather than ethics



## Open consultation meetings and patient focus group

Potential changes to the law were not discussed explicitly in the open consultation meetings, nor in the patient focus group; however, discussions at these events were broadly positive about the techniques overall. The 'key messages' section of the focus group report also demonstrates this positive sentiment. This could suggest that many of those in London, even more of those in Manchester, and participants in the focus group would probably support changing the law to allow these techniques to be made available in licensed HFEA clinics.

## Open consultation questionnaire

In the open consultation questionnaire, respondents were asked whether they believe the law should be changed to allow mitochondria replacement techniques to be made available to people who are at risk of passing on mitochondrial disease to their child. The question was answered by 1,055 respondents. A majority of these respondents argued against changing the law, while a substantial minority argued in favour. A small number of respondents made a distinction between both techniques, almost exclusively saying they would support a law change for MST, but not for PNT. When answering this question many respondents referred to or reiterated arguments made in responses to earlier questions.

A small number of respondents made specific comments in relation to a possible change in the law. Those arguing against a law change sometimes referred to the international context and saw it as problematic that the UK would be the first or only country to allow the use of these MST and PNT. Several respondents argued that other methods should be considered before forging ahead with these new techniques: *"Other methods (such as repairing faulty mitochondria) are already being developed by scientists and should be examined further instead of considering PNT and MST."*

Respondents arguing in favour of law change, and particularly those adding caveats to their support, highlighted a variety of criteria they think need to be met. Most of these said that the techniques need to be proven safe and/or efficient before introducing legislation allowing them to be offered to people at risk of passing on mitochondrial disease. Respondents also suggested that further work needs to be undertaken to specify which of the techniques should be allowed, and in which circumstances: *"PNT raises more problems [for me], considering that it involves the destruction of potentially viable embryos. However, on the assumption that this would be performed at a very early stage, it might well be that the benefits are worth the worry if it becomes evident that PNT is safer and/or dramatically cheaper than MST."*

## Summary

Participants in the deliberative public workshops discussed this issue specifically, with nearly 8 out of 10 supporting the techniques being made available. In the open consultation questionnaire those respondents who were against the techniques being made available tended to focus largely on ethical concerns, such as the use of embryos, and interference with the natural or spiritual aspect of reproduction. Based on the views and attitudes expressed in response to other issues, we think it is reasonable to conclude that most of those involved in other strands of the consultation apart from the open consultation questionnaire would support a change in the law that will allow these techniques to be used in a clinical setting.



# Medical frontiers: Debating mitochondria replacement

## Annex II: Deliberative public workshops

Report to HFEA

February 2013

OPM  
252B Gray's Inn Road,  
London WC1X 8XG

tel: 0845 055 3900  
fax: 0845 055 1700  
email: [info@opm.co.uk](mailto:info@opm.co.uk)  
web: [www.opm.co.uk](http://www.opm.co.uk)



Client	HFEA
Document title	Medical frontiers: Debating mitochondria replacement: deliberative public workshops
Date modified	22/02/2013
Status	Final
OPM project code	8984
Author	Sanah Sheikh
Quality assurance by	Diane Beddoes
<b>Contact details</b>	
Main point of contact	Tim Vanson
Telephone	020 7239 7806
Email	tvanson@opm.co.uk

If you would like a large text version of this document, please contact us.



---

# Contents

Executive summary .....	1
1. Introduction .....	7
1.1 Background and context .....	7
1.2 Methodology .....	8
2. Understanding the science – series one .....	10
2.1 Overview of journey .....	10
2.2 Factors that facilitated learning .....	10
3. Emerging views on mitochondria replacement techniques – series one .....	12
3.1 Support for and concerns about mitochondria replacement techniques .....	12
3.2 Views on ethical and social issues .....	13
3.3 Factors that shaped emerging views.....	14
4. Initial support for new techniques – series two.....	16
5. Views on specific ethical and social issues – series two .....	18
5.1 Attitudes towards DNA from three people and identity .....	18
5.2 Attitudes towards germline therapy.....	22
5.3 Impact on attitudes towards these techniques .....	24
6. Other information and evidence that shaped support for techniques – series two.....	27
6.1 Uncertainty about risks and science.....	27
6.2 The importance of regulation .....	28
7. Final support for new techniques – series two .....	29
8. Messages for Secretaries of State – series two .....	32
Appendix A – Profile of participants .....	33
Appendix B – Workshop programmes .....	35
Appendix C – List of experts and workshop materials .....	37

## Executive summary

The Office for Public Management (OPM), in partnership with Forster and Dialogue by Design, was commissioned by the Human Fertilisation and Embryology Authority (HFEA) to conduct a multi-method research and engagement project looking at the possible social and ethical issues relating to two techniques for the avoidance of mitochondrial disease: pronuclear transfer (PNT)<sup>1</sup> and maternal spindle Transfer (MST)<sup>2</sup>.

As part of this research and engagement, OPM ran three deliberative public workshops each consisting of two series. The workshops aimed to explore the in-depth attitudes of a group of randomly selected members of the public and to understand the journey that participants go on as they become increasingly engaged with and knowledgeable about the issues.

Series one workshops were held in Newcastle, Cardiff and London in July 2012. These workshops focused on helping participants to understand the potential treatment techniques – pronuclear transfer (PNT) and maternal spindle transfer (MST). For series two, the groups were reconvened in the same locations in July and August 2012. The reconvened workshops focused on the potential social and ethical issues relating to the techniques.

At each workshop in both series, participants worked in three groups of 8-10. Each group comprised of people with a range of different demographic characteristics.

In terms of key findings, participants' views remained broadly in favour of the two new techniques over the course of the two days. The principal reason given for this was largely because the techniques give parents the opportunity to have healthy children who are genetically their own, which is not possible using current techniques. In order to form considered opinions, participants used a range of comparisons and analogies, for example with adoption, organ donation and sperm donation, in their discussions.

Participants' views were also shaped by information on the amount and role of mitochondrial DNA in a person's genetic makeup that was described by scientists in the video. The importance that participants placed on individual and personal choice for patients also shaped their views on the techniques. There were some participants who had some concerns about the techniques, due to doubts about the robustness of the scientific evidence presented on day one.

### 1. Understanding the science – series one

Series one workshops were designed to help participants to develop their understanding of the science in a step-by-step process. First, they learned about and reviewed basic concepts such as organisms, cells and DNA. They were then introduced to the more complex topics of mitochondrial disease and the new techniques. Learning was supported by a short biology quiz and an animated briefing video. An expert on the science was on hand to answer any

---

<sup>1</sup> Pronuclear transfer involves transferring the pronuclei from an embryo with unhealthy mitochondria and placing them into a donor embryo which contains healthy mitochondria and has had its pronuclei removed. A pronucleus is a small round structure containing nuclear DNA seen within an embryo following fertilisation. A normal embryo should contain two pronuclei, one from the egg (maternal pronucleus) and one from the sperm (paternal pronucleus).

<sup>2</sup> The maternal spindle is a structure within the egg containing the mother's nuclear DNA. Maternal spindle transfer involves transferring the spindle from the intended mother's egg, with unhealthy mitochondria, and placing it into a donor egg with healthy mitochondria.

questions that participants had (see Appendix C for a list of the experts who staffed the workshops and the supporting materials).

Participants' initial discussions about mitochondria and mitochondrial disease raised a range of questions and concerns, particularly about the pathology of the disease, its transmission, prevalence and diagnosis. Concerns about the potential severity of mitochondrial disease led to questions by some participants about why the public had not heard about the disease before. Facilitator observation and participant feedback over the course of the day indicated that input from the scientists was very valuable: they were engaging, spoke in lay terms about complex topics and helped participants grasp the building blocks needed to support the later social and ethical discussions. Additionally, participants also found the handouts and the bespoke video useful too. These gave them clear and accessible information that was easy to follow.

## 2. Emerging views on mitochondria replacement techniques – series one

Overall, participants were fairly positive about the new techniques at this stage of the dialogue. The majority of participants were in favour of the new techniques because they felt these guaranteed parents a healthy child that was *genetically their own*, which is something they felt was important to a great many parents. They spent some time discussing the differences between the two new techniques. A small number of participants were against the use of PNT on the grounds that it involved manipulating and disposing of embryos. More often, participants felt that the use of embryos – and thus also use of PNT – might be an issue for 'other people'. These 'others' were often named as 'religious groups', who it was felt would be the most likely to object.

Participants raised questions and concerns about what, if any, risks were associated with the techniques, and what research had been done to date about success rates and long term safety. They were also keen to learn about the regulatory assurances for these techniques. These questions were either answered by the science expert or a representative from the HFEA present at the workshop, or if the questions related to social and ethical issues, they were noted and discussed at the second workshop.

At all three locations, participants asked about the cost of implementing these new techniques. They questioned whether investing in techniques to eradicate mitochondrial disease is appropriate when health funding is severely constrained. The argument was made largely on the basis of the low prevalence of the disease compared to diseases such as cancer. A majority did think that the techniques could save the healthcare system a great deal of money over the long term, since it would not have to treat people with mitochondrial disease in the future. Discussions about costs often led to conversations about the importance of affordable and fair access to these new treatments should they be approved.

Participants recognised that some people might feel that these techniques are akin to 'playing god' and could result in a 'slippery slope' to 'designer babies' and 'aborting disabled people'. However, most participants focused instead on the potential for these techniques to eradicate disease and give parents the opportunity to have a healthy child. Indeed, from the outset of series one, it was clear that most participants were more interested in these techniques as a means to address disease than from the perspective of reproductive ethics.

A number of factors shaped participant's emerging views on, and levels of support for the new techniques. The most influential were comparisons with available techniques and where the choices should lie. In discussion of pre-implantation genetic diagnosis (PGD) and prenatal diagnosis (PND), participants made a lot of negative comments about PND in

particular. They felt that the new techniques could offer a better alternative because they avoid the disease altogether, rather than PGD and PND which test to see whether mitochondrial disease is present in embryos or foetuses. In general, these comparisons with existing techniques resulted in broad support for the new techniques.

A second influential factor was the **importance of allowing choice. Participants placed great weight on personal and individual choice** and did not think it was appropriate to restrict access to these new techniques to individuals and families just because some people, who they tended to identify as 'religious groups', might be opposed.

### 3. Views on specific ethical and social issues – series two

The second series focused on the ethical and social issues associated with the two new techniques. Discussion was supported by a number of tools, including bespoke scenarios, a video, and brief presentations from bioethicists, followed by a question and answer session.

At the start of the day participants identified the issues they felt it was important to cover. This was followed by some focussed discussion on two specific ethical and social issues:

- DNA from three people and what that might mean for the child and/or donor
- The techniques as germline therapy

To stimulate discussion participants were provided with short scenarios that illustrated these issues. Following initial discussions about the scenarios they also watched videos and heard from ethics experts, both of which presented a range of opinions on the issues involved. In order to track changes in attitudes, participants were asked to complete an ethics questionnaire, which included questions relating to these two issues, at the start and end of the day. In the sections below we will outline participants' views on these two issues, the factors that shaped and changed their views, and the impact these discussions had on their support for the new techniques.

#### 3.1 Attitudes towards DNA from three people and identity

Participants across the three locations had a range of reactions to the first scenario to which they were introduced. This presented the story of Susie, a little girl born as a result of the mitochondrial techniques who wondered about her mitochondrial donor. One area where participants generally agreed was that Susie had the 'right to know' about how she was conceived.

When considering the fact that a child born from the new techniques would have nuclear DNA from both parents and mitochondrial DNA from a donor, hereafter described as **DNA from three people**, there was more variability in participants' views and about how this may impact on identity. Discussions over the course of the day suggested that most participants rejected the 'three parent' label because they felt that the contribution of mitochondrial DNA to a child's personal characteristics was negligible. However, there were also a few participants who felt that the fact that the donation of healthy mitochondria enabled the child to exist was very important and should give the donor some sort of parental status. At the end of the day, participants were more likely to not be concerned by the 'DNA from three people' issue. Analysis of the ethics questionnaires revealed that 57% of participants reported that they were 'not very' or 'not at all' concerned at the end of the day, compared with half (51%) at the start of the day.

There was also variability in participant's views on **whether a child born from these techniques should be able to access information about the donor**. Discussions

indicated that those participants who supported the anonymity of the mitochondrial donor felt quite strongly that the rights of the donor should be protected, and that donors should be given the choice as to whether they want their identity to be revealed to the child. On the other hand, there were also participants who felt that children should have the opportunity to know the identity of the donor, if they wanted. At the end of the day, a larger number of participants favoured the anonymity of the donor. Analysis of the ethics questionnaires revealed that more than four out of ten participants (45%) either strongly disagreed or tended to disagree that any child born after these techniques should have the right to know about the individual who donated the mitochondria, compared with 31% at the start of the day. However, the number of participants favouring the child's right to know about the donor did not change very much – from 33% at the start of the day, to 31% at the end of the day – which indicates that these participants tended to remain steadfast in their views.

A number of factors contributed to helping participants form and change their views about these issues. All discussion groups at each of the three locations used a range of **comparisons and analogies**, for example with adoption, organ donation and sperm donation, in their discussions. Many were influenced by presentations from the experts in which they made comparisons between mitochondrial donation and blood transfusion or bone marrow donation. Participant's views on this issue were also shaped by information on the **amount and role of mitochondrial DNA** in a person's genetic makeup that was described by scientists in the video. Many participants picked up on a comment by an expert in a video about the small number of mitochondrial genes compared to nuclear genes. These comparisons, analogies and information about mitochondrial DNA meant that by the end of the workshop participants were more likely to not be concerned about the issue of DNA from three people. Some participants' views on the issue were also shaped by the **importance they placed on the rights of the child** born from these techniques and this meant that these participants tended to remain steadfast in their attitudes towards children being able to find out about their donors.

### 3.2 Attitudes towards germline therapy

The second scenario focused on Martin and Jane, parents of a child with mitochondrial disease who disagree about whether to use these new techniques to conceive another child, and therefore alter the germline of future generations. Discussions indicated that initially, a majority of participants supported Jane, who wants to have another child via the techniques and several participants felt that Martin was being 'unreasonable'. A number of participants agreed that Martin would change his mind with a better understanding of the science, and many also felt that generally it was important to give parents more information to enable them to make the right decision.

Participants also discussed the extent to which uncertainty about the impact of these techniques on future generations should factor into whether these techniques should be licensed. At this stage participants tended to feel that despite the information and evidence presented on the known risks and uncertainty they were 'worth it' if it meant that the parents could have a healthy child. The risks involved were therefore acknowledged by participants, but did not raise very much concern about the techniques representing germline therapy. Some participants also felt that there is always uncertainty when it comes to new treatments.

Analysis of the ethics questionnaires revealed that in the course of the day, attitudes towards germline therapy remained stable, with 64% not at all or not very concerned about germline therapy at the beginning of the day and 62% at the end. Participants' views on the germline therapy issue were largely shaped by **the importance they placed on individual and**



**personal choice for parents.** Findings from the ethics questionnaire also highlighted the importance that participants placed on individual choice throughout the day. Participants were most likely to feel that couples themselves should make the decision about treatment (in consultation with their doctor), without the involvement of an expert regulator. This continued to be the case, and in fact increased slightly (from 35% to 40%), by the end of the day.

#### 4. Other information and evidence that shaped support for techniques – series two

After discussion about the two specific ethical issues, participants were given the opportunity to watch a further video which presented a range of opinions on the potential social and ethical issues relating to safety, risks, regulation and monitoring. A number of discussion groups picked up on a reference in the video by a scientist to a study on fish about the potential for factors present in cytoplasm (which may or may not involve mitochondria), to influence the number of vertebrae that are formed. For a few participants in each of these groups the mention of this study raised doubts about the robustness of the scientific evidence presented on day one<sup>3</sup>. They felt that this was new information which had not been made available during the first day of the dialogue and questioned whether they had been given all the relevant scientific information. This strong response was felt by a few participants, while many others either did not pick up on the comment, or felt that it was part of the inevitable uncertainty in science and did not cause them concern. What is clear is that for some participants their **trust in the safety of these techniques is relatively fragile, and easily disrupted by new information.**

A few participants also picked up on concerns by a scientist in the video that if the techniques are not licensed in the UK they will become available in other nations with less stringent regulation regimes. These participants tended to agree that it was **important for these techniques to be introduced in a regulated environment.** Participants felt that regulation would ensure the fairness and affordability of the techniques and that they are only used for the purposes of reducing the incidence of disease.

#### 5. Changes in views over the series two workshops

In series two workshops, participants recorded their responses to the following question:

*'If the treatment can be shown to be safe, to what extent would you support or reject it being made available to families through HFEA licensed clinics?'*

Responses were marked on a scale of 1 to 10, with 1 indicating 'reject' and 10 indicating 'support' in their response to the question.

They did this on three occasions throughout the day. The purpose of this was to provide us with a broad indication of whether and how new information, evidence or discussion impacted on their views of the treatments. On the final occasion, we asked participants to

---

<sup>3</sup> The reference to this study was dropped from later versions of the video used in the consultation as it was not felt to be relevant because of the lack of transferability of the implications of it to humans and the fact it related to science rather than ethics

explain why their response was on a particular place on the scale. Overall, participants' views did not change greatly throughout the course of the series two workshops, remaining broadly in favour of the techniques. The principal reason for this was largely because the techniques give parents the opportunity to have healthy children who are genetically their own, which is not possible using current techniques.

## 6. Messages for Secretaries of State

Some groups used the last session to express their support for the introduction of the techniques, alongside their conditions. The fundamental reason given for supporting the techniques is that the state should not preclude individuals from having this choice available to them. In other words, participants felt that the choice about whether or not these techniques were appropriate to use was one to be made by parents in discussion with health professionals. Many participants identified a number of requirements associated with their support for the techniques (1, below). Others were more cautious and their support was contingent upon other things happening before they felt a decision could be made. While there was a breadth of the discussions over the two days, the final points across the three locations were relatively similar.

### 1. Support for the techniques with caveats and conditions:

- Individuals need to be provided with all the relevant information they require to make an informed choice. This includes information on the potential and long-term risks, any uncertainties, and the pros and cons of the two different techniques or any alternative treatments
- The techniques must be introduced in a regulated environment
- Parents who choose to access these techniques should be offered counselling
- Donors' identity should be protected
  - Although different views remain about whether some information should be available to the child
- Fair access to these techniques is essential and they should be available on the NHS, to all who might benefit from them, free of charge
- The techniques are to be used to produce a healthy child and for no other purposes

### 2. Requirements before support can be given:

- A more comprehensive scientific assessment of safety and efficacy must be completed; some participants expected human trials a stage prior to wider licensing
- There needs to be more information about how individuals will be able to access the techniques, with an emphasis on the importance of fair, equitable and affordable access
- There needs to be more information about mitochondrial disease provided to the public, along with information on testing and diagnosis



# 1. Introduction

## 1.1 Background and context

Mitochondria are present in almost all human cells. They are often referred to as the cell's 'batteries' as they generate the majority of a cell's energy supply. For any cell to work properly, the mitochondria need to be healthy. Unhealthy mitochondria can cause genetic disorders known as mitochondrial disease.

There are many different conditions that are linked to mitochondrial disease. They can range from mild to severe or life threatening, and can have devastating effects on the families that carry them. Currently there is no known cure and treatment options are limited. For many patients with mitochondrial disease preventing the transmission of the disease to their children is a key concern.

Mitochondrial disease can be caused by faults in the genes within a cell's nucleus that are required for mitochondrial function or by faults within the small amount of DNA that exists within the mitochondria themselves. It is the latter form of mitochondrial disease that could be avoided using two new medical techniques, termed pro-nuclear transfer (PNT)<sup>1</sup> and maternal spindle transfer (MST)<sup>2</sup> which UK researchers are working on.

These techniques are at the cutting edge, both of science and ethics and are currently only permitted in research. They involve removing the nuclear DNA from an egg or embryo with unhealthy mitochondria, and transferring it into an enucleated donor egg or embryo with healthy mitochondria.

The Human Fertilisation and Embryology Act (1990) (as amended) ('the Act') governs research and treatment involving human embryos and related clinical practices in the UK. The Act currently prevents the clinical use of these techniques (or any other technique that involves genetic modification of gametes and embryos to treat patients). However, in 2008 the Act was amended, introducing new powers which enable the Secretary of State for Health to permit techniques which prevent the transmission of serious mitochondrial disease. The Secretary of State for Health and the Secretary of State for Business, Innovation and Skills asked the Human Fertilisation and Embryology Authority (HFEA) to seek public views on these emerging techniques. On considering advice from the HFEA the Government will decide whether to propose regulations legalising one or both of the procedures for treatment.

The HFEA, together with the Sciencewise Expert Resource Centre<sup>4</sup>, therefore commissioned OPM (in partnership with Forster and Dialogue by Design) to conduct a multi-method research and engagement project looking at the possible social and ethical issues and arguments relating to the techniques. The project consisted of five strands:

1. Deliberative public workshops
2. Public representative survey
3. Patient focus group
4. Open consultation meetings
5. Open consultation questionnaire

This research provides the evidence base that will inform the HFEA's advice to the Secretary of State.

---

<sup>4</sup> The Sciencewise Expert Resource Centre (Sciencewise-ERC) is the UK's national centre for public dialogue in policy making involving science and technology issues

The **deliberative public workshops** aimed to explore the in-depth attitudes of a group of randomly selected members of the public and to understand the journey that participants go on as they become increasingly engaged with and knowledgeable about the issues.

This report presents the detailed findings from these workshops.

## 1.2 Methodology

Three deliberative public workshops were held in Newcastle, Cardiff and London in July 2012. The groups were reconvened for a further three workshops in July and August 2012. Participants were randomly selected members of the public recruited to represent a broad spectrum of age, gender, socio-economic status and family circumstances (see Appendix A for the demographic profile of participants).

Thirty people were recruited to each workshop. At each workshop participants were representatively distributed into three groups, giving a total of nine discussion groups at each of the two days. The overall numbers involved at each workshop and the size of the table groups meant that each session could elicit a suitable breadth and depth of contributions.

Each group discussion was facilitated by an independent and experienced facilitator. One facilitator also led the plenary discussions (the workshop programmes can be found in Appendix B).

Participants received a thank you payment for attending the workshops, which is standard practice in deliberative workshops with members of the public. They were given to help compensate participants for their time and to encourage them to attend both the first and second workshops.

The first workshops in each location focused on the scientific building blocks that would help people discuss the social and ethical issues relating to the techniques. This involved running a short biology quiz and providing written information sheets, a specially made video and a presentation by a scientist working directly on the techniques concerned (see Appendix C for workshop materials and links to the videos).

The overall purpose of the second meeting was to engage participants in the potential social and ethical issues that relate to the new techniques, building on the science covered in the first meeting. At the start of the second day, the dialogue participants were asked to record on a scale of 1 to 10, with 1 indicating 'reject' and 10 indicating 'support' in their response to the following key question:

*'If the treatment can be shown to be safe, to what extent would you support or reject it being made available to families through HFEA licensed clinics?'*

Participants were then asked to revisit the statement at two further points in the day, to determine the extent to which new information, evidence and discussions had an impact on their support for the treatments. The data captured were analysed and the average/mean score for each discussion group (9 discussion groups), for each location (3 locations) and the overall average/mean score was calculated. We provide an overview of these mean scores, and how they varied over the course of the day in the body of the report.

Participants were asked to explore and discuss two potential ethical and social issues over the course of the day. In order to track changes in attitudes, participants were asked to complete an ethics questionnaire, which included questions relating to these two issues, at

the start and end of the day. An analysis of these findings is presented in the body of the report.

Discussion was supported by scenarios describing different perspectives on the ethical questions to which the techniques give rise, presentations by bioethicists, a video of a patient talking about the experience of having mitochondrial disease, and a second video showing scientists, bioethicists and social commentators expressing a range of different views.

## 2. Understanding the science – series one

### 2.1 Overview of journey

The three series one workshops in Newcastle, Cardiff and London were designed to provide participants with the scientific knowledge and understanding that would help them to develop informed opinions towards the social and ethical issues relating to the new techniques. We felt it was important not to assume participants' levels of understanding and to provide them with a straightforward way of either refreshing existing knowledge or of learning something new.

Each series one workshop started with a biology quiz where participants worked in small groups and gathered information on basic concepts such as cells, DNA and mitochondria from handouts and posters. Next, we showed a video which provided more detailed information on the concepts explored in the discovery exercise and also familiarised participants with mitochondrial disease. A scientist was also on hand to answer any questions (see Appendix C for a list of the expert at the workshops and the supporting materials).

Levels of knowledge about mitochondria and mitochondrial disease were very low across participants, with the exception of a few individuals who had done some research prior to the workshop. More participants were aware of some of the broader issues relating to genetics and assisted reproduction and had some knowledge of the basic biology, though levels of knowledge varied across participants.

Initial discussions about the science resulted in a range of questions and concerns. Most notably, all groups had questions about the pathology of mitochondrial disease, its transmission, prevalence and diagnosis. A number of participants also had concerns about families and, in particular, women who may not know they carry the disease before they start a family of their own. Participants raised concerns about the potential severity of mitochondrial disease which led to questions by some about why the public had not heard about the disease before and what was being done to treat and eradicate the disease.

Participants reported having thoroughly enjoyed the learning process and that the subject matter had been *“interesting”* and *“fascinating”*.

### 2.2 Factors that facilitated learning

Facilitator observation and feedback from participants over the course of the day highlighted that a number of factors relating to the design of the workshops contributed to participants' ability to grasp the scientific concepts introduced on the first day. For example, the participation of an **engaging scientist** who went from table to table and facilitated question and answered questions was extremely valuable. The scientist was approachable and enthusiastic and most importantly, able to explain complex scientific concepts and answer questions using layperson's terms. He/she assumed that participants had no previous knowledge of the science and therefore started with the basic concepts, which gave participants the time and space they needed to slowly build up their understanding.

Participants also felt that the handouts provided worked well because they provided them with **clear and accessible information** that was easy to follow. The use of diagrams and the specially made video in particular was felt to be helpful by many participants. The **sequencing of learning sessions** also proved helpful. At the first session they learnt about

and reviewed basic concepts such as organisms, cells and DNA before being introduced to the more complex topics of mitochondrial disease and the new techniques.

In addition to the above factors relating to the design of the first workshops, the fact that the **subject matter was new** to and not part of participants' every day life, also meant that they were interested and focused on learning over the course of the day.

## 3. Emerging views on mitochondria replacement techniques – series one

### 3.1 Support for and concerns about mitochondria replacement techniques

After the initial discovery stage, participants were introduced to mitochondrial disease and the new techniques for avoiding the disease. Materials used to support this included written hand-outs and a video and discussion with the science expert. As well as learning about the new techniques participants also learned about the current options currently available to couples who want to avoid transmitting the disease to their children. These are: adoption, using a donor egg, pre-implantation genetic diagnosis, and prenatal diagnosis.

Overall, most participants were fairly positive about the new techniques at this stage of the dialogue. The majority were in favour of the new techniques because they felt that, unlike the current options available, the new techniques guaranteed that parents would be **able to have a healthy child** and avoid passing on mitochondrial disease completely. Some participants also felt that the techniques meant that the disease would also no longer be passed down the germline to future generations. Many participants reported that they understood how difficult it can be to have a severely disabled child and felt positively about the potential for these techniques to result in healthy children.

Another reason participants felt positively about the new techniques was because they felt that they allowed parents to **have a child that was genetically their own**. These participants placed a great deal of emphasis on the 'right of parents' to be able to pass on their own genes to their children.

Participants spent some time discussing the **differences between the two techniques**. In a few groups, the discussion covered the difference between the two techniques and the use of embryos in one (PNT) in contrast with the use of eggs in the other (MST). A small number of participants were against the use of PNT on the grounds that it involved manipulating and disposing of embryos and that this was inappropriate from a moral and ethical perspective. The more predominant view amongst participants was that objections about the use of embryos and hence PNT were more likely to come from 'other people', with these others often being identified as 'religious groups'. Participants argued that objections from a small group of people should not stand in the way of medical progress or prevent access to these techniques for those who need them.

Two out of the three discussion groups at the workshop in London felt that PNT was the better option. This was on the basis of information from the science expert, who said that the pronucleus was larger and therefore easier to see and access than the spindle. Other reasons cited for favouring PNT over MST was that the former involves working with an already fertilised egg, while the latter does not guarantee that the egg would fertilise. On the whole, participants felt that what was most important was to test which technique had the highest success rates and was the safest.

Once participants felt confident about their understanding of the new techniques they felt able to raise some questions. These included questions about the **risks associated with the techniques**, for the mother, child and future generations; information relating to long term-safety; the nature of **research** carried out to date and whether animal trials had been successful. Some participants had questions about the **regulatory environment** for

reproductive techniques and reported having little knowledge of regulatory bodies. These questions were either answered by the science expert or a representative from the HFEA present at the workshop, or if the questions related to social and ethical issues, they were noted and discussed at the second workshop.

A number of participants continued to raise questions about the **pathology, prevalence and diagnostic testing** of mitochondrial diseases. They wanted reassurance that the proper diagnostic testing and records would be in place to ensure that all women that carried the disease were aware of its presence in their germline before they started a family.

### 3.2 Views on ethical and social issues

In addition to their questions on the science itself, participants in this first series of workshops also raised and discussed spontaneously a number of ethical and social issues.

In all three locations and in most discussion groups, participants asked about the **cost of developing and funding** the new techniques. Mindful of current constraints on healthcare funding, they questioned whether it was right to invest in techniques to eradicate mitochondrial disease when the prevalence of the disease was much lower than the prevalence of other diseases, such as cancer.

On the whole, participants tended to feel that the investment was 'worth it' for a range of reasons. The majority felt that the techniques had the potential to save the healthcare system money that it would otherwise have to spend on treating and supporting people who developed mitochondrial disease in the future. Some participants wanted evidence that this would be the case and that the benefits of the treatments would outweigh the cost. Others felt that although the prevalence of the disease was lower than that of other diseases, its severity meant that investment was warranted. Some participants felt that investment is warranted because scientists are closer to developing effective preventative techniques than they are for other diseases. They noted too that other diseases - such as cancer - already receive a lot of funding. A few participants supported the investment because of the potential for learning from the treatments. They felt that scientists and doctors might learn about how to prevent other diseases. Lastly, some argued that it is important for the UK to be leading research and development of these new techniques.

Discussion about costs and funding often led to conversations about **access** to these new treatments, should they be approved. Affordability and fairness are important to participants, who stressed that it is important to ensure that the techniques are available on the NHS and not accessible to private patients only.

Participants discussed the 'slippery slope' argument and the potential for these techniques to open the way to '**designer babies**' selected on the basis of personal characteristics. Participants in one group felt that this argument would be raised by those who don't understand the science, implying that they, having understood the science, did not feel that the 'slippery slope' argument was valid. Overall, participants supported techniques used for health reasons – such as the two techniques under discussion – but not those selecting for personal characteristics. This led some to report that their views on the acceptability of the techniques would change if mitochondrial DNA was found to have an impact on personal characteristics.

In all three locations, participants discussed the issue of '**playing God**.' They felt that some people could see the new techniques as a step towards 'aborting disabled people'. They discussed the 'boundaries' of genetic testing and whether it was fair for people to make



judgments about what constitutes a good quality of life. A minority of participants felt unable to support these – or any techniques involving genetic testing – because of their concerns about these issues. However, most participants focused instead on the potential for these techniques to eradicate disease and give parents the opportunity to have a healthy child. Indeed, from the outset of series one, it was clear that most participants were more interested in these techniques as a means to address disease than from the perspective of reproductive ethics.

### 3.3 Factors that shaped emerging views

A number of factors shaped participants emerging views on and level of support for the new mitochondrial techniques.

First, all discussion groups across the three locations found it helpful to make **comparisons with the current available techniques** in trying to weigh the pros and cons of the new techniques. As mentioned earlier, many participants noted, almost immediately, that the new techniques were preferable to the existing option of pre-implantation genetic diagnosis (PGD) because they guaranteed that the child would not have mitochondrial disease. They also noted that unlike adoption and the use of donor eggs, the new techniques would allow parents to have a child that is genetically related to both parents. Some participants described using a donor egg as ‘having someone else’s baby’ which they recognised may not be what parents want.

Participants drew on the experience of friends or family to relate how adoption, although valuable from a moral and social perspective, can be a long and arduous process. Another factor raised in the discussion of adoption was that it can be easier to adopt toddlers than babies, which can be seen as a disadvantage. Some participants felt that the new techniques would mean there would be less take up of adoption and therefore an increase in the number of children waiting to be adopted. One participant, who had been adopted, felt that much of the discussion was misguided and argued that she was as much her parent’s own child as any genetically related offspring would be, and very far from being ‘someone else’s baby’.

PGD and prenatal diagnosis (PND) were discussed in most small groups: PND in particular was viewed very negatively. Several participants felt that the potential for PND to result in terminations made it contentious and for a small number of participants it was unacceptable because they opposed termination of pregnancies altogether. For others the impact on the parents was a primary consideration, with a positive test result giving parents a potentially traumatic decision to make. Many of those who felt negatively about PND thought the new techniques could offer a better alternative because they avoid the disease altogether, rather than testing to see whether the embryo or fetus is affected. In general, these comparisons with existing techniques resulted in broad support for the new techniques.

The scope for **personal and individual choice** played an important role in determining participants’ emerging views on the new mitochondrial techniques. For example, participants did not tend to think it was appropriate to restrict access to these new techniques because some people, who they identified ‘religious groups’, might oppose them on moral and ethical grounds. As discussed earlier, participants acknowledged arguments about ‘playing God’ and the ‘slippery slope’ but felt strongly that parents should have the opportunity to choose for themselves. Participants did however welcome the debate and acknowledge the importance of different groups expressing their views on genetic treatments.

Finally, participants’ emerging views were a function of the fact that at this stage in the dialogue they had been provided with **incomplete information**. The purpose of the series



one workshop was to focus on the science underpinning the new techniques. Further information relating to social and ethical issues was not provided until the second series. In this absence of information participants therefore had a number of concerns which were broadly in line with the social and ethical issues to be discussed during the second series. These included questions about regulation, costs and access to the new techniques, progress in animal trials and the known risks associated with the new techniques. Some participants therefore had reservations about the techniques because they had not yet had a chance to hear about and reflect on such issues. Nevertheless, at the end of the first series many participants felt positively towards the new techniques.

The series one workshops ended with participants being encouraged by facilitators to reflect on the issues discussed and talk about them with families and friends.

## 4. Initial support for new techniques – series two

The series two workshops were held in the same locations as series one – Newcastle, Cardiff and London – and brought together the same participants. The focus was on the social and ethical issues relating to the two techniques to which they had been introduced to in series one.

Before the discussions began, participants were asked to complete a brief questionnaire that included questions about their views on some of the issues to be discussed. This exercise was repeated at the end of the day.

At the start of the dialogue between participants, we asked them to record their response to the following question:

*'If the treatment can be shown to be safe, to what extent would you support or reject it being made available to families through HFEA licensed clinics?'*

Responses were on a scale of 1 to 10, with 1 indicating 'reject' and 10 indicating 'support.'

This exercise was repeated at two further points in the day. The purpose of this was to provide us with a broad indication of whether and how new information, evidence or discussion impacted on their views of the treatments. The overall mean score, across discussion groups and locations, at the start of the day was 8.2 which indicates that the participants started the day with fairly high support for the new techniques. This is not surprising since the first day had been primarily about understanding the science underpinning these techniques and participants had only just started to discuss the social and ethical issues associated with the techniques.

The table below provides an overview of how mean scores varied across locations and discussion groups.

**Table 1: Mean scores across locations at the start of the day**

	Group 1	Group 2	Group 3	Mean at location
<b>Cardiff</b>	7.5	8.3	8.4	<b>8.0</b>
<b>London</b>	5.9	9.7	7.5	<b>7.7</b>
<b>Newcastle</b>	8.4	9.4	9.1	<b>9.0</b>

*Base sample (first scoring): Cardiff = 28, London = 26, Newcastle = 28*

For one group the mean score was low (group 1 in London); this group expressed greater concerns about justifying investment in these techniques compared to investment in eradicating diseases with higher prevalence. Across the three locations, some groups also had individuals who felt more strongly about the risk of parents 'playing God' or the risk of these techniques leading to others which allow the selection of personal characteristics. Additionally, lower mean scores were also shaped by participants' desire for more information about the regulation of and risks associated with these techniques.

On the other hand, higher mean scores were generally shaped by participants' feeling that the new techniques were positive because they gave parents the opportunity to have healthy

children that were also genetically their own, something that they recognised none of the existing techniques to avoid mitochondrial disease were able to guarantee.

## 5. Views on specific ethical and social issues – series two

Series two workshops began with an overview of some of the potential social and ethical issues associated with the new techniques. Following this, participants focused on two specific ethical and social issues:<sup>5</sup>

- DNA from three people and what that might mean for the child and/or donor
- The techniques as germline therapy

To stimulate discussion participants were provided with short scenarios that illustrated these issues. Following initial discussions about the scenarios they watched videos and heard from ethicists or bioethicists. These stimuli mapped out some of the main dimensions of the debates that surround these techniques. In the sections below we outline participants' views on these two issues, the factors that shaped and changed their views, and the impact these discussions had on their support for or rejection of the new techniques.

### 5.1 Attitudes towards DNA from three people and identity

#### 5.1.1 Overview of attitudes and concerns

Participants across the three locations had a range of responses to the first scenario, which presented the story of Susie, a little girl born as a result of the mitochondrial techniques who wondered about her mitochondrial donor. Participants tended to agree **that Susie should know how she was conceived** and identified a number of reasons why this was important. Some took a fairly straightforward 'rights' perspective whilst others argued more pragmatically that medically relevant genetic information would be important to Susie and her healthcare providers. Some participants felt that giving children this type of information would be essential because long-term monitoring of individuals born of these techniques would be necessary. Participants expressed these views prior to watching the video and hearing from the ethicists and continued to hold them after discussion of the points raised in these materials.

There was more **variability in participants' views on the child having DNA from three people and how this might impact on identity**. Discussions over the course of the day suggested that most participants rejected the 'three parent' label because they felt that the contribution of mitochondrial DNA to a child's personal characteristics was negligible. Some participants argued that the relationship between the donor and the child was more like that of a grandparent; genetic but not directly so. However, a few participants felt that the donation of healthy mitochondria had enabled the child to exist and this should give the donor some sort of parental status.

Some participants discussed whether the mitochondrial DNA would have an impact on the identity of the child. Most participants felt it would not, particularly if the nature of their conception was properly and expertly explained to the child. Many argued that a 'search for identity' was something that all young people experienced. Several participants took a

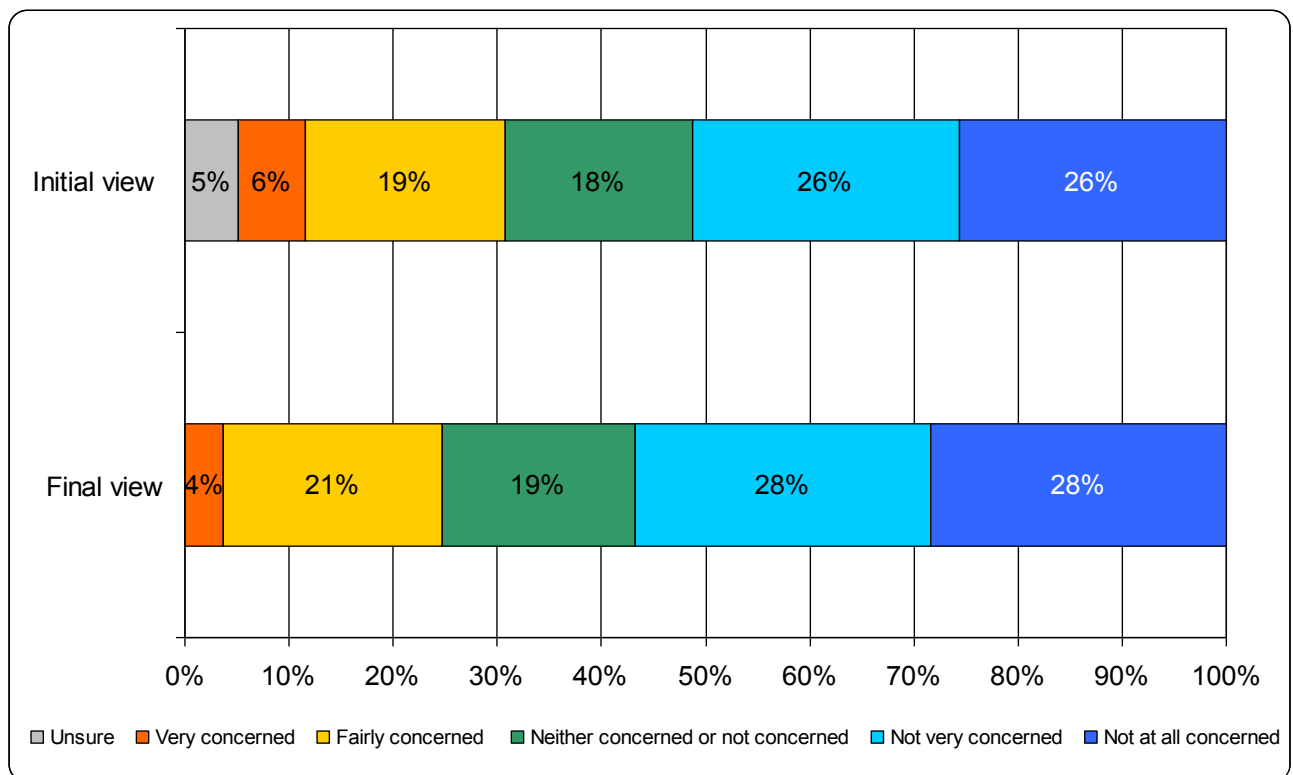
---

<sup>5</sup> Participants were asked to consider the following key ethical issues which were identified during stakeholder workshops and interviews earlier in the project.

slightly different perspective, discussing the emotional impact on the child and drawing parallels with adopted children who are keen to find their biological parents as they seek to establish their identity.

The findings from the ethics questionnaires distributed at the start and close of series two workshops show that views on the 'DNA from three people' question remained relatively stable throughout the discussion. At the end of day, the questionnaire shows that a majority of participants (56%) were more likely to be 'not very' or 'not at all' concerned about an egg or embryo resulting from the mitochondrial techniques containing genetic information from a third person. This is a small increase on the proportion holding this view at the start of the day (51%). With respect to those who had begun the day being 'very' or 'fairly' concerned about this (26%) approximately the same proportion (25%) held similar views at the end of the day (25%).

**Figure 1: Any resulting egg or embryo from the mitochondrial techniques will contain a small amount of genetic information in its mitochondria from a third person (the donor). What is your reaction to this?**



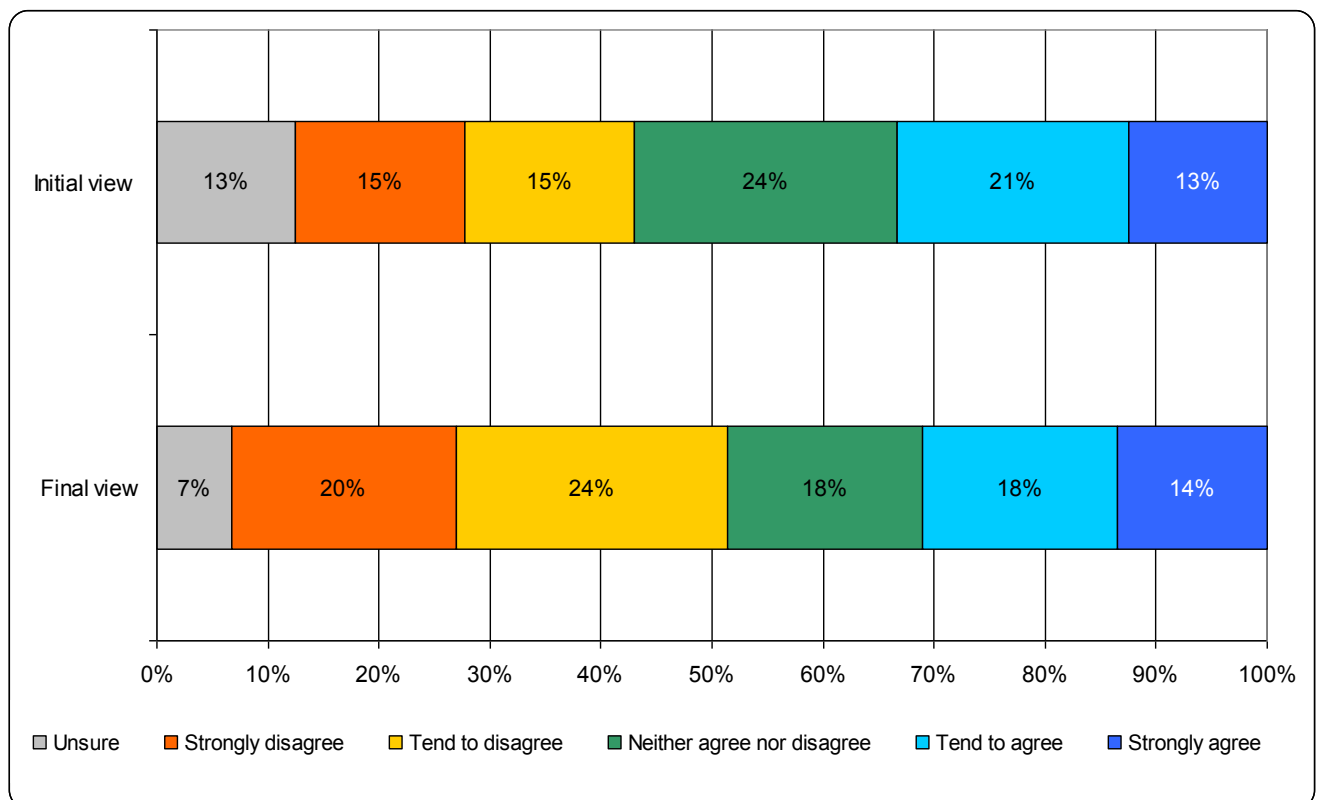
Base sample is number of participants completing ethics questionnaire at the start and end of the day:  
Initial = 78, Final = 81

Participants' views on **whether a child born from these techniques should be able to access information about the donor** were varied. In discussions, participants who supported anonymity for the mitochondria donor strongly argued that the donor's rights should be protected: they felt that donors should be given the choice as to whether they want their identity to be revealed to the child. Some participants felt that not protecting the privacy of donors could potentially result in fewer people making donations. Others felt that anonymity was appropriate because the contribution of mitochondrial DNA was not significant enough, and that it was similar to an organ transplant where donors also have anonymity.

Some participants argued, in contrast, that children should have the right to know the identity of the donor, if they wanted. They felt that the majority of children would probably not want to know but that the opportunity should be open to those who did want this information. These participants felt that donors should be fully informed before donation and accept responsibility for the fact that a child may come searching for them at some point in the future. Participants in one group suggested a third way, where a 'donor profile' with descriptive but not identifying information about the donor be made available to the child if they chose.

Findings from the closing questionnaire suggest that a majority of participants favour anonymity for the donor, as illustrated in Figure 2 below. A total of 45% of participants<sup>6</sup> either strongly disagree or tend to disagree that any child born after these techniques should have the right to access the individual who donated the mitochondria, compared with 31%<sup>7</sup> at the start of the day. However, the number of participants favouring the child's right to know about the donor did not change very much – from 33% at the start of the day to 31% at the end of the day – which indicates that these participants tended to remain steadfast in their views. Additionally, of the 5% who were initially 'unsure' and shifted their position, equal numbers ended the day either concerned or not concerned.

**Figure 2: Any child born after these techniques should have the right to access the individual who donated the mitochondria**



*Base sample is number of participants completing ethics questionnaire at the start and end of the day:  
Initial = 72, Final = 74*

<sup>6</sup> Has been rounded up

<sup>7</sup> Has been rounded up

### 5.1.2 Factors that shaped and changed views

A number of factors contributed to helping participants form and change their views about the use of DNA from three people and the implications of this for the child and donor. Throughout their discussions, participants used a range of **comparisons and analogies** to help them structure and convey their arguments and attitudes. For example, participants discussing whether or not children born from these techniques should have access to the identity of their donors tended to make comparisons with adoption. Comparisons with adoption also helped participants to visualise how the use of DNA from three people might impact on the identity of the child. As the discussion progressed, the value of the comparison with adoption waned as participants began to argue that the relationship between a parent giving up a child for adoption and that child, and the relationship between someone donating mitochondrial DNA and the child born with this mitochondrial DNA were two very different types of relationship. Instead, they moved towards an analogy with sperm or organ donation. These were seen as more appropriate and more helpful to discussions about the '3 parent' label and the rights of the donor and the child.

Many participants took into account the comparison made by experts, between mitochondrial donation and blood transfusion or bone marrow donation. This perhaps provides some explanation for the decrease in the proportion of participants concerned about the child having DNA from three people (Figure 1) between the start and the end of the day. However, a number of participants continued to feel that mitochondrial donation was more significant than a blood, organ or bone marrow donation and therefore continued to be concerned about the DNA from three people issue.

Participants' views on this issue were also shaped by **information on the amount and role of mitochondrial DNA** in a person's genetic makeup. In the video shown to participants, one expert mentioned the small number of mitochondrial genes compared to nuclear genes, while another stressed that while there are few mitochondrial genes they are clearly important. Participants in most discussion groups picked up on these statements, and most felt that the first statement confirmed their view that the 'three parent' label was unwarranted and even 'misleading'. A few participants felt that the small amount of mitochondrial genes from the donor meant that this would not be an issue in terms of the identity of the child.

For a few participants, their uncertainty about the appropriateness of particular analogies and comparisons – for example, with blood transfusions - was strengthened by the thought that whilst the quantity of DNA was small, the relationship between quantity and effect was neither direct nor straightforward. On the whole, however, participants' concern about the DNA from three people tended to reduce over the course of the day and, although this cannot be confirmed, the information in the video and that presented by the expert scientists might well have played some role in this reduction.

Some participants' views were also shaped by the **importance they placed on the right of the child** born from these techniques. This relates primarily to the child having the right to access information about the donor if they choose. However they also argued that a blanket approach was not appropriate and that access to information about a donor should 'depend on the child's need'. This meant that participants tended to remain steadfast in their attitudes towards the anonymity of the donor. As discussed earlier, the number of participants favouring the child's right to know about the donor did not change very much – from 33% at the start of the day to 31% at the end of the day.

## 5.2 Attitudes towards germline therapy

### 5.2.1 Overview of attitudes and concerns

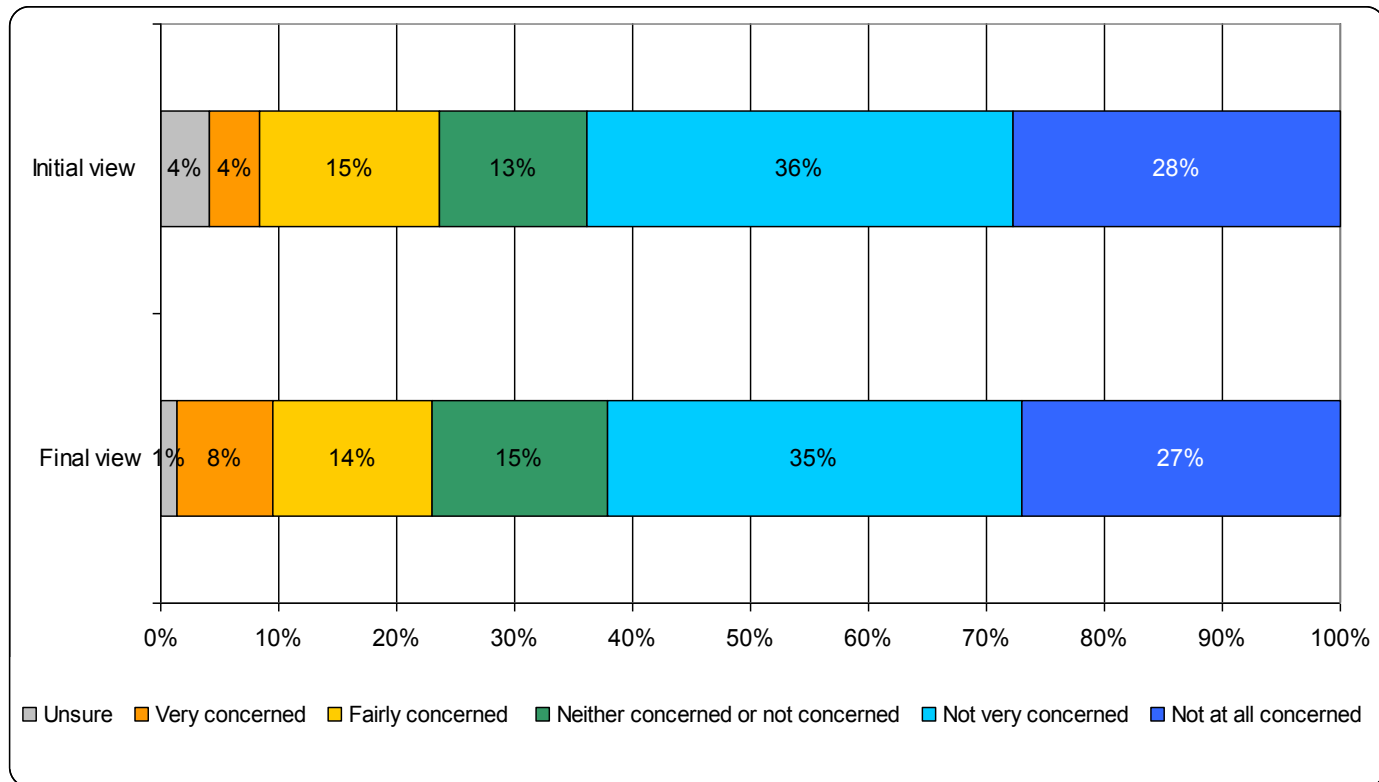
The second scenario focused on Martin and Jane, parents of a child with mitochondrial disease who disagree about whether to use these new techniques to conceive another child, and thereby alter the germline of future generations. In initial discussion of this scenario, participants were more likely to support Jane, who wants to have another child and to use the techniques to avoid the possibility that this child will have mitochondrial disease. Several participants felt that Martin was being 'unreasonable'. They felt that Jane was right in wanting treatment to prevent the disease being transmitted to their next child and that she was acting in the child's best interest. After further discussion, however, some felt that Martin's concerns might be based on a lack of information and that he would change his mind with a better understanding of the science. Many felt that, in general, parents should have the information that will enable them to make the right decision. However, participants also acknowledged that decision making can be difficult and that needing to take difficult decisions can have a negative impact on a couple's relationship. They were also concerned about how siblings might feel and about the impact of ongoing monitoring of any child born from these techniques. Several groups felt that counselling should be available to parents in this situation. Most participants were not greatly concerned about the implications of these techniques for future generations, except for the possibility that mitochondrial disease could be eradicated and health outcomes for children born from these techniques thereby improved.

Participants discussed the extent to which uncertainty about the impact of these techniques on future generations should be a factor in whether or not they should be licensed. At this stage of discussion, participants tended to feel that the information and evidence with which they had been presented suggested that the known risks and uncertainty were 'worth it' if it meant that the parents could have a healthy child. That is, participants acknowledged that there were risks in germline therapies but were not greatly concerned by these. Some participants also felt that there is always uncertainty when it comes to new treatments.

These discussions meant that throughout the day, **attitudes towards germline therapy** remained stable, with 64% not at all or not very concerned about germline therapy at the beginning of the day and 62% at the end. This is illustrated in the chart below.



**Figure 3: The techniques to avoid mitochondrial disease would involve altering the make-up of an egg or embryo, specifically the mitochondria. The donated healthy mitochondria would replace the intended mother's faulty mitochondria and would then be passed down to the child and, in turn, to that child's children and beyond. This is called germline therapy, because the change goes down through the generations (the germline). Assuming that scientists could show that this is safe, how do you feel about this?<sup>8</sup>**



Base sample is number of participants completing ethics questionnaire at the start and end of the day:  
Initial = 72, Final = 74

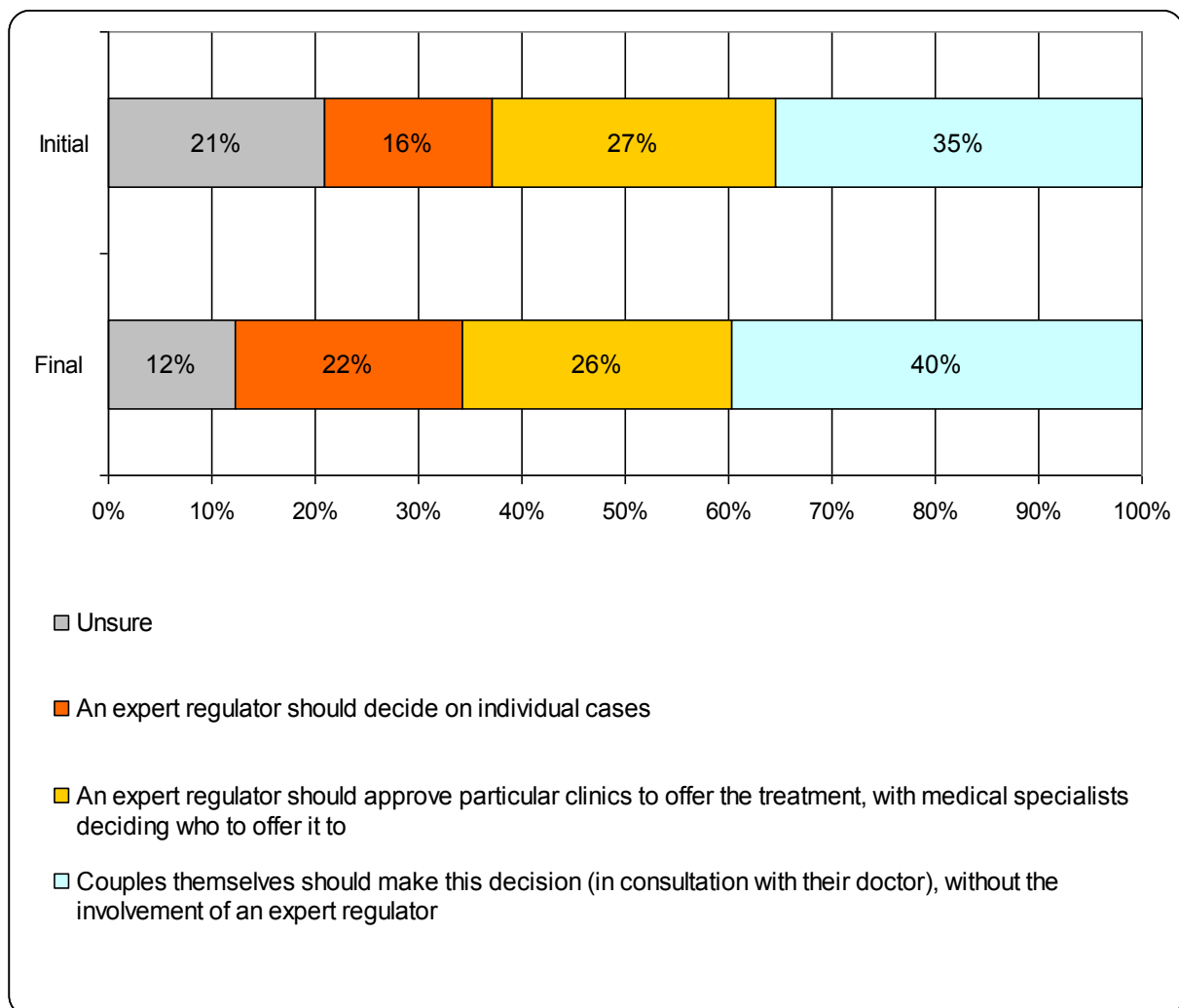
### 5.2.2 Factors that shaped and changed views

One main factor shaped participants' views on the germline therapy issue, which has been discussed previously and was a recurrent theme throughout this work: the importance of **individual and personal choice for parents**. Most participants stated that parents should be able to make the decision about using the techniques and altering the germline: that is, that the government should not prevent parents from having this choice by deciding against the techniques being available to those who might need them. They recognised the complexity of the issues and debate and that views would be varied and often strongly held. However, holding choice open to parents was seen as paramount. What the scenario illustrated was that making the choice would be difficult and that parents would need support in order to take the course that was right for them.

<sup>8</sup> It should be noted that prior to considering this question, participants were made aware that mitochondria are only inherited maternally; therefore the issue of inheritance to subsequent generations is only relevant if the offspring are female.

Findings from the ethical questionnaire reinforced the importance that participants placed on individual choice. They were most likely to feel that couples themselves should make the decision about treatment (in consultation with their doctor), without the involvement of an expert regulator (Figure 4, below). The proportion holding this view increased slightly throughout the day, from 35% at the start of the day to 40%, at the end.

**Figure 4: Currently, these techniques cannot be offered to couples as the law only allows the techniques to be carried out in research. However, Parliament may have an opportunity to change the law to allow these techniques to be offered to couples. If Parliament did change the law, who do you think should decide whether individual couples should have the treatment?**



*Base sample is number of participants completing ethics questionnaire at the start and end of the day: Initial = 62, Final = 73*

### 5.3 Impact on attitudes towards these techniques

The discussions about the two specific ethical issues – DNA from three people and germline therapy – did not appear to have a significant positive or negative impact on participants' support for the new techniques. After discussion of these issues, they recorded their second response to the question described at the start of this section:

*'If the treatment can be shown to be safe, to what extent would you support or reject it being made available to families through HFEA licensed clinics?'*

Again, they used a scale of 1 to 10, with 1 indicating 'reject' and 10 indicating 'support'. At this stage of the day, the overall mean score across discussion groups and locations was 8.4, only slightly higher than at the start of the day when it was 8.2. The table below provides an overview of how mean scores changed from the start of the day across locations and groups.

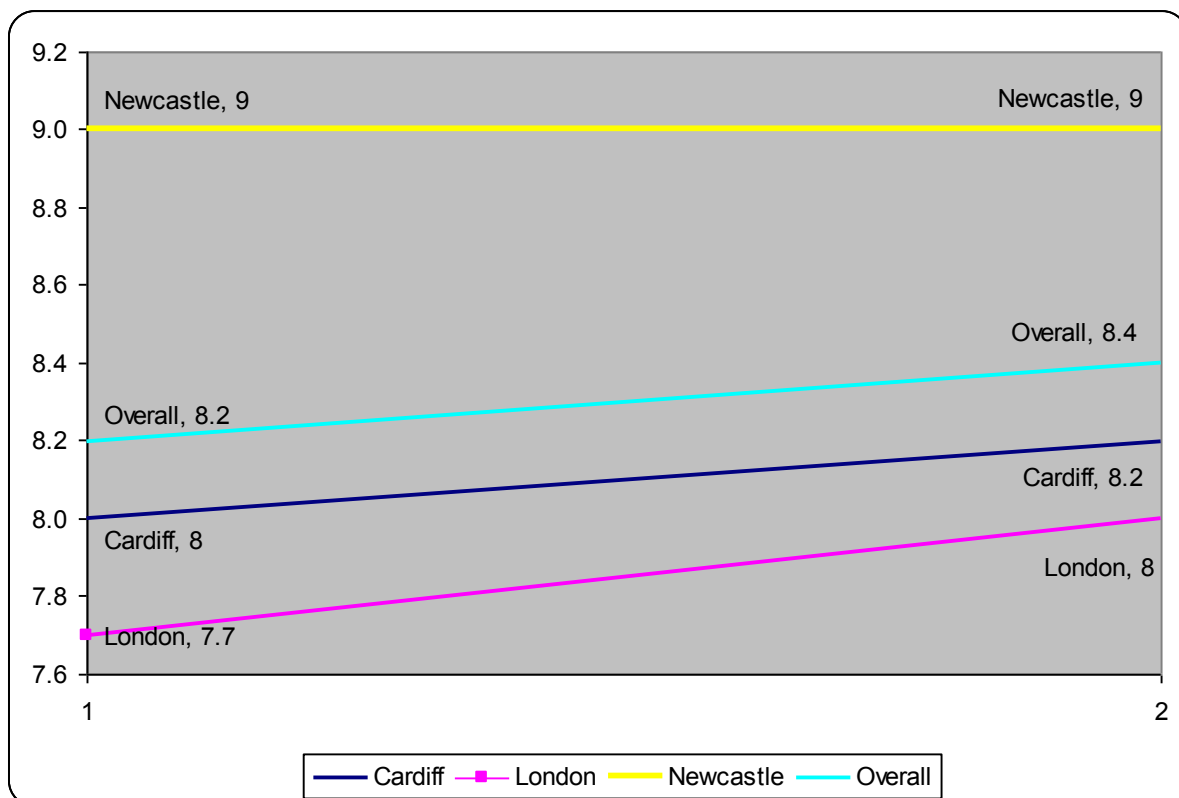
**Table 2: Change in mean scores across locations**

	Group 1	Group 2	Group 3	Mean at location
<b>Cardiff</b>	7.5 → 8.5	8.3 → 8.1	8.4 → 8.1	<b>8.0 → 8.2</b>
<b>London</b>	5.9 → 5.9	9.7 → 9.5	7.5 → 8.1	<b>7.7 → 7.8</b>
<b>Newcastle</b>	8.4 → 8.7	9.4 → 9.4	9.1 → 8.9	<b>9.0 → 9.0</b>

Base sample (second scoring): Cardiff = 29, London = 26, Newcastle = 28

Additionally, the chart below illustrates how the mean scores at each location and the overall mean score changed from the start of the day.

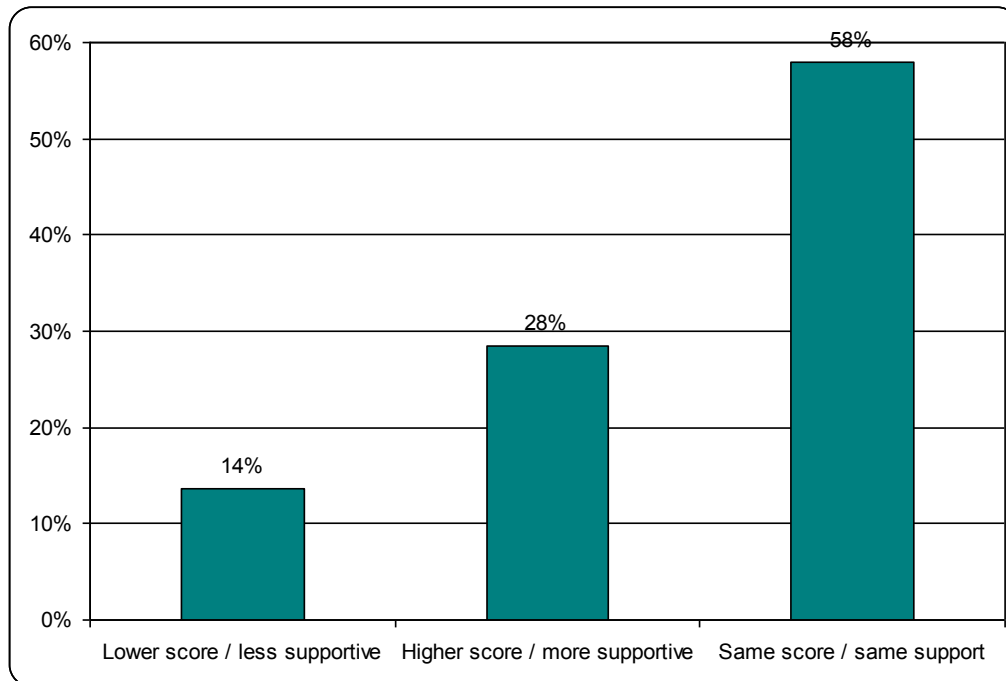
**Figure 5: Change in mean scores across locations**



As the chart above illustrates, the mean level of support at two locations increased very slightly and stayed the same at one location. These findings indicate that participants generally remained steadfast in their support for the new techniques regardless of discussions about the two ethical issues. At an individual level, almost sixty percent of

participants (58%) reported the same scores at the first and second scoring sessions, with a further 28% reporting a higher score at the second scoring session and only 14% reporting a lower score. This is illustrated in the chart below.

**Figure 6: Direction of change in individual scores / support for techniques – first and second scoring sessions**



*Base sample (first and second scoring): 81 participants*

As discussed in previous sections, the importance which participants placed on individual choice appears to have contributed to the continued support for the techniques throughout the dialogue workshops. Mostly, participants differentiated between techniques that aim to determine personal characteristics, which they did not support and those aimed at preventing disease, which they were more likely to support. Many found the argument focussed on quantity to be persuasive: they thought that the small quantity of mitochondrial DNA when compared with the quantity of nuclear DNA meant the ethical issues had less importance. Participants continued throughout the day to see the new techniques as a means to prevent disease and give parents the opportunity to have healthy children. While they recognised and discussed the ethical objections, these were outweighed by their ethical commitment to parental choice.

## 6. Other information and evidence that shaped support for techniques – series two

After discussion about the two specific ethical issues, participants watched a video presenting a range of opinions on some of the social and ethical issues relating to safety, risk, regulation and monitoring. This video generated further conversations and discussions which continued to shape the participants' views about the techniques.

In the sections below we discuss two further factors that shaped participants' views:

- Uncertainty about risks and science
- The importance of the techniques being introduced in a regulated environment, in order to ensure that the technology isn't misused

### 6.1 Uncertainty about risks and science

After watching the video discussing some of the social and ethical issues relating to safety and risk, participants raised questions about the certainty of the science. Some argued that more testing and trials should be done before the techniques were made available to the public. This view was prompted primarily by a reference made in the video to a study on fish about the potential for factors present in cytoplasm (which may or may not involve mitochondria), to influence the number of vertebrae that are formed. For a few participants in each of these groups the mention of this study raised doubts about the robustness of the scientific evidence presented on day one<sup>9</sup>. They felt that this was new information which had not been made available during series one and questioned whether they had been given all the relevant scientific information. This strong response was expressed by a few participants only: others either did not pick up on the comment, or felt that it was part of the inevitable uncertainty in science and did not cause them concern. What is clear is that for some participants their **trust in the safety of these techniques is relatively fragile, and easily disrupted by new information**. Some of these participants therefore suggested that it would be better if the techniques were trialled with a small group of people before being made available to the wider public.

Other participants focussed on some scientists' view that monitoring and follow-up is of prime importance, given that there is **uncertainty about the risks** associated with the techniques. Participants agreed that monitoring is an important part of breakthroughs in medicine. However, there was some concern that the demands of monitoring may be too much of a burden on some people and that they may therefore choose to withdraw. Some also questioned the feasibility of tracking and monitoring people born from this technique for the rest of their life, especially if they were opposed to such monitoring. Again, some participants suggested that trialling the techniques on a small group of people first would make monitoring and therefore risk assessment easier.

---

<sup>9</sup> The reference to this study was dropped from later versions of the video used in the consultation as it was not felt to be relevant because of the lack of transferability of the implications of it to humans and the fact it related to science rather than ethics.

## 6.2 The importance of regulation

A few participants picked up on concerns by a scientist in the video that if the techniques are not licensed in the UK they will become available in other nations with less stringent regulation regimes. These participants tended to agree that it was **important for these techniques to be introduced in a regulated environment**. This was to ensure that the techniques are only used for the purposes of reducing the incidence of disease. It was also related to practical concerns regarding fairness and availability, with participants feeling that regulators had a role to play in ensuring that the techniques would be available to all people and not just those able to afford private treatment.

## 7. Final support for new techniques – series two

Towards the end of the series two workshops, participants were again asked to record their response to the following key question:

*'If the treatment can be shown to be safe, to what extent would you support or reject it being made available to families through HFEA licensed clinics?'<sup>10</sup>*

On this last occasion the overall mean score across discussion groups and locations, was 7.8, showing that participants ended the day with fairly high support for the new techniques. However, this was lower than the mean score of 8.2 at the start of the day and the mean score of 8.4 in the middle of the day. The table below provides an overview of how mean scores varied across locations and discussion groups at the end of the day. As this illustrates, there is quite a difference between groups that have very high support for the techniques with mean scores close to or over 9 (e.g., group 2 in London or Newcastle), and those who appear to be more reserved in their support, with mean scores close to or lower than 5 (e.g., group 1 in Cardiff or London).

**Table 3: Mean score responses to question: 'If the treatment can be shown to be safe, to what extent would you support or reject it being made available to families through HFEA licensed clinics?'**

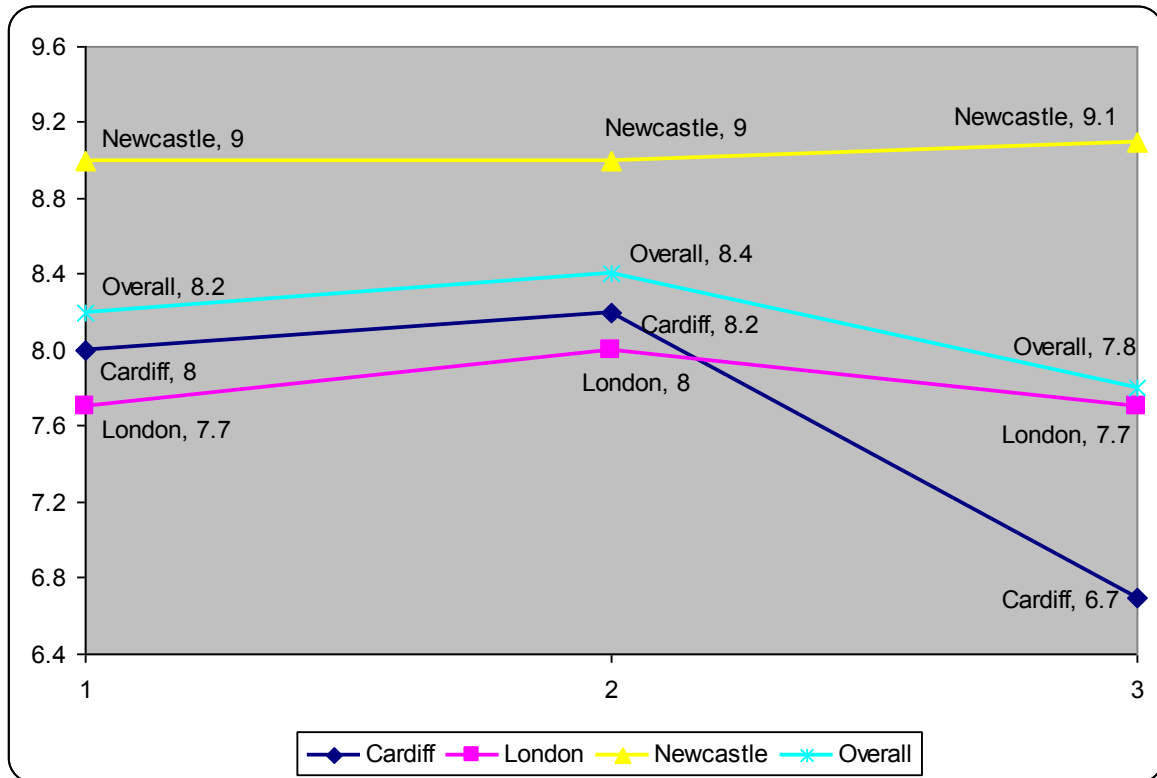
	Group 1	Group 2	Group 3	Mean at location
<b>Cardiff</b>	4.8	8.8	6.5	<b>6.7</b>
<b>London</b>	5.8	9.4	8.1	<b>7.7</b>
<b>Newcastle</b>	8.6	9.8	8.9	<b>9.1</b>

*Base sample (final scoring) = Cardiff = 28, London = 25, Newcastle = 28*

Additionally, the chart below highlights how the mean scores of each location and the overall mean score changed over the course of the day.

<sup>10</sup> As on previous occasions, responses were recorded on a scale of 1 to 10, with 1 indicating 'reject' and 10 indicating 'support'

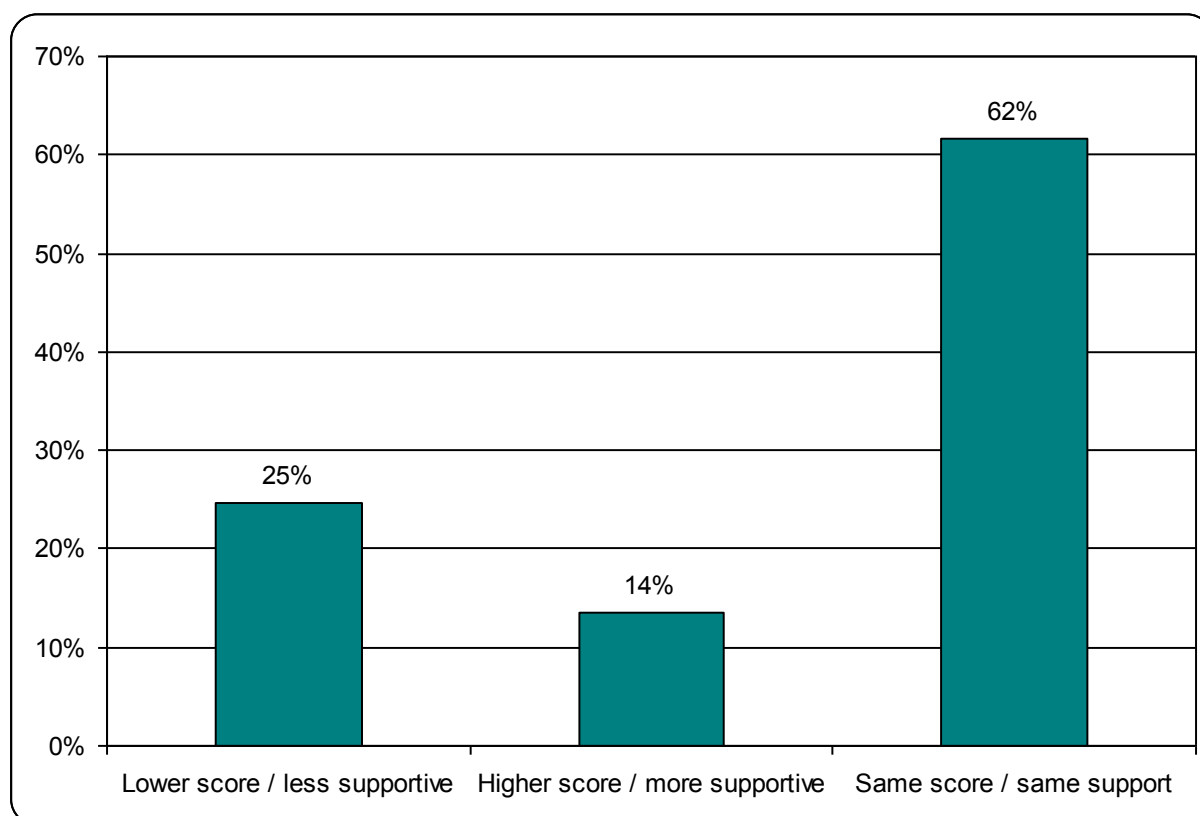
**Figure 7: Changes in mean scores, across location and overall, in response to the question: 'If the treatment can be shown to be safe, to what extent would you support or reject it being made available to families through HFEA licensed clinics?'**



In London, Cardiff and overall, there was a slight rise in the mean between the first and second scoring sessions. In the final scoring session the mean drops, and in Cardiff it does so quite dramatically. In Newcastle the mean score stays more or less constant over the course of the day. This drop in the overall mean score and two location mean scores suggests that issues around risk and uncertainty had an impact on views and, in particular, that participants were concerned about the study on the fish model (see section 6.1). These concerns had an impact on the extent to which participants felt able to support these techniques being available to anyone who might need them. This may have also been a contributing factor in the quarter of the participants (25%) who changed their views in a negative direction, becoming less supportive of the techniques (see Figure 8 below). This illustrates that for some participants, trust in the safety of these techniques is relatively fragile, and easily disrupted by new (contradictory) information, even when it is introduced late on in the process.

Levels of support in some sub-groups within a location – for example, group 2 in Cardiff and in London and all groups in Newcastle either stayed the same or increased over the course of the day. Analysis of table discussions suggests that this is at least in part because participants remained focused on the potential health benefits offered by these techniques and on the importance of individual and personal choice. More than six out of ten participants (62%) reported the same score at the second and final scoring sessions. Fourteen percent (14%) of participants increased their level of support for the techniques. These findings are highlighted in the chart below:



**Figure 8: Direction of change in individual scores / support for techniques – second and third scoring sessions**

*Base sample (second and third scoring): 81 participants*

## 8. Messages for Secretaries of State – series two

In the final session of the series two workshops, participants summarised their views into short messages to convey to the Secretaries of State with responsibility for making a decision about the licensing of these techniques. Some groups used this opportunity to express their support for the introduction of the techniques, alongside their conditions. Others were more circumspect, outlining the things they wanted to happen before a decision could be taken. Across all three locations, the final points raised were similar and illustrate broad agreement amongst a majority of participants.

### 8.1. Support for the techniques, with caveats and conditions (see below):

- Individual choice is important and parents should be able to choose to use these techniques
- Individuals need to be provided with all the relevant information they need to make an informed choice. This includes information on the potential risks, any uncertainties and the pros and cons of the two different techniques
- The techniques must be introduced in a regulated environment
- Parents who choose to use these techniques should be offered counselling
- Donors' identity should be protected
  - Although different views remain about whether some information should be available to the child
- Fair access to these techniques is essential and they should be available on the NHS, to all who might benefit from them, free of charge
- The techniques are to be used to produce a healthy child and for no other purposes

### 8.2 Requirements before support can be given:

- A more comprehensive scientific assessment of safety and efficacy must be done, for example through human trials first
- There needs to be more information about how individuals will be able to access the techniques, with an emphasis on the importance of fair, equitable and affordable access
- There needs to be more information about mitochondrial disease provided to the public, along with information on testing and diagnosis

## Appendix A – Profile of participants

	Cardiff		London		Newcastle	
	N	% of total	N	% of total	N	% of total
<b>Gender</b>						
Male	13	43	13	43	15	50
Female	16	54	14	47	15	50
Not answered	1	4	3	10	0	0
<b>Ethnicity</b>						
White British / White Other	20	67	16	53	24	80
Mixed	2	7	0	0	0	0
Asian	4	13	6	20	4	13
Black	3	10	6	20	2	7
Not answered	1	3	2	7	0	0
<b>Age</b>						
18 - 24	6	20	4	13	6	20
25 - 34	4	13	5	17	6	20
35 - 44	9	30	5	17	5	17
45 – 54	5	17	7	23	6	20
55 – 64	3	10	5	17	4	13
65 +	3	10	2	7	3	10
Not answered	0	0	2	7	0	0

<b>Socio economic group<sup>11</sup></b>						
A	2	7	0	0	3	10
B	4	13	11	37	4	13
C1	7	23	9	30	10	33
C2/D/E	16	53	8	27	13	43
Not answered	1	3	2	7	0	0
<b>Follows science issues on television/radio/papers</b>						
Yes	15	50	14	47	14	47
No	14	47	14	47	16	53
Not answered	1	3	1	7	0	0
<b>No. of participants who attended both days<sup>12</sup></b>	29 out of 30		26 out of 30		28 out of 30	

<sup>11</sup> Social grade was decided by asking the potential participant to identify the job of head of the household and the response was coded to the appropriate NRS Social Grade (<http://www.nrs.co.uk/>) by the recruiter. The level of social grade is decided on different criteria depending on the type of job. For example it could be number of people responsible for, type of qualification needed, level of skill needed etc.

<sup>12</sup> All participants attended day 1.

## Appendix B – Workshop programmes

### Day 1

Time	Session
9.30 – 10.00	Arrival, registration, coffee and complete initial questionnaire
10.00 – 10.25	<b>PLENARY: Welcome, introductions and overview of the day</b> HFEA OPM
10.25 – 10.45	<b>Small group discussion: understanding initial views / knowledge</b>
<b>10.45 – 11.00</b> <b>Coffee break</b>	
11.00 – 11.30	<b>Bluff your way in biology</b> Small group discovery session
11.30– 12.15	<b>What is mitochondrial disease?</b> Video
11.45 – 12.15	<b>Mitochondrial disease and techniques for avoiding mitochondrial disease.</b> Table discussions
12.15 – 12.30	<b>Review of the morning</b> Plenary
<b>12.30 – 13.15</b> <b>Lunch</b>	
13.15 – 13.40	<b>Expert question and answer session</b> Plenary
13.40 – 14.10	<b>What is new about these techniques? How are they different from assisted reproduction techniques that are currently permitted?</b> Table discussions
14.10 – 14.30	<b>What have you discovered today and what more do you need to know?</b> <b>What will you tell your friends and family about today?</b> Working tea time – small table discussions
14.30 – 14.50	<b>Summing up the day and looking forward</b> <b>Quiz (chance to win a box of chocolates....)</b>
14.50 – 15.00	<b>PLENARY: Close and thanks</b> <b>Evaluation questionnaires and ‘thank you’ payments.</b>

## Day 2

Time	Session
9.30 -10.00	<b>Arrival, registration, coffee</b> Participants complete ethics questionnaire and return to registration desk (or table facilitator, whichever is easiest).
10.00 – 10.10	<b>PLENARY: Welcome back</b> OPM & HFEA
10.10 – 11.00	<b>PLENARY: Recap of the issues</b> Video: patient experience
<b>Coffee break</b> <b>11.00 – 11.15</b>	
11.15 – 12.45	<b>Small table discussion</b> Identifying social and ethical issues Scenarios and deliberation on two specific issues: <ul style="list-style-type: none"> <li>• DNA from three people</li> <li>• Germ line therapy</li> </ul> Video and expert presentation Rapid table feedback
<b>Lunch break</b> <b>12.45 – 13.30</b>	
13.30 – 14.15	<b>PLENARY</b> Issues and discussion Video
14.15 – 14.35	<b>Small table discussion</b> Reviewing the issues What's most important? What messages do we want to give to the Secretaries of State?
14.50 – 14.55	<b>PLENARY: Final feedback, thanks and close</b> What we will do with your contributions. How to stay involved
14.55 – 15.00	<b>Evaluation and ethics questionnaires and 'thank you' payments</b> Leave us your contact details if you'd like to stay in touch with the project.

## Appendix C – List of experts and workshop materials

Location	Dates	Experts
Cardiff	Day 1 14 <sup>th</sup> July	Dr Lyndsey Butterworth, Research Associate, Institute for Ageing and Health, Newcastle University
	Day 2 28 <sup>th</sup> July	Dr Sheelagh McGuinness, Fellow, Birmingham Law School, University of Birmingham
London	Day 1 14 <sup>th</sup> July	Professor Mary Herbert, Professor of Reproductive Biology, North East England Stem Cell Institute (NESCI), Newcastle University
	Day 2 28 <sup>th</sup> July	Dr Iain Brassington, School of Law, Manchester University
Newcastle	Day 1 21 <sup>st</sup> July	Professor Doug Turnbull, Professor of Neurology, North East England Stem Cell Institute (NESCI), Newcastle University
	Day 2 4 <sup>th</sup> August	Professor Steve Wilkinson, Professor of Bioethics, Keele University

**1 - Information handouts** – A series of handouts were provided to participants. These covered the aims of the public dialogue; some of the basic science; information about mitochondrial disease; the research and regulation and a glossary of terms.

**2 - Bluff Your Way in Biology** – Each participant was asked to take part in a short quiz on the basic biology associated with mitochondria replacement, drawing on information posters that were placed around the room. Participants could work alone or in groups and were encouraged to share their learning on completing the quiz. The quiz handout sheet is set out below.

### **Bluff your way in biology – discovery session**

You have 20 minutes to use the resources in the room to collect information that will help you to answer three questions:

- What is a cell?
- What is DNA?
- What are mitochondria
- What do mitochondria do?

There are large posters on the wall and the same information is provided on handouts round the room. We have our expert on hand too, who will be happy to answer any questions you have.

You can tackle this in any way you like:

- Work as a team on all three questions
- Work in pairs or threes, each one gathering some information on one question and then come back together to discuss what you've found out
- Work individually and share learning afterwards.

There is a grid on which to record what you find out.



What is a cell?	
What is DNA?	
What are mitochondria?	
What do mitochondria do?	

**3. Briefing videos** – As part of the dialogue, two short and accessible briefing videos were produced using a vox pops and animations with a voiceover to introduce the key issues.

**Mitochondria Replacement – the science video**<sup>13</sup> – This video demonstrated what mitochondria are, and how the new techniques to prevent mitochondrial disease would work.

**Mitochondria Replacement – the ethics video**<sup>14</sup> – This video highlights some of the ethical considerations. This includes issues of identity and parentage; changing the germline; and the individual risks and benefits of the new techniques.

---

<sup>13</sup> Available at: <http://vimeo.com/45389280>

<sup>14</sup> Available at: <http://closeupresearch.com/ethics.html>



# Medical frontiers: Debating mitochondria replacement

## Annex III: Public representative survey

Report to HFEA

February 2013

OPM  
252B Gray's Inn Road,  
London WC1X 8XG

tel: 0845 055 3900  
fax: 0845 055 1700  
email: [info@opm.co.uk](mailto:info@opm.co.uk)  
web: [www.opm.co.uk](http://www.opm.co.uk)

Client	HFEA
Document title	Medical Frontiers: Debating mitochondria replacement: public representative survey
Date modified	22/02/2013
Status	Final
OPM project code	8984
Author	Kai Rudat
Quality assurance by	Robin Clarke
<b>Contact details</b>	
Main point of contact	Tim Vanson
Telephone	020 7239 7806
Email	tvanson@opm.co.uk

If you would like a large text version of this document, please contact us.



---

# Contents

Executive Summary .....	1
1. Introduction .....	3
2. Methodology and reporting .....	4
3. Key Findings .....	5
3.1 General attitudes towards medical research and treatments for genetic diseases .....	5
3.2 Awareness of IVF and Mitochondrial Disease .....	7
3.4 Attitudes to the Regulation of Genetic Treatments .....	9
Appendix A – Survey .....	12
Appendix B – Sample Profile .....	15
Appendix C – Results tables .....	17

## Executive Summary

The Office for Public Management (OPM), in partnership with Forster and Dialogue by Design, was commissioned by the Human Fertilisation and Embryology Authority (HFEA) to conduct a multi-method research and engagement project looking at the possible social and ethical issues relating to two techniques for the avoidance of mitochondrial disease: pronuclear transfer (PNT)<sup>1</sup> and maternal spindle transfer (MST)<sup>2</sup>.

As part of this research and engagement, OPM ran a short representative survey of the public. Demographic quotas were set to ensure that the selected sample was representative of the UK population. In total, 979 face-to-face interviews were completed. The key findings are presented below.

### 1. General attitudes towards medical research and treatments for genetic diseases

The results indicate that the UK population holds very positive attitudes about the benefits of medical research: nine out of ten respondents agree that such research ‘can do a lot to reduce human suffering’ and that it ‘creates new knowledge and treatments which will benefit the wider healthcare system’. Whilst the responses point to a universal perception of medical research as beneficial, responses to the question about ‘*unforeseen negative side effects*’ show that half of the population has concerns about side effects.

Attitudes towards the treatment of people with genetic diseases are also highly positive: almost nine out of ten members of the public are in favour of providing people with serious genetic conditions with ‘healthcare and treatment to help manage their conditions’ and three-quarters feel that ‘families at risk of having a child with a serious genetic disease should be able to avoid that risk through genetic testing’.

### 2. Awareness of IVF and Mitochondrial Disease

The UK population shows a high level of awareness of IVF with 86% of respondents saying that they are aware of it. However, awareness in London and amongst Black and Minority Ethnic (BME) groups and related faith communities is lower (for example, awareness among Muslims was 51%).

The survey indicates that around one in ten of the UK population has experience of genetic diseases in their family or immediate circle of friends.

**Awareness of mitochondrial disease is relatively low** with just over a quarter (28%) reporting that they have heard of the disease. Awareness of mitochondrial disease is strongly correlated with education, rising from 10% of those with low educational levels to 25% with

---

<sup>1</sup> Pronuclear transfer involves transferring the pronuclei from an embryo with unhealthy mitochondria and placing them into a donor embryo which contains healthy mitochondria and has had its pronuclei removed. A pronucleus is a small round structure containing nuclear DNA seen within an embryo following fertilisation. A normal embryo should contain two pronuclei, one from the egg (maternal pronucleus) and one from the sperm (paternal pronucleus).

<sup>2</sup> The maternal spindle is a structure within the egg containing the mother’s nuclear DNA. Maternal spindle transfer involves transferring the spindle from the intended mother’s egg, with unhealthy mitochondria, and placing it into a donor egg with healthy mitochondria.

medium levels of education and 46% to those with high levels; subsequently there is a similar gradient by social class<sup>3</sup>. There are only small variations by faith.

### 3. The Genetic Treatment of Mitochondrial Disease

The survey sought to establish general attitudes towards the testing of embryos during IVF. Two thirds (65%) expressed a positive attitude and 8% a negative attitude; 27% were undecided or unsure. In terms of sub group differences, the results show a drop off in positive ratings the testing of embryos during IVF for those who describe themselves as Christian and a more marked drop-off among Muslims. Although there are variations, negative attitudes are still confined to small minorities of Christians (9%) and Muslims (14%).

Asked to give their 'initial reaction' on the new techniques, between 44% and 56% expressed a positive initial reaction while between 10% and 15% had a negative reaction. These results suggest that respondent's support for medical research and sympathy towards those affected continued even as the more ethically difficult subjects of PNT and MST were explained.

### 4. Attitudes to the Regulation of Genetic Treatments

When asked about the potential regulation of treatments for mitochondrial disease the findings suggest that the UK public have a range of preferences.

The option of couples being allowed to decide for themselves was favoured by over a third of respondents (36%). Slightly more (39%) favoured the involvement of a regulator of some kind – with a fifth (20%) selecting the option of an expert regulator deciding on an individual basis, and a similar amount (19%) calling for an expert regulator to approve particular clinics, with medical specialists deciding who to offer it to. A further one quarter were unable to express a preference.

---

<sup>3</sup> See Methodology and Reporting (Section 2) for an explanation of how level of education and social class were ascertained.

# 1. Introduction

Mitochondria are present in almost all human cells. They are often referred to as the cell's 'batteries' as they generate the majority of a cell's energy supply. For any cell to work properly, the mitochondria need to be healthy. Unhealthy mitochondria can cause genetic disorders known as mitochondrial disease.

There are many different conditions that are linked to mitochondrial disease. They can range from mild to severe or life threatening, and can have devastating effects on the families that carry them. Currently there is no known cure and treatment options are limited. For many patients with mitochondrial disease preventing the transmission of the disease to their children is a key concern.

Mitochondrial disease can be caused by faults in the genes within a cell's nucleus that are required for mitochondrial function or by faults within the small amount of DNA that exists within the mitochondria themselves. It is the latter form of mitochondrial disease that could be avoided using two new medical techniques, termed pro-nuclear transfer (PNT)<sup>1</sup> and maternal spindle transfer (MST)<sup>2</sup> which UK researchers are working on.

These techniques are at the cutting edge, both of science and ethics and are currently only permitted in research. They involve removing the nuclear DNA from an egg or embryo with unhealthy mitochondria, and transferring it into an enucleated donor egg or embryo with healthy mitochondria.

The Human Fertilisation and Embryology Act (1990) (as amended) ('the Act') governs research and treatment involving human embryos and related clinical practices in the UK. The Act currently prevents the clinical use of these techniques (or any other technique that involves genetic modification of gametes and embryos to treat patients). However, in 2008 the Act was amended, introducing new powers which enable the Secretary of State for Health to permit techniques which prevent the transmission of serious mitochondrial disease. The Secretary of State for Health and the Secretary of State for Business, Innovation and Skills asked the Human Fertilisation and Embryology Authority (HFEA) to seek public views on these emerging techniques. On considering advice from the HFEA the Government will decide whether to propose regulations legalising one or both of the procedures for treatment.

The HFEA, together with the Sciencewise Expert Resource Centre<sup>4</sup>, therefore commissioned OPM (in partnership with Forster and Dialogue by Design) to conduct a multi-method research and engagement project looking at the possible social and ethical issues and arguments relating to the techniques. The project consisted of five strands:

1. Deliberative public workshops
2. Public representative survey
3. Patient focus group
4. Open consultation meetings
5. Open consultation questionnaire

This research provides the evidence base that will inform the HFEA's advice to the Secretary of State.

The **public representative survey** explored attitudes towards the genetic treatment of mitochondrial disease. The findings from this survey help to build up understanding of public

---

<sup>4</sup> The Sciencewise Expert Resource Centre (Sciencewise-ERC) is the UK's national centre for public dialogue in policy making involving science and technology issues



perception and to contextualise the wider consultation. This report provides a summary of the main findings.

## 2. Methodology and reporting

The aim of the survey was to ascertain awareness and attitudes towards the development of the new medical techniques of a representative sample of the UK public. A random location methodology was used to select respondents. It involved making a random selection of 175 sample points covering the whole of the UK. For each sample location, demographic quotas were set to ensure that the sample reflected the profile of the UK population.

Respondents were contacted by interviewers in the 175 sample points; they were not members of panels and had not been pre-contacted for any other purpose. Interviews were carried out in August 2012. In total, 979 face-to-face interviews were completed; a profile of the sample can be found in Appendix B.

The survey consists of ten questions and was included in a UK omnibus survey. It aimed to gauge the awareness and attitudes of respondents by asking a series of yes/no questions as well as the extent to which they agree or disagree with a series of statements, using a five point scale and a 'don't know' option. Throughout this report references are made to particular survey questions. A full copy of the survey can be found in Appendix A.

This report shows responses to the questions asked as the percentage of the overall sample. Where less than 0.5% of respondents answered a question, this is shown as '\*\*' to indicate that at least one respondent endorsed this answer but the number who did so was less than 0.5% of the sample.

The report contains few comparisons between sub-groups since views were held relatively consistently between sub-groups, or because variations were relatively small and lacked consistency. However two factors produced more consistent variations:

- **Education:** a number of questions showed consistent variations for education (and subsequently for social class)
- **Faith:** there also were some variations by faith, showing a difference between respondents who reported that they had 'no religion' and those who reported they were 'Christian' or 'Muslim'. The sample sizes for other faith groups were too small to allow for any systematic comparisons

While these differences were notable, they did not point to any polarisation of views. Instead they suggest that some views were held less or more strongly but were broadly on the same continuum.

### *Note about the sub-group classifications*

**Education level** was ascertained by asking respondents to indicate their highest level of education qualification held – where low equals no qualifications, medium equals O-Level, GCSE, A-level, GNVQ or similar and high equals a degree, postgraduate, NVQ/SVQ level 4 or HNVQ.

**Social grade** was decided based on the job of the head of the household. The interviewer asked for the job role and then coded it at the end of the interview. In the case of respondents who were retired, they were asked for the previous job if on private pension, or if on state pension only, then automatically classified as an 'E'. The NRS social grades are the standard categories used in social research in the UK. They are decided on different

criteria depending on the type of job. For example, it could be number of people responsible for, type of qualification needed, level of skill needed etc.

### 3. Key Findings

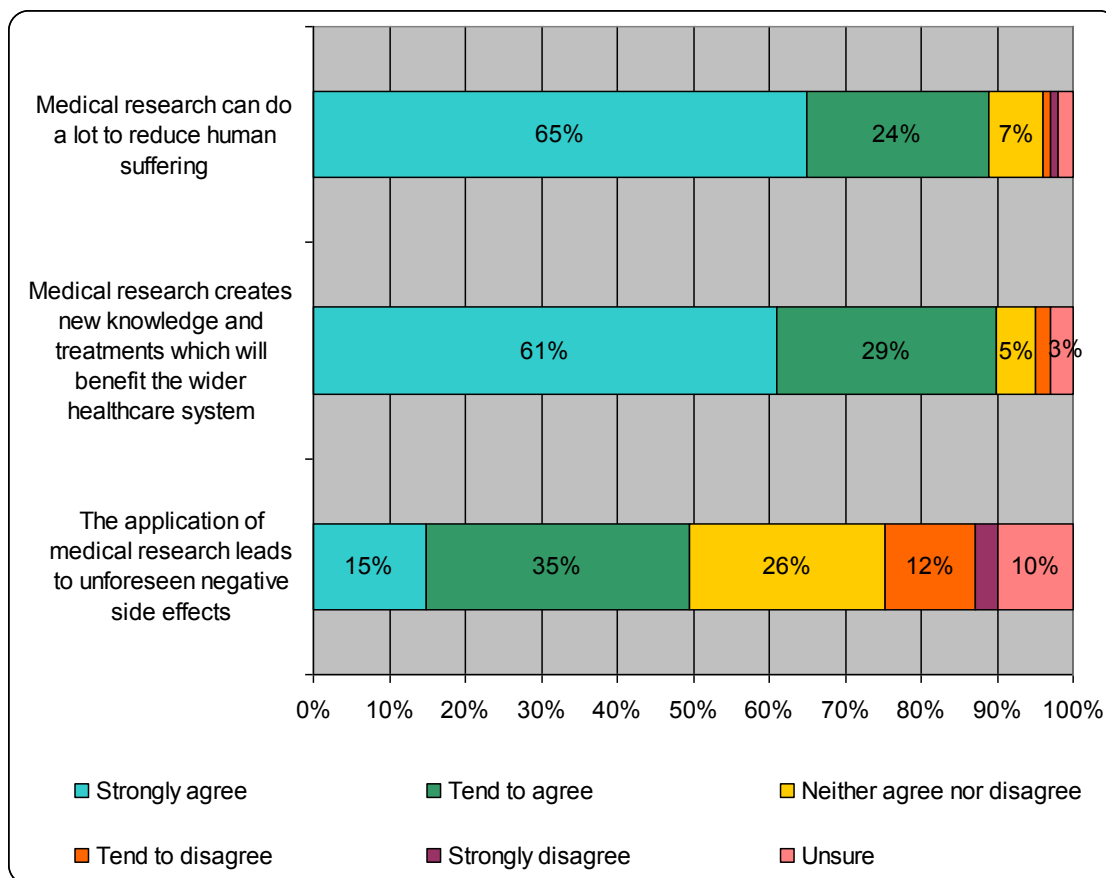
#### 3.1 General attitudes towards medical research and treatments for genetic diseases

Figure 1 shows responses to three general questions about medical research. Responses indicate that those who took part in the survey hold very positive attitudes about the benefits of medical research: nine out of ten respondents agree that such research 'can do a lot to reduce human suffering' and that it 'creates new knowledge and treatments which will benefit the wider healthcare system'; almost two-thirds hold these views 'strongly' and only very small minorities (2%) disagree with the statements.

Whilst these responses point to a universal perception of medical research as beneficial, responses to the question about 'unforeseen negative side effects' show that half of the population has concerns about side effects. Fifteen percent disagree with the statement about side effects and 36% are either unsure or feel they can neither agree nor disagree with the statement.

There are no systematic variations between different sub-groups on the first two items; however on the question about side effects, Muslims express slightly more concern (61%).

**Figure 1. Attitudes towards medical research and treatments for generic diseases**

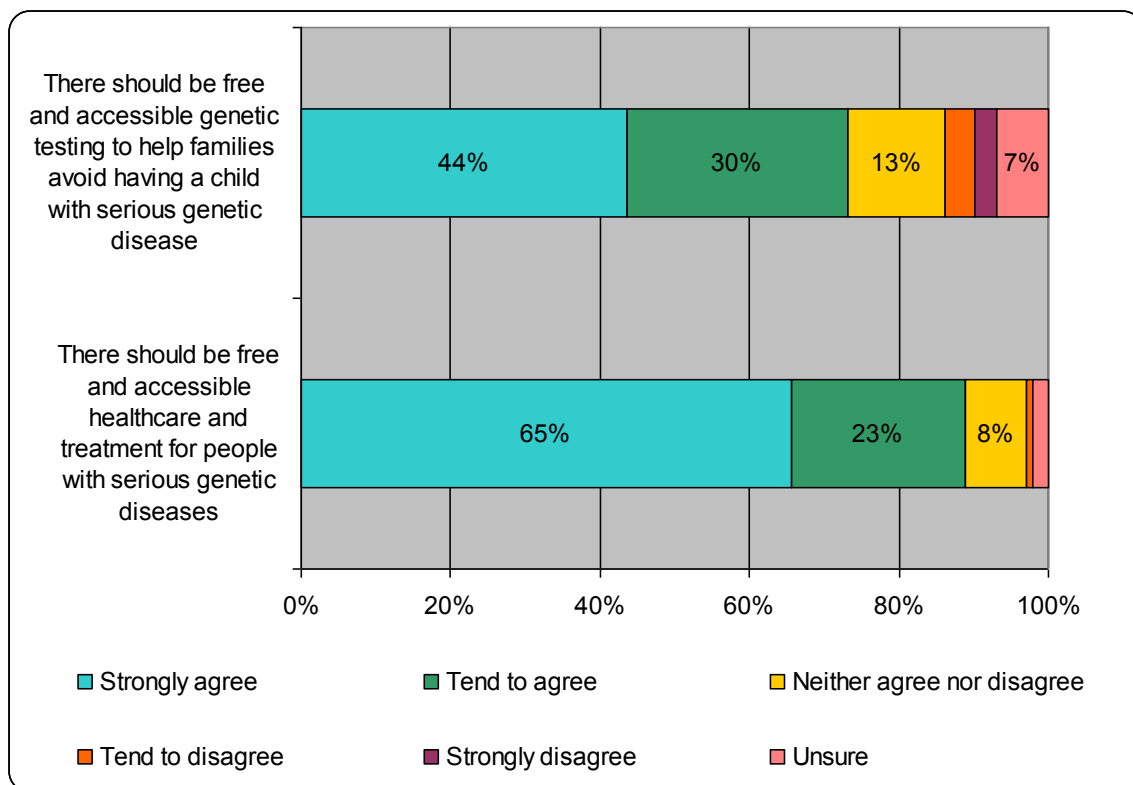


Base: All (979)

Attitudes towards the treatment of people with genetic diseases also are highly positive: almost nine out of ten members of the public are in favour of providing people with serious genetic conditions with 'healthcare and treatment to help manage their conditions' and three-quarters feel that 'free and accessible genetic testing to help families avoid having a child with serious genetic disease' should be made available. The question about genetic testing receives slightly more opposition (7%) as well as more uncertainty (20% are either unsure or undecided).

There are no major variations in attitudes for the first statement. For the second statement, respondents who reported that they had 'no religion' are slightly more positive (Mean Score of 1.31) compared with Christians (MS 1.14) or Muslims (MS 0.96) (see Appendix C for a full breakdown of the mean scores).

**Figure 2. Attitudes towards the treatment of people with genetic diseases**



Base: All (979)

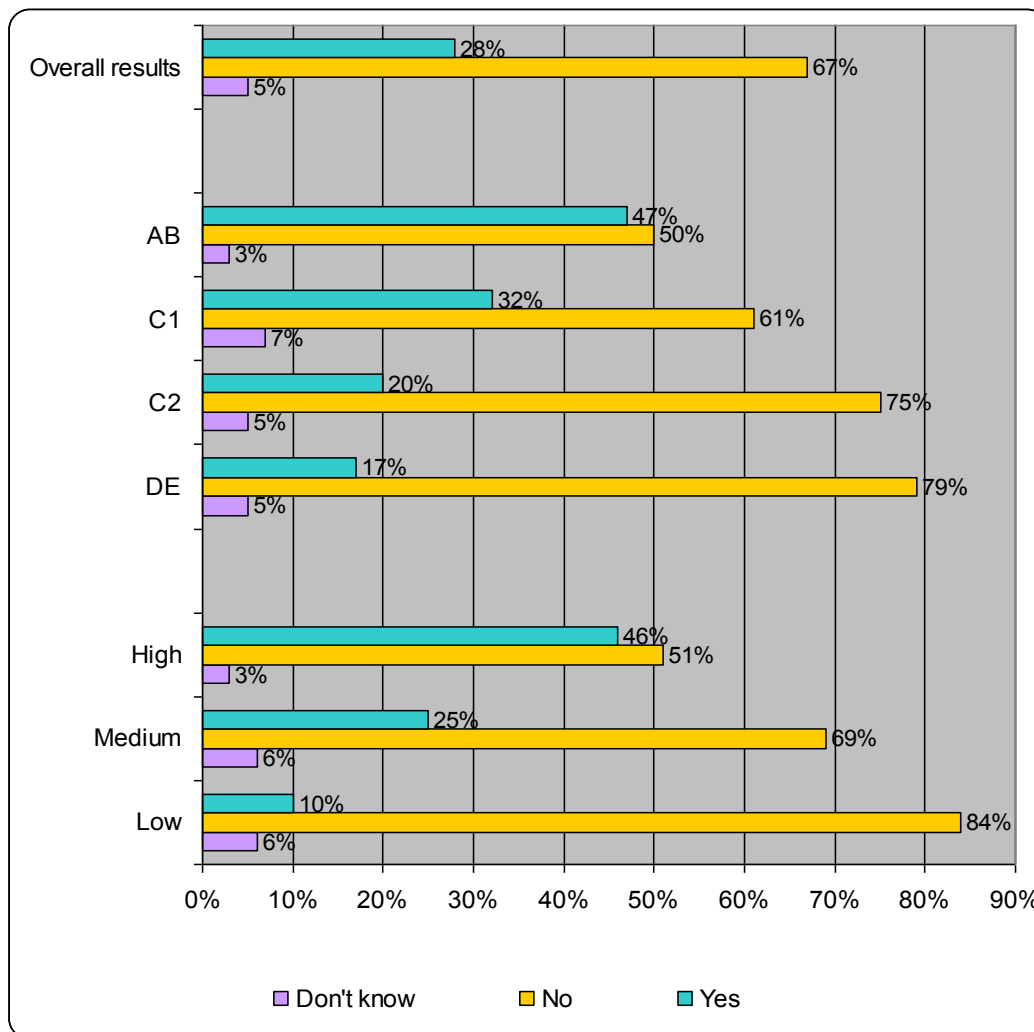
### 3.2 Awareness of IVF and Mitochondrial Disease

The UK population shows a high level of awareness of IVF (Q3) - 86% of respondents are aware and only 14% unaware. However, awareness in London is particularly low – 65%; this is linked to similarly lower levels of awareness among BME groups and related faith communities (for example, awareness among Muslims is 51%).

Around one in ten of the UK population has experience of genetic diseases in their family or immediate circle of friends (Q5).

Awareness of mitochondrial disease is relatively low with just over a quarter (28%) reporting that they have heard of the disease. Awareness of mitochondrial disease is strongly correlated with education, rising from 10% of those with low educational levels to 25% with medium levels of education and 46% to those with high levels; subsequently there is a similar gradient by social class (awareness among social class DE is 17%, C2 – 20%, C1 – 32% and AB 47%. There are small variations by faith; among those who report they have no religion, 34% have heard of mitochondrial disease, among Christians the figure is 26%, and among Muslims 22%.

**Figure 3. Awareness of mitochondrial disease: overall, by social class and educational level**



Base: All (979)

### 3.3 The Genetic Treatment of Mitochondrial Disease

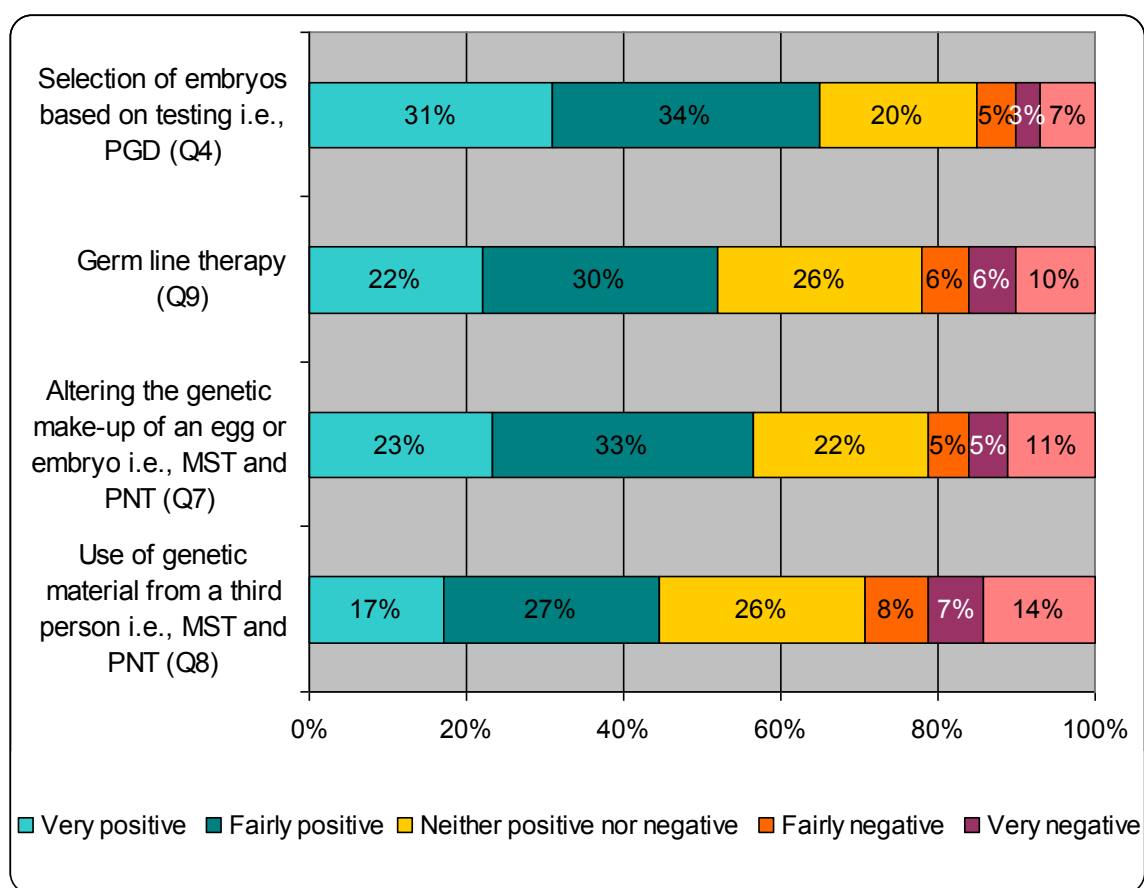
The survey included several questions (see Appendix A for full question wording) about specific aspects of genetic treatments. The first question was asked more generally, prior to asking questions about mitochondrial disease. It sought to establish general attitudes towards the testing of embryos during IVF. Two thirds (65%) expressed a positive attitude and 8% a negative attitude; 27% were undecided or unsure. The mean score analysis (see Appendix C) shows that there was a drop off in positive ratings for those who describe themselves as Christian and a more marked drop-off among Muslims. Although there are variations, negative attitudes are still confined to small minorities of Christians (9%) and Muslims (14%).

Questions 7 to 9 (see Appendix A) seek to understand respondents 'initial reaction' to different aspects of potential treatments for mitochondrial disease, which are outlined in Figure 3 below. The results will inform the HFEA's consultation about the ethical and social issues surrounding new techniques that will require a change in the law.

As shown in Figure 3 below, across the three treatment questions, between 44% and 56% expressed a positive initial reaction while between 10% and 15% a negative reaction. The proportion undecided or unsure is quite high, between 33% and 40%. This reflects both the unfamiliarity of mitochondrial diseases and the complexity of the techniques.

These results suggest that respondent's positivity towards medical research and sympathy towards those affected (see Section 3.1) continued, even as the more ethically challenging subjects of PNT and MST were explained.

The analysis of the mean score differences (see Appendix C) shows that education and faith have some influence on people's attitudes towards these treatments, but that these differences are not profound, with fewer than one-in-five of the groups expressing negative attitudes.

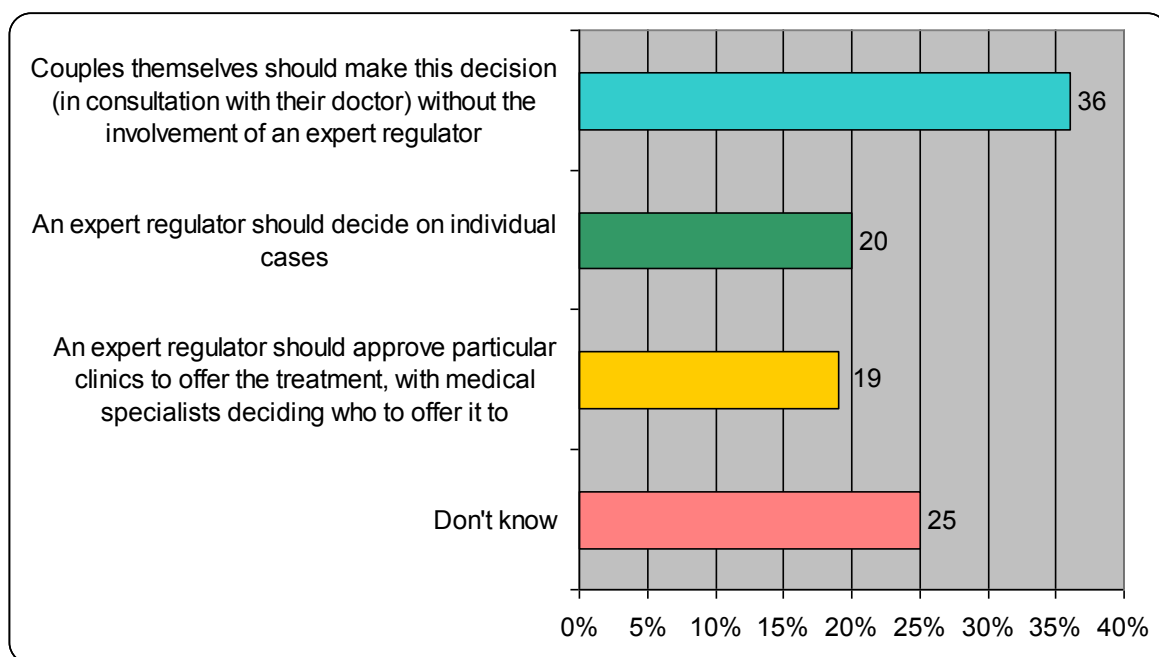
**Figure 4: Attitudes to the genetic treatment of mitochondrial disease**

Base: All (979)

### 3.4 Attitudes to the Regulation of Genetic Treatments

When asked about the potential regulation of treatments for mitochondrial disease (Q10) respondents expressed a range of preferences.

The option of couples being allowed to decide for themselves was favoured by over a third of respondents (36%). However, slightly more (39%) favoured some kind of involvement of a regulator – with a fifth of respondents (20%) selecting the option of an expert regulator deciding on an individual cases, and a similar amount (19%) calling for an expert regulator to approve particular clinics, with medical specialists deciding who to offer it to. A further one quarter (25%) were unable to express a preference.

**Figure 5. Attitudes to the regulation of genetic treatments**

Base: All (979)

As shown in Table 1 below, the mean score analysis shows small variations, but these are largely influenced by variations in the proportions who did not express an opinion.

**Table 1: Attitudes to the regulation of genetic treatments**

	Expert regulator decides on individual basis	Expert regulator approves clinics and medical specialists decide who to treat	Couples decide without expert regulator	Don't know
Education Level				
- low	17%	12%	39%	31%
- medium	21%	18%	37%	24%
- high	20%	26%	31%	23%
Religion				
- none	22%	16%	42%	20%
- Christian	20%	22%	35%	23%
- Muslim	24%	7%	18%	51%



## Appendix A – Survey

### Q1. To what extent you agree or disagree with the following statements?

Medical research can do a lot to reduce human suffering

Medical research creates new knowledge and treatments which will benefit the wider healthcare system

The application of medical research leads to unforeseen negative side effects

Strongly agree

Tend to agree

Neither agree nor disagree

Tend to disagree

Strongly disagree

Unsure

### Q2. To what extent you agree or disagree with the following statements?

There should be free and accessible healthcare and treatment for people with serious genetic diseases

There should be free and accessible genetic testing to help families avoid having a child with serious genetic disease

Strongly agree

Tend to agree

Neither agree nor disagree

Tend to disagree

Strongly disagree

Unsure

**Q3. IVF is where a couple having difficulties conceiving have eggs and sperm mixed in a laboratory to create an embryo. The embryo is then grown for a few days and placed into the woman's womb where it has a reasonable chance of leading to a normal pregnancy. Have you heard of IVF (in-vitro fertilisation) before?**

Yes

No

**Q4. Techniques are already available to test embryos during IVF for a specific genetic disease. Couples who know they have a high chance of having a child with a serious genetic disease can use this technique to have a child without that disease and not use the embryos that have tested positive. How would you describe your attitude to this?**

Very positive

Fairly positive

Neither positive nor negative

Fairly negative

Very negative

Unsure

**Q5 Can I just check if you, a member of your family or your immediate circle of friends have any direct experience of inherited genetic disorders such as cystic fibrosis, Huntington's disease, muscular dystrophy or sickle cell anaemia?**

Yes

No

Don't know

**Q6. Some people are born with, or develop, genetic diseases – such as cystic fibrosis, Huntington's disease, muscular dystrophy or sickle cell anaemia – which they inherit from one or both of their parents. These diseases are caused by an alteration in an individual's genetic material that leads to a variety of physical or learning impairments.**

**A small proportion of these genetic diseases are inherited just from the mother and are difficult to avoid. These are called mitochondrial disease and can often be severe. Have you heard of mitochondrial disease before today?**

**Have you heard of mitochondrial disease before today?**

Yes

No

Don't know

**Q7. Scientists are developing techniques which could remove the chance of these mitochondrial diseases by altering the genetic make-up of an egg or embryo during IVF. What is your initial reaction to this?**

Very positive

Fairly positive

Neither positive nor negative

Fairly negative

Very negative

Unsure

**Q8. In order for this to happen, you would need to replace abnormal mitochondria in the intended parent's egg or embryo with healthy mitochondria from a donor egg or embryo. This means that any resulting egg or embryo will contain a small amount of genetic material in its mitochondria from a third person (other than the mother and father). What is your reaction to this?**

- Very positive
- Fairly positive
- Neither positive nor negative
- Fairly negative
- Very negative
- Unsure

**Q9. As I said before, the techniques to avoid mitochondrial disease would involve altering the make-up of an egg or embryo, specifically the mitochondria. The donated healthy mitochondria would replace the intended mother's faulty mitochondria and would then be passed down to the child and, in turn, to that child's children and beyond. This is called germline gene therapy, because the change goes down through the generations (the germline). Assuming that scientists could show that this is safe, what is your reaction to this?**

- Very positive
- Fairly positive
- Neither positive nor negative
- Fairly negative
- Very negative
- Don't know

**Q10. Currently, these techniques cannot be offered to couples as the law only allows them to be carried out in research. However, Parliament may have an opportunity to change the law to allow these techniques to be offered to couples. If Parliament did change the law, who do you think should decide whether individual couples should have the treatment?**

An expert regulator should decide on individual cases

An expert regulator should approve particular clinics to offer the treatment, with medical specialists deciding who to offer it to

Couples themselves should make this decision (in consultation with their doctor), without the involvement of an expert regulator

## Appendix B – Sample Profile

The sample profile is reported as the total number of interviews obtained, the number obtained for each sub-group, the unweighted proportion of each sub-group within the overall sample, and the weighted proportion within the overall sample. For example, the achieved sample included 12% of people under the age of 25; this age group makes up 15% of the UK population and the achieved sample was weighted to make up 15% of the weighted sample. Throughout the report, weighted percentages are reported.

<b>Sample Profile</b>			
	<b>Number of interviews</b>	<b>Unweighted %</b>	<b>Weighted %</b>
<b>Total</b>	979	100%	100%
<b>Gender</b>			
- female	547	56%	51%
- male	432	44%	49%
<b>Age</b>			
- 16 to 24	117	12%	15%
- 25 to 34	186	19%	16%
- 35 to 44	145	15%	17%
- 45 to 55	154	16%	17%
- 55 to 64	139	14%	14%
- 65+	238	24%	20%
<b>Education level</b>			
- low	234	24%	20%
- medium	484	49%	51%
- high	258	26%	28%
<b>Social class</b>			
- AB	205	21%	20%
- C1	238	24%	29%
- C2	196	20%	22%
- DE	340	35%	29%
<b>Religion</b>			
- no religion	251	26%	27%

- Christian	578	59%	57%
- Muslim	42	4%	4%
- others (combined)	63	6%	7%
- refused to say	46	5%	5%

## Appendix C – Results tables

**Table 1: Attitudes to medical research**

Q1: To what extent do you agree or disagree with the following statements?

	Medical research can do a lot to reduce human suffering	Medical research creates new knowledge and treatments which will benefit the wider healthcare system	The application of medical research leads to unforeseen negative side effects
Strongly agree (+2)	65%	61%	15%
Tend to agree (+1)	24%	29%	35%
Neither agree nor disagree (0)	7%	5%	26%
Tend to disagree (-1)	1%	2%	12%
Strongly disagree (-2)	1%	*	3%
Unsure	2%	3%	10%
Mean Score	1.55	1.53	0.51

**Table 2: Attitudes to the treatment of genetic diseases**

Q2: To what extent do you agree or disagree with the following statements?

	People with serious genetic diseases should be provided with healthcare and treatment to help manage their condition	Families at risk of having a child with a serious genetic disease should be able to avoid that risk through genetic testing
Strongly agree (+2)	65%	44%
Tend to agree (+1)	23%	30%
Neither agree nor disagree (0)	8%	13%
Tend to disagree (-1)	1%	4%
Strongly disagree (-2)	*	3%
Unsure	2%	7%
Mean Score	1.55	1.16

**Table 3: Attitudes to the genetic treatment of mitochondrial disease**

Q4: Attitude/reaction to ...

	Selection of embryos based on testing (Q4)	Altering the genetic make-up of an egg or embryo (Q7)	Use of genetic material from a third person (Q8)	Germ line therapy (Q9)
Very positive (+2)	31%	23%	17%	22%
Fairly positive (+1)	34%	33%	27%	30%
Neither positive nor negative (0)	20%	22%	26%	26%
Fairly negative (-1)	5%	5%	8%	6%
Very negative (-2)	3%	5%	7%	6%
Unsure	7%	11%	14%	10%
Mean Score	0.91	0.73	0.47	0.63
<b>Mean Score Variations</b>				
Education Level				
- low	0.87	0.55	0.24	0.38
- medium	0.96	0.79	0.52	0.70
- high	0.86	0.73	0.52	0.68
Religion				
- none	1.10	0.97	0.70	0.85
- Christian	0.89	0.64	0.37	0.56
- Muslim	0.59	0.64	0.60	0.47



---

# **Medical frontiers: debating mitochondria replacement**

## **Annex IV: Summary of the 2012 open consultation questionnaire**

---

**Report to: Human Fertilisation and Embryology Authority**

**February 2013**

**Prepared by Dialogue by Design**

Dialogue by Design  
252B Gray's Inn Road  
London WC1X 8XG

Telephone: 020 7042 8000  
Email: [facilitators@dialoguebydesign.com](mailto:facilitators@dialoguebydesign.com)  
Website: [www.dialoguebydesign.net](http://www.dialoguebydesign.net)

Company registration no. in England and Wales: 3856988  
VAT registration no. 123 4151 58

# Contents

---

<b>Executive Summary</b>	<b>4</b>
<b>Chapter 1            Introduction</b>	<b>8</b>
<b>Chapter 2            The consultation process</b>	<b>10</b>
2.1   Summary of consultation activities	10
2.2   Responses	10
2.3   About the respondents	11
<b>Chapter 3            Methodology</b>	<b>14</b>
3.1   Receiving responses	14
3.2   Analysing responses	14
3.3   About this report	16
<b>Chapter 4            Question 1: permissibility of new techniques</b>	<b>19</b>
4.1   Headline findings	19
4.2   Summary of comments	20
4.2.1   Arguments for the introduction of the techniques	20
4.2.2   Arguments against the introduction of the techniques	23
4.2.3   Other considerations	25
<b>Chapter 5            Question 2: changing the germ line</b>	<b>29</b>
5.1   Headline findings	29
5.2   Summary of comments	30
5.2.1   Uncertainty and risk	30
5.2.2   Social implications	32
5.2.3   Ethical implications	34
5.2.4   The science of the germline	35
<b>Chapter 6            Question 3: implications for identity</b>	<b>39</b>
6.1   Headline findings	39
6.2   Overview of comments	40
6.2.1   Reflections on identity	40
6.2.2   Ethical implications	42
6.2.3   Social implications	43
6.2.4   Comparing with other procedures	49
<b>Chapter 7            Question 4a: the status of the mitochondria donor</b>	<b>51</b>
7.1   Headline findings	51
7.2   Summary of comments	51
7.2.1   Comparing mitochondrial donation	51
7.2.2   The mitochondrial donor	55

<b>Chapter 8</b>	<b>Question 4b: the status of the mitochondria donor</b>	<b>58</b>
8.1	Headline findings	58
8.2	Summary of comments	60
8.2.1	Option 1 (no information) & option 2 (some information but not identity)	60
8.2.2	Option 3 (information and ability to contact once child is 18)	62
8.2.3	Option 4	64
8.2.4	Option 5	66
8.2.5	Other comments	66
<b>Chapter 9</b>	<b>Question 5: regulation of mitochondria replacement</b>	<b>67</b>
9.1	Headline findings	67
9.2	Overview of comments	69
9.2.1	Responses to option 1 (clinics and patients to decide)	69
9.2.2	Responses to option 2 (regulatory framework; clinics and patients decide)	71
9.2.3	Responses to option 3 (regulator decides)	73
9.2.4	Responses to option 4 (mitochondria replacement should not be permitted)	74
<b>Chapter 10</b>	<b>Question 6: should the law be changed?</b>	<b>76</b>
10.1	Headline findings	76
10.2	Overview of comments	78
10.2.1	Arguments against a change in law	78
10.2.2	Arguments in favour of a change in law	80
10.2.3	Other legal and regulatory considerations	82
10.2.4	Other considerations	84
<b>Chapter 11</b>	<b>Question 7: further considerations</b>	<b>85</b>
11.1	Headline findings	85
11.2	Overview of comments	86
11.2.1	Arguments against the introduction of the techniques	86
11.2.2	Arguments for the introduction of the techniques	88
11.2.3	Other considerations	89
11.2.4	Context and decision making	92
<b>Appendix</b>		<b>95</b>
A.1	Consultation questions	95
A.2	Responding organisations	97
A.3	Analysis: List of themes	100
A.4	Analysis: List of codes applied per question	101

## Executive summary

---

### About the consultation

The Office for Public Management (OPM), in partnership with Forster and Dialogue by Design (DbyD), was commissioned by the Human Fertilisation and Embryology Authority (HFEA) to conduct a multi-method research and engagement project looking at the possible social and ethical issues relating to two techniques for the avoidance of mitochondrial disease: pronuclear transfer (PNT)<sup>1</sup> and maternal spindle transfer (MST)<sup>2</sup>.

As part of this research and engagement, *Medical Frontiers: debating mitochondria replacement*, an **open consultation** ran from 17 September to 7 December 2012.

Respondents were invited to consider a range of information presented on the consultation website, and to respond to seven questions using the online questionnaire.

A total of **1,836 responses** were received, the majority of which were via the consultation website. Respondents include stakeholder organisations, individuals with personal experience of mitochondrial disease, as well as many members of the public.

The consultation process was managed by Dialogue by Design (DbyD), a company specialising in managing large or complex consultation processes. DbyD received, processed and analysed all responses to the consultation in close liaison with the HFEA.

It is important to note that the open consultation provided an opportunity to participate for individuals and organisations keen to have their views heard. As anyone who wanted to could participate, the views expressed **cannot be considered representative of the wider population**.

### Emerging themes

The consultation questionnaire asks respondents to consider a number of questions relating to making MST and pronuclear transfer PNT techniques available to people at risk of passing on mitochondrial disease to their child.

Throughout responses to all consultation questions a number of themes are highlighted repeatedly, mostly as part of a narrative that is either supportive of the introduction of the techniques, or one that articulates opposition.

**Respondents who argue against** the introduction of mitochondria replacement techniques often express concern that such a move would cross an ethical boundary or amount to inappropriate interference with the natural or spiritual aspect of reproduction. Many specify that they believe it is problematic that children born as a result of the techniques will carry DNA from three people, for a range of reasons further discussed below. Another strand to some respondents' opposition is the creation and destruction of embryos as part of PNT, which in their view is unethical.

---

<sup>1</sup> Pronuclear transfer involves transferring the pronuclei from an embryo with unhealthy mitochondria and placing them into a donor embryo which contains healthy mitochondria and has had its pronuclei removed. A pronucleus is a small round structure containing nuclear DNA seen within an embryo following fertilisation. A normal embryo should contain two pronuclei, one from the egg (maternal pronucleus) and one from the sperm (paternal pronucleus).

<sup>2</sup> The maternal spindle is a structure within the egg containing the mother's nuclear DNA. Maternal spindle transfer involves transferring the spindle from the intended mother's egg, with unhealthy mitochondria, and placing it into a donor egg with healthy mitochondria.

**Respondents who argue in favour** of the introduction of mitochondria replacement techniques often emphasise the benefits of the techniques to families affected by mitochondrial disease. Many say they believe it is important - some say there is an ethical imperative - to avoid or eradicate the disease, sometimes referring to the suffering that patients may endure. Respondents who support the techniques also tend to employ arguments about the genetic significance of donated mitochondria (or mitochondrial DNA), which they believe is limited and therefore not a great concern. This is further explored in the sections below.

An additional theme emerging both in responses arguing against the techniques and in responses arguing in favour is the **management of risk**. For many respondents supporting mitochondria replacement in principle it is crucial that sufficient evidence is available about the safety of the techniques before they are allowed in a clinical setting. Other respondents highlight that risks cannot be fully managed and that this is part of the reason why they oppose the introduction of mitochondria replacement techniques.

## Consultation questions

Responses to each of the seven consultation questions are discussed below, focusing on issues specific to those questions.

### Question 1

Asked for their **views on offering MST and PNT** to people at risk of passing on mitochondrial disease to their child, just over 500 respondents say they do not think the techniques should be permitted, while almost 500 say that they support the introduction of both techniques. Most respondents with direct or indirect experience of mitochondrial disease argue in favour of the introduction of the techniques.

Where respondents support one technique in particular, they tend to prefer MST because this technique replaces mitochondria in eggs rather than embryos.

### Question 2

Respondents are asked in question 2 whether they think there are social and ethical implications to **changing the germline**.

Those in favour of the techniques argue that there are **no negative implications** or that these are outweighed by the positives. Respondents who oppose the introduction of the techniques specify a range of potential implications, highlighted below.

With regard to the germline the most prominent concern expressed is that consequences of the techniques will affect many **generations down the line**, and that these consequences are to some extent unknown.

Another potential implication outlined in some respondents' views is that making changes to the germline for this purpose could **lead to other changes** becoming more acceptable: many respondents identify the idea of germline change with cloning or the creation of designer babies.

Others argue that any change to the germline is inappropriate because there is no way for all those affected to give **consent**; a view contradicted by a few who see making choices for subsequent generations as a very ordinary part of being a parent.

### Question 3

When asked in question 3 whether they think the techniques have social or ethical implications relating to **a person's sense of identity**, respondents' comments differ widely.

Respondents who believe such implications will be **minor or non-existent** often argue that identity is more a social than a genetic concept, that mitochondrial DNA has no function in determining an individual's characteristics, and that other procedures currently used (including adoption and gamete donation) are likely to have similar or greater implications.

Respondents who consider that implications are likely often say that knowing they carry DNA from three people may saddle children with questions about who they are, and who their parents are, which they say will have a detrimental impact on their **well-being**. Some respondents argue that adopted or donor-conceived children suffer from identity issues and that children resulting from mitochondria replacement could experience similar problems, or worse. A number of respondents think that children born as a result of using PNT might also feel unhappy about the creation and destruction of embryos as part of their conception.

Many respondents believe that parents will be able to **mitigate** any identity implications by being open about how the child is conceived.

#### Question 4a

The consultation questionnaire asks how respondents **view the status of a mitochondria donor** compared to other, existing types of donor. Views differ diametrically on this topic, with mitochondria donation seen as similar to, and different from, each existing type of donation by roughly equal numbers of respondents.

The most frequently made comparisons are with **gamete donation**, closely followed by **tissue, organ and bone marrow donation**. Generally speaking it is the genetic significance of mitochondria donation that informs respondents' comparisons, with those believing mitochondrial DNA is of greater significance more inclined to compare with gamete donation, and others more inclined to compare with organ, tissue or bone marrow donation.

#### Question 4b

This question asks respondents about their views on possible models for governing the disclosure of **information about the mitochondria donor** to the child.

The consultation questionnaire outlines three possible models, each of which are supported by more than 100 respondents. Most of these believe **children should not know the identity** of their mitochondria donor, with opinion divided on whether medical and personal information should be available. About 150 respondents think **children should be able to contact their mitochondria donor** once they reach the age of 18. Some respondents offer alternatives to the models proposed in the question, including suggestions for more flexible arrangements.

Respondents often indicate that their preference is informed by whether or not they regard the mitochondria donor as **a third parent** of the child, with those who think of the donor as a parent more inclined to favour a model that allows contact.

Several respondents think that donors should **consent** to the information that is disclosed, in particular for the model where the donor's identity would be made available to the child. Others argue that the disclosure of identity is part of the responsibilities of the donor.

Respondents who oppose the introduction of the techniques generally do not discuss the models and reaffirm their **opposition** instead.

#### Question 5

In question 5 respondents are asked to indicate a preference for one of three possible **models of regulation** if the law were to be changed to allow mitochondria replacement to be carried out in specialist clinics.

Almost half of the respondents to this question decline to express such a preference, and instead note their objection to mitochondria replacement.

Of those respondents who indicate a preference for a particular model of decision making, close to half opt for a system in which **clinics and individual patients** would make a case-by-case decision about whether or not to use mitochondria replacement (option 1). This preference is often associated with a view that a central regulatory board may lack sensitivity to individual circumstances and a feeling that individual patients should be empowered to choose the best option for their own families.

A similar number of respondents prefer an option that includes a **role for the regulator** (option 2 and option 3). Many feel that an external regulatory framework would provide a buffer against abusive profiteering and promote fairness by making sure that the same criteria are applied for all applications for treatment.

Most respondents who think there is a role for the regulator express a preference for a **broad regulatory framework** in which the regulator sets overall criteria within which patients and clinicians can decide on a case-by-case basis. A minority of respondents express a preference for a model in which a central regulator would maintain responsibility for making decisions about particular cases.

### Question 6

In question 6 of the consultation questionnaire, respondents are **asked whether they believe the law should be changed** to allow mitochondria replacement techniques to be made available to people who are at risk of passing on mitochondrial disease to their child.

A majority of these respondents argue against changing the law, while a substantial minority argue in favour.

Those **arguing against a law change** sometimes refer to the international context and see it as problematic that the UK would be the first or only country to allow the use of MST and PNT. Several respondents argue that other methods should be considered before forging ahead with these new techniques.

Respondents **arguing in favour of law change**, and particularly those adding caveats to their support, highlight a variety of criteria they think need to be met. Respondents also suggest that further work is undertaken to specify which of the techniques (MST and/or PNT) should be allowed, and in which circumstances.

### Question 7

The final consultation question asks respondents whether there are any **other considerations** they think decision makers should take into account.

In addition to reiterating points they made in response to earlier questions, some respondents highlight that decision makers should particularly consider the **views of certain groups** such as patients and relatives, scientists, and religious groups. With regard to the latter there are responses urging decision makers to not give undue consideration to these.

## Chapter 1 Introduction

---

Mitochondria are present in almost all human cells. They are often referred to as the cell's 'batteries' as they generate the majority of a cell's energy supply. For any cell to work properly, the mitochondria need to be healthy. Unhealthy mitochondria can cause genetic disorders known as mitochondrial disease.

There are many different conditions that are linked to mitochondrial disease. They can range from mild to severe or life threatening, and can have devastating effects on the families that carry them. Currently there is no known cure and treatment options are limited. For many patients with mitochondrial disease preventing the transmission of the disease to their children is a key concern.

Mitochondrial disease can be caused by faults in the genes within a cell's nucleus that are required for mitochondrial function or by faults within the small amount of DNA that exists within the mitochondria themselves. It is the latter form of mitochondrial disease that could be avoided using two new medical techniques, termed pro-nuclear transfer (PNT) and maternal spindle transfer (MST) which UK researchers are working on.

These techniques are at the cutting edge, both of science and ethics and are currently only permitted in research. They involve removing the nuclear DNA from an egg or embryo with unhealthy mitochondria, and transferring it into an enucleated donor egg or embryo with healthy mitochondria.

The Human Fertilisation and Embryology Act (1990) (as amended) ('the Act') governs research and treatment involving human embryos and related clinical practices in the UK. The Act currently prevents the clinical use of these techniques (or any other technique that involves genetic modification of gametes and embryos to treat patients). However, in 2008 the Act was amended, introducing new powers which enable the Secretary of State for Health to permit techniques which prevent the transmission of serious mitochondrial disease. The Secretary of State for Health and the Secretary of State for Business, Innovation and Skills asked the Human Fertilisation and Embryology Authority (HFEA) to seek public views on these emerging techniques. On considering advice from the HFEA the Government will decide whether to propose regulations legalising one or both of the procedures for treatment.

The HFEA, together with the Sciencewise Expert Resource Centre<sup>3</sup>, therefore commissioned OPM (in partnership with Forster and Dialogue by Design) to conduct a multi-method research and engagement project looking at the possible social and ethical issues and arguments relating to the techniques. The project consisted of five strands:

1. Deliberative public workshops
2. Public representative survey
3. Patient focus group
4. Open consultation meetings
5. Open consultation questionnaire

As part of this range of activities to seek views of members of the public, the HFEA conducted a open consultation on mitochondria replacement in the autumn of 2012. This report provides a

---

<sup>3</sup> The Sciencewise Expert Resource Centre (Sciencewise-ERC) is the UK's national centre for public dialogue in policy making involving science and technology issues.



summary of the responses to the consultation, which was run by an independent specialist company.

The findings of the consultation have also informed the Summary of Evidence which is published separately, and also contains findings from other dialogue and research activities. The overview report also contains an introduction to the techniques and the issues the HFEA is considering as part of their duty to provide recommendations to Government.

## Chapter 2      The consultation process

---

### 2.1      Summary of consultation activities

The HFEA's public consultation on *Medical Frontiers: debating mitochondria replacement* ran from 17 September to 7 December 2012. It followed an intensive and wide-ranging programme of dialogue and research carried out in the spring and summer of 2012, and the findings from these stages informed the consultation questionnaire. This report covers the public consultation only; please see the Summary of Evidence for summaries of other engagement activities. The purpose of the public consultation was to gather public views on the social and ethical impact of making the proposed techniques available to patients. The HFEA will consider these views when they prepare their recommendations to Government.

The consultation was open to all. Respondents were invited to consider a range of information presented on the consultation website, and to respond to seven questions using the online questionnaire. Although the consultation website encouraged respondents to consider the information presented, respondents may have preferred to respond without considering this information, or to use other sources to inform their response. Respondents were not asked to indicate which information they consulted, so this has not been used as a variable in the analysis or the report.

The consultation documents recommended the use of the online questionnaire, but responses made via email or post were also accepted while the consultation was open. The consultation was managed by Dialogue by Design (DbyD), a company specialised in managing large or complex consultation processes.

The public consultation was an open process, which means that respondents cannot be considered a representative sample of the UK population, as one would expect to find in a survey or referendum. Rather, the consultation attracted responses from individuals and organisations who chose to respond. Its main purpose is to help the HFEA understand the range of views held by respondents as well as the arguments underpinning these views. Although it can be helpful to consider how many respondents express certain views, this is not the primary aim of the consultation or indeed this report.

The HFEA also held two public meetings in London and Manchester, which gave members of the public a chance to share their views in person. The events included a panel of experts who gave some information about the techniques and took questions from the attendees, as well as a chance for members of the public to discuss the issues. These meetings have been reported on separately and have also been covered in the Summary of Evidence.

### 2.2      Responses

A total of 1,836 responses to the consultation were received. Most of these were submitted via the consultation website. Additionally, 524 letters and emails were received. A further 45 respondents completed a response form.

**Table 1 Overview of response types**

Response type	Count
Online questionnaire	1,260
Paper-based response form	45
Letters and emails	524
Total	1,836

Not all respondents answered all consultation questions. In fact, some respondents answered none of the questions, but sent a generic letter or email in which they set out their views. Table 2 below provides an overview of the number of responses each consultation question received.

**Table 2 Overview of responses per consultation question**

Question	Count of responses
Question 1	1,235
Question 2	1,114
Question 3	1,084
Question 4a	987
Question 4b	1,039
Question 5	1,143
Question 6	1,055
Question 7	883
Other responses, not specific to consultation questions	503

## 2.3 About the respondents

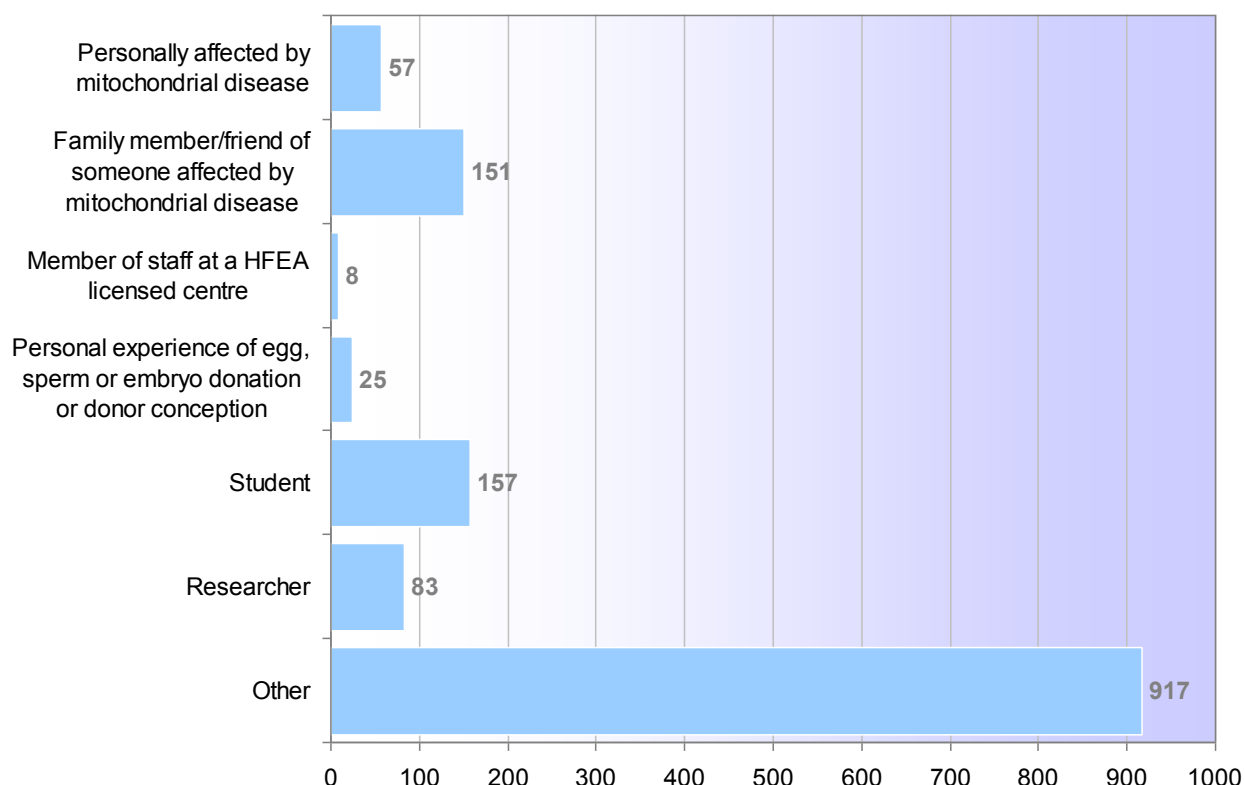
Respondents who used either the consultation website or a response form were asked to answer a small number of questions about themselves, specifying their background and the nature of their interest in the consultation. The responses to these questions are summarised here.

A total of 66 respondents specified that their response was submitted on behalf of an organisation. A list of organisations who participated in the consultation is provided in appendix 2.

The questionnaire also asked respondents to select from a series of listed options which best described them. Respondents could select more than one option if appropriate. An overview of the responses to this question is given in figure 1 below. This respondent information could not be collected for those who responded by email or letter.

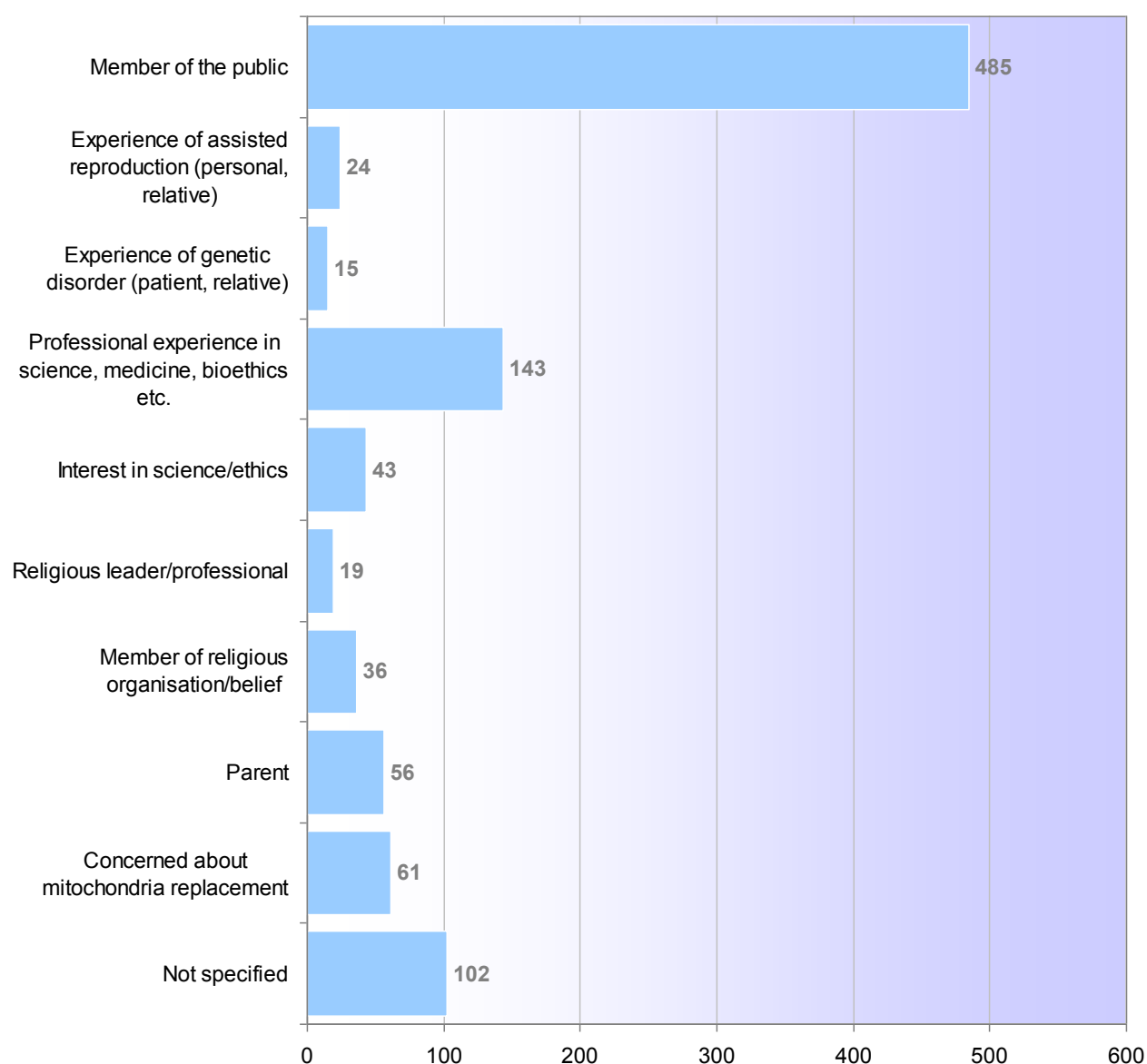
Figure 1 shows that most respondents did not describe themselves as belonging to one of the categories specified in the questionnaire, with 917 respondents choosing 'Other'. Of those who did identify with listed options, 157 respondents indicated they were students and 83 that they were researchers. A total of 151 respondents specified that they were a family member or friend of someone affected by mitochondrial disease; 57 respondents indicated that they themselves were affected. Also, 25 respondents indicated that they had personal experience of egg, sperm, embryo donation or donor conception and 8 respondents identified themselves as staff members at a HFEA licensed centre.

**Figure 1**      **Respondent types (online only)**



As is shown above, the majority of respondents who completed the 'About you' question ticked 'Other' and many of these specified further their interest in the consultation. Roughly half of the respondents who selected 'Other' identified themselves as 'members of the public' or 'citizens'. Smaller numbers of respondents included details about their scientific or professional background, their religious beliefs or involvement, or their experience of related diseases or procedure. A rough breakdown of the respondents within the 'other' category is shown in figure 2. Please note that many respondents included a fair bit of information, therefore sometimes respondents have been counted in multiple categories.

**Figure 2 Respondent type ‘other’: further breakdown based on self-description**



### **Individuals, organisations and organised responses**

It is worth noting that respondents include individuals responding on behalf of themselves (or a small group of people), organisations responding on behalf of their staff or membership, as well as individuals responding in their capacity of supporters of an organisation or group. This is common for open consultation processes: there is no selection of respondents other than the choice of individuals and organisations to respond.

As discussed in section 2.1 above and further clarified in chapter 3, this needs to be kept in mind when considering the summary of responses. In particular, it is possible (and common for this type of high-profile consultation) that a proportion of the responses are a result of initiatives from groups or organisations to raise the prominence of specific points of view. This may have influenced the numbers of responses expressing either strong support for or strong opposition to mitochondria replacement.

## Chapter 3 Methodology

---

### 3.1 Receiving responses

Responses were received in a number of formats: online response forms (via the website), letters and emails. All responses were received by DbyD, at which point they were assigned a unique reference number and entered into the DbyD analysis system.

#### Online response forms

Online responses were imported directly into the DbyD analysis system. Whilst the consultation was open, users were able to update or amend their submission. If respondents updated their submission this was imported into the analysis database with a clear reference that it had been modified, to ensure that any new information was taken into account during the analysis.

#### Paper response forms

Response forms received by post were logged and scanned, then manually written or copied into the analysis database by data entry staff. The data entry process followed the questionnaire structure so that these responses could be analysed in the same way as online responses. Data entry was monitored by the DbyD transcription team to ensure that responses were accurately captured.

#### Emails

Respondents were able to send responses directly to DbyD by email. These responses were logged, imported into our analysis system and analysed alongside the online responses.

#### Letters

Letters sent to DbyD were logged, scanned and written into the database by data entry staff. The data entry process was monitored by the DbyD transcription team to ensure that responses were accurately captured. Once data entry was complete responses were imported to the analysis system and analysed alongside the online responses.

#### Responses sent to the HFEA

A small number of responses were sent directly to the HFEA, either by post or by email. The HFEA informed respondents that their response would be considered as part of the consultation and securely transferred the responses to DbyD, where they were entered into the analysis system as described above.

#### Late submissions

The consultation ended at midnight on Friday 7<sup>th</sup> December. To make allowances for potential delays in the email and postal systems offline responses which arrived no later than Tuesday 11 December 2012 were included in the analysis and this report.

### 3.2 Analysing responses

#### Developing an analysis framework

In order to analyse the responses, and the variety of views expressed, an analytical framework was created. The purpose of the framework was to enable analysts to organise responses by key themes and issues so that key messages as well as specific points of detail could be captured and reported.

A three-tier approach was taken to coding, starting with high level themes, splitting into sub-themes and then specific codes. As an example, a response to question 1 containing a concern about changes to the germ line would be coded into (theme) *Arguments against* - (sub-theme) *Altering DNA* - (code) *impact on germ line/lineage*. Some themes were used more often for particular questions, while others were used equally across the questions as respondents raised similar issues. Table 3 provides a full list of the top level themes used and Table 4 provides an extract from the coding framework showing the use of themes, sub-themes and codes. The full list of themes and codes are available in appendices 3 and 4.

Each code is intended to represent a specific issue or argument raised in responses. The data analysis system allows the analysts to populate a basic coding framework at the start (top-down) whilst providing scope for further development of the framework using suggestions from the analysts engaging with the response data (bottom-up). We use natural language codes (rather than numeric sets) since this allows analysts to suggest refinements and additional issues, and aids quality control and external verification.

**Table 3 Coding framework: themes**

Theme	Acronym
Acceptability	AC
Arguments against	AG
Arguments in favour	FA
Considerations	CO
Consultation process	CP
Decision making	DM
Donation status	DS
Information	IN
Legal Status	LS
Other	O
References	RF
Science	SC
Social and ethical	SE

**Table 4**      **Coding framework: example codes for SC and SE themes**

Theme	Sample codes
Science	SC - DNA - natural mixing SC - Mitochondria - function/form SC - Mt DNA - does not affect identity/traits SC - Mt DNA - may affect identity/traits SC - other procedures - organ/tissue/blood donation
Social and ethical	SE - Ethical - end does not justify means SE - Ethical - ethical imperative to intervene SE - General - similar to other procedures SE - Social - child awareness/understanding SE - Social - donor/child relationship SE - Social - overall societal impact

### Applying the analysis framework

The analysis team, supervised by the senior analysts who developed the coding framework, worked systematically through each response to the consultation, applying the relevant codes to capture the issues raised. The application of a code from the framework was done simply by highlighting the relevant text and recording the selection. A single response would receive multiple codes to capture the various issues raised by each respondent.

The coding of responses to each question was regularly checked and reviewed by senior analysts to ensure quality and consistency. In addition, HFEA was able to view analysed responses throughout the analysis stage and provide feedback on the coding when required.

## 3.3 About this report

This report provides a summary of the responses to the HFEA consultation on *Medical frontiers: debating mitochondria replacement*. It gives a flavour of the issues raised in response to each of the consultation questions.

As outlined above, this report is produced to help the HFEA understand the range of views held by respondents as well as the arguments underpinning these views. For that reason it is not written with a view to identify majority views, or to emphasise points made by greater numbers of responses only. Rather the report aims to present minority views alongside those held by many, so that each issue is discussed in a manner that does as much justice as possible to the wealth of suggestions presented in responses.

### Summarising a variety of response types

The structure of this report mirrors the structure of the consultation questionnaire (see appendix 1), with a chapter dedicated to each consultation question. Each chapter summarises views expressed in response to the question it covers. This includes comments from stakeholder organisations as well as individuals. The report aims to provide an accurate summary of all respondents' views and efforts were made to ensure that it amply covers responses from organisations as well as individuals.



Chapter 2 includes a breakdown of respondent categories based on what respondents indicated when asked to define their interest in the consultation. Where relevant the report specifically looks at the responses from a particular category of respondents, for instance to consider the views of those with experience of gamete donation on the status of the mitochondria donor.

As specified in chapter 2, not all respondents used the consultation questionnaire: some 500 responses received as emails and letters did not refer to the consultation questions. Non-questionnaire responses were analysed in the same way as questionnaire responses, making up an additional 'question' in the database. In the report, the issues most prominently discussed in these responses are discussed in the most relevant chapter, i.e. comments about changing the law are discussed in chapter 10. As these responses are not directly addressing the consultation question, they are discussed separately from the other responses, and set apart by a different layout.

Both among questionnaire and non-questionnaire responses there are numerous respondents making similarly or identically worded arguments. This indicates that there may have been initiatives to encourage people to respond to the consultation in a certain way. While this does not make such responses less valid or valuable than others, it is important that readers of the report are aware of this. To accommodate this, the report clarifies where particular views are made by many respondents using the same words or suite of arguments.

### **Numbers and quantifying terms**

Where the report refers to how many respondents have raised a specific issue, it is important to keep in mind that this was an open and qualitative consultation process rather than a way to establish dominant views across a representative cross-section of the public. The numbers in the report are useful in clarifying where issues are seen as important by many or by a few respondents. Beyond that, however, they cannot be seen to serve any statistical purposes. This is also true for the numbers reported on in chapters 8 and 9, where the closed questions of the questionnaire are discussed and charts are included to summarise responses.

Similar to the above, the report contains words like 'many', 'some', 'a few' in order to indicate the distribution of opinions among respondents on particular topics. In this way these terms help clarify whether viewpoints discussed are raised by greater or smaller numbers of respondents. The words are only very rarely used in relation to the total number of respondents to the consultation. Rather, the use of these words depends on their context, i.e. 'many' should not be regarded as indicating a precise numeric range.

### **Info-graphics**

The following chapters of the report each contain an info-graphic presenting a diagram of the topics emerging in responses to the consultation question discussed in that chapter. These diagrams aim to clarify how the report breaks down the wide range of issues relating to each consultation question; they do not indicate any further or deeper interpretation of the data.

### **Quotes**

Throughout the following chapters quotes from respondents have been used to illustrate the points raised. Where responses from organisations are quoted, the name of the organisation is mentioned; individual respondents are not identified by name when quoted.

### **Use of the terms social and ethical**

Several consultation questions ask respondents to consider whether the techniques have social or ethical implications. As part of the analysis of these and other questions a distinction was made between implications, or issues, that could be described as ethical and others that would primarily

be social. The distinction used throughout the analysis brands arguments relating to ideologies and value systems as *ethical* and arguments relating to impact on individuals or groups in society as *social*. This distinction has been used consistently across the consultation questions. In this regard it is important to remember that the report merely aims to summarise responses; further interpretation is outside the scope of this report.

## Chapter 4      Question 1: permissibility of new techniques

### 4.1      **Headline findings**

The first question asks:

**Q1: Having read the information on this website about the two mitochondria replacement techniques – maternal spindle transfer and pro-nuclear transfer, what are your views on offering (one or both of) these techniques to people at risk of passing on mitochondrial disease to their child? You may wish to address the two techniques separately.**

1,235 responses were made to this question.

Most respondents took this opportunity to express their view about the acceptability the techniques - with approximately equal numbers supporting and opposing their introduction into clinical practice. Most respondents commented on the acceptability of the techniques taken together or without distinguishing between them: 349 state that they consider both acceptable, while 106 agree but with some caveats, but 502 say they are not acceptable. Among those commenting on the MST technique alone, 20 say the technique is acceptable, compared to 3 who agree with caveats and 2 respondents who say it is not acceptable. Conversely, no respondents commenting on the PNT technique alone say that it is acceptable, but 3 say it is acceptable while acknowledging some caveats, and 24 state that it is not acceptable.

Proponents of the techniques tend to focus on social outcomes, particularly the potential to avoid disease and allow parents the opportunity to have a healthy child. Some feel that if the techniques are possible, there is an ethical obligation to implement them. In contrast those opposing the techniques are more likely to discuss ethical issues, often arguing that use of the techniques would amount to inappropriate interference with the natural or spiritual aspect of reproduction. Others focus on the use of embryos, particularly in relation to PNT, arguing that any artificial or in-vitro manipulation of embryos is unethical. Where respondents support one technique in particular, they tend to prefer MST because it involves eggs rather than embryos. A few respondents say they favour PNT, sometimes stating that this technique has a greater success rate.

Looking at respondent types, there is a visible pattern with regard to their view on the acceptability of the techniques. Among those who describe themselves as 'other', there are 453 respondents stating that the techniques are not acceptable and 156 respondents saying they are. For each of the other respondent categories, such as 'student' and 'family member or friend affected by mitochondrial disease', more respondents say they find the techniques acceptable than unacceptable. Of the respondents describing themselves as personally affected by mitochondrial disease 36 think the techniques are acceptable and three think they are not.

#### **Non-questionnaire responses**

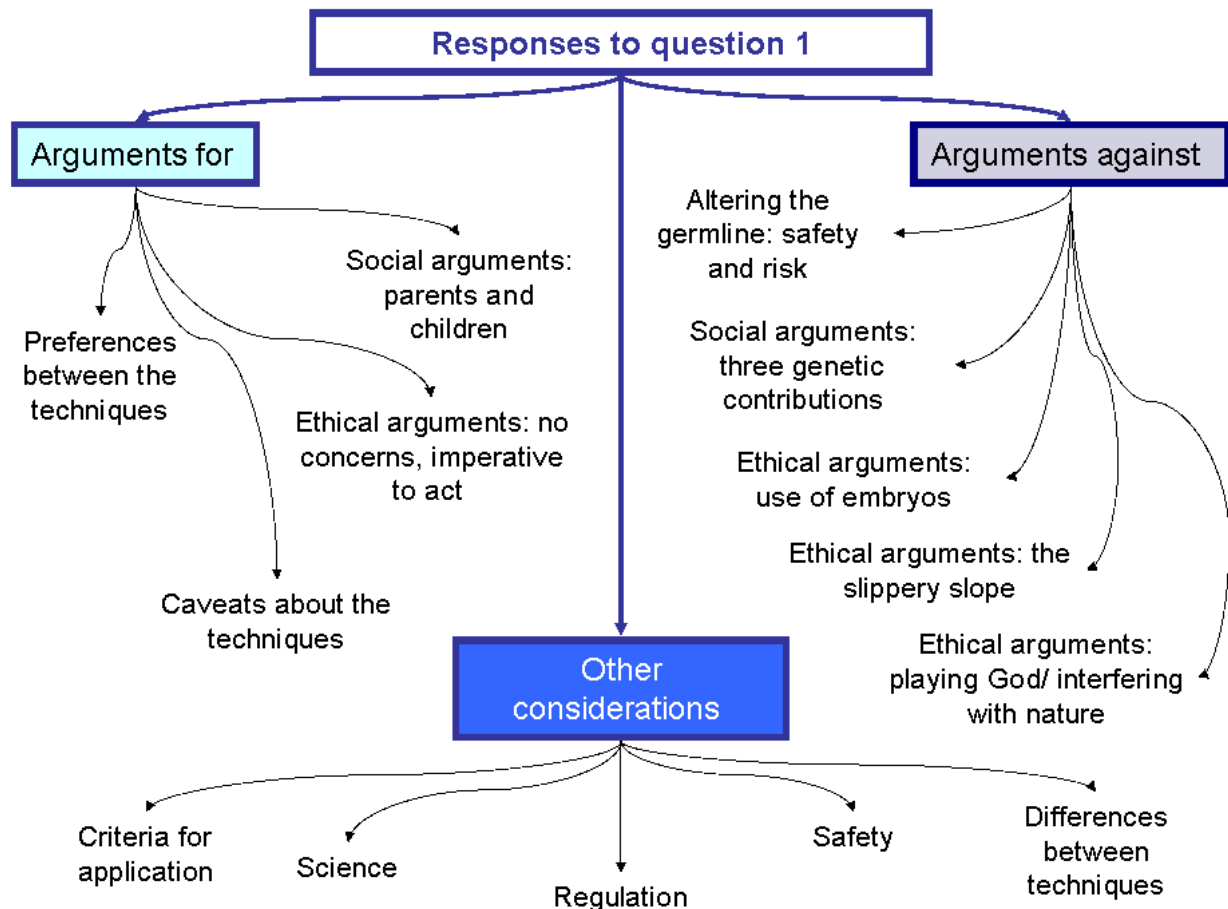
Comments on the permissibility of the techniques are also abundant in the 503 non-questionnaire responses to the consultation. These responses include a large number of letters and emails which make a similar range of arguments, often using very similar wording. Some 300 respondents state that they do not think either of the techniques are acceptable. Often this statement is accompanied by concerns about the use of embryos and/or the idea that children will carry DNA from three people. Respondents also express concern about possible unintended long-term consequences of mitochondria replacement. Some respondents believe the techniques will lead to

the acceptance of cloning and/or designer babies. A substantial number of those who argue against the techniques refer to their religion.

Some 40 respondents who sent a letter or email believe that mitochondria replacement techniques are acceptable. Many of these refer to a particular case of a child that was born with mitochondrial disease, while others sometimes point to the impact of the disease on patients and families more generally.

These arguments and others raised by respondents to question 1 are explored in more detail below under the following sub-headings:

**Figure 3 Responses to question 1**



## 4.2 Summary of comments

### 4.2.1 Arguments for the introduction of the techniques

60 respondents express their support for the introduction of the two techniques without adding any further explanation. Around 400 respondents give an explanation of their support, as summarised here. Stakeholder organisations expressing support include the British Medical Association, the Humanist Society Scotland, and the Association of Clinical Embryologists (ACE) Executive Committee.

#### **Social argument: parents and children**

The most common reason given by those in support of the techniques is the importance of the health of children, with many respondents seeing the techniques as an opportunity to prevent

future suffering which should not be passed up. As in the quote below, a large proportion of those responding in favour of the introduction of the techniques feel that the outcomes of these techniques are so obviously positive that there is no real reason to oppose them.

“If by introducing both these techniques, we can wipe out mitochondrial diseases and the suffering that goes with it, then it can only be a good thing.”

Individual, Personally affected by mitochondrial disease; Family member/friend of someone affected by mitochondrial disease

Some respondents focus more specifically on the principle of avoiding or eradicating disease, seeing it as a categorically positive step, and supporting both research and introduction of new techniques which can prevent disease. Other respondents talk more generally about scientific progress as beneficial to society. Some respondents specifically address mitochondrial disorders, with some arguing that the potential severity of the symptoms means the benefits of the techniques outweighs any risks or costs they perceive. Personal experience of mitochondrial disease, and other hereditary disorders, is a factor for many respondents who support the techniques.

Another of the most prevalent arguments for introducing the techniques comes from respondents who talk about the benefits to current and potential parents, describing the techniques as giving them a ‘chance’ to have a healthy child, without passing on the disorders. In relation to the experience of potential parents some respondents talk about the emotional experience of a parent who fears passing on a disorder to their child, particularly where the severity cannot always be anticipated. One participant who describes their own family experiences with mitochondrial disease states:

“One cannot underestimate the amount of emotional and psychological damage inflicted on parents knowing they have passed the mitochondrial disease to their children.”

Individual, Family member/friend of someone affected by mitochondrial disease

### **Ethical arguments: no concerns, imperative to act**

There are two main strands of ethical argument from those supporting the introduction of the new techniques in question one. Many respondents simply state that they see no significant ethical concerns in the use of the techniques. Some specify that they have no ethical concerns within the clinical context of mitochondrial disorders, and a few explicitly disagree that this could lead to other uses. Others feel that because the techniques involve mitochondrial rather than nuclear DNA there is no reason to be concerned about the involvement of a third person’s genetic material.

The second major ethical argument for the techniques comes from respondents who feel there is a moral or ethical imperative to intervene wherever suffering can be prevented. Respondents including the British Medical Association and the Humanist Society Scotland talk about a positive duty to help those who are disadvantaged, others feel it is morally unacceptable to restrict the availability of potentially beneficial techniques. These respondents feel that the techniques under consultation will reduce the incidence of mitochondrial disease, and that it is unethical not to take the opportunity to achieve this. For others the imperative is to give parents the opportunity to have a healthy child, or the right to choose to do so:

“The chance to have a healthy baby is something that should be available to all couples regardless of their medical history and this is a step towards that.”

Individual, Student

## Caveats about the techniques

There are 105 respondents including the Church of England (Mission and Public Affairs Council), the Nuffield Council on Bioethics, the Academy of Medical Sciences and the British Fertility Society who qualify their support for the techniques proposed, suggesting that there are further criteria that must be met before they would consider them acceptable. By far the most common group of criteria is to do with the safety and efficacy of the techniques. Some respondents make general statements, for example that the techniques should be made available as soon as they are 'safe', while others call more specifically for further trials or evidence to verify their safety. As noted above, many respondents who do not offer a preference between the two techniques suggest that further research to determine which is the most effective, should determine which technique is used.

"Maternal spindle transfer (MST) and pro-nuclear transfer (PNT) have the potential to prevent mitochondrial disease in future generations, giving affected parents the opportunity to have children without the fear of passing on the condition, or of passing on the risk of having affected children to their own children.

"Both of these techniques are at a research stage and there is not sufficient data available to determine which is better on the grounds of safety, efficacy and feasibility. We do not believe they should be differentiated between at this point. Research into both of these techniques should continue to assess whether they are viable as potential clinical treatments.

We recognise that the two techniques used are different and could raise varying ethical concerns for different people. However the Nuffield Council concluded it was ethical for both to be explored further. Subject to further information about effectiveness and safety, when balancing the benefits of each technique, some people may wish to consider the different methods used by each technique as a factor in this decision...

...We support the Nuffield Council of Bioethics conclusion that "if the PNT and MST techniques are proven to be acceptably safe and effective, on balance it would be ethical for families wishing to use them to do so. This should, however, be subject to the offer of an appropriate level of information and support."

Organisation, AMRC and Genetic Alliance

## Preferences between the techniques

A number of responses to this question either support maternal spindle transfer only (20), or express a preference for maternal spindle transfer over pronuclear transfer (72). The majority of these respondents discuss the fact that the MST technique involves the use of unfertilised gametes, in comparison to the use of embryos in PNT, therefore preferring MST for a range of reasons. Respondents give a range of views on this issue, with some focusing on their own personal beliefs, and others talking more about social perceptions. Some respondents express their belief that life starts at conception, and feel that PNT is unacceptable as it conflicts with that belief. Others describe feeling more 'comfortable' with MST because it involves unfertilised eggs, with some adding the caveat that if PNT is more effective this should be authorised over MST. A few respondents discuss the views of others - suggesting that because some people may feel that the use of embryos is ethically unacceptable, MST is to be preferred.

A related argument expressed by a few respondents is that both techniques should be made available, to ensure that those who feel that the use of embryos is unacceptable are still able to benefit from the research.

"I believe it is important that this option is available, in order to ensure that as many people as possible can benefit from these techniques without regard to their views on whether life starts at conception."

Individual, Other

Of respondents who do not express a preference for one technique or the other, a few specifically state that they say no real difference between the two, but more common is for respondents to say that they prefer whichever technique is proved safer or more effective.

#### **4.2.2 Arguments against the introduction of the techniques**

31 respondents express their opposition to the introduction of the two techniques without adding any further explanation. Stakeholder organisations who argue against mitochondria replacement techniques include the Church of Scotland, ProLife Alliance, and Human Genetics Alert.

##### **Ethical arguments: use of embryos**

The most commonly cited argument against the introduction of the two proposed techniques is that the creation and destruction of human embryos is unethical (231). A handful of these respondents identify themselves as either personally affected by mitochondrial disease or having a family member or friend affected by mitochondrial disease; 200 of the respondents proposing this argument describe themselves as 'other'. While many respondents note that this argument applies specifically to the case of pronuclear transfer, there are many who do not specify which technique they are referring to and a few who suggest that both involve destruction of embryos. There are also a much smaller number of respondents who express similar concerns about the ethical acceptability of the destruction of eggs, as in maternal spindle transfer.

Respondents give detailed accounts of why they feel the use of embryos in PNT is inappropriate, with a range of views. Some respondents state clearly their belief that life starts at conception, and any process that results in the discarding of an embryo is tantamount to the death of a living human. Some of these respondents use terms such as 'the sanctity of life', with a few citing specific passages from the Bible to elaborate their view. Others focus on the fact that a donor embryo is created alongside the intended parents embryo, with the transfer process resulting in only one viable embryo. They see the act of creating an embryo for this purpose, with no expectation that it will have the opportunity to develop, as an act of instrumentalisation - treating human life as a means to an end, rather than an end in itself. Some argue against this on more direct ethical grounds - believing the techniques to be fundamentally immoral, while others express concern about how the parent or child would be affected by knowledge of the 'sacrifice' of one embryo to create another.

"This ethical dilemma would not only have to be tackled by parents but may also have to be tackled by the resulting child who may feel troubled that their life came at the cost of another's."

Individual, Other

##### **Ethical arguments: playing God and/or interfering with nature**

Another key argument made by those opposing the introduction of the techniques is that they represent an 'over-stepping' of an ethical boundary by altering a predetermined outcome (70). Some respondents describe this boundary in religious terms, referring to 'playing God', or suggest that for science to take responsibility for the creation of human life undermines their belief that creation is a process outside of the human domain.

“...there are many in this country who believe our creator God himself has spoken to us about how we should live to please him. It is clear throughout the bible that fiddling with his created order in this way would not only be wrong and yet another expression of our rebellion against him, but would have negative consequences for us as a human race, as he is our good creator and his design MUST be for our good.”

Individual, Other

While many of these responses argue that the techniques are unacceptable on principle, some also discuss potential negative consequences, suggesting that as procreation is a divine act it could not be recreated by science without causing harm.

Other respondents make similar arguments about overstepping boundaries, but refer to nature or evolution, arguing that using these techniques would subvert the process of natural selection which governs all biological life. Some of these respondents are concerned about unforeseen consequences of manipulating the genome, citing our incomplete knowledge. Others suggest that the expression of genetic disorders and associated failure to reproduce acts as a limiting factor on the spread of genetic mutations which would be harmful at a species level. They suggest that by overcoming this ‘natural’ process the techniques proposed will ultimately have detrimental consequences.

“It is not imperative that people have their own biological children, in fact such conditions are nature's way of preventing weaknesses being passed from generation to generation.”

Individual, Other

Both strands of this argument are sometimes couched in terms of the greater good, with respondents anxious to note their compassion for individual sufferers of mitochondrial disorders, while maintaining that ultimately no positive benefit would be served by the introduction of the techniques.

### **Ethical arguments: the slippery slope**

Opposition to the techniques proposed is often accompanied with concern that if they were to be introduced, this would leave the door open for other, less acceptable measures to be taken. Some 70 respondents, including LIFE Charity, refer to ‘designer babies’ as shorthand to describe the use of assisted reproductive techniques to select characteristics of a child before birth. Some respondents talk about the outcome: expressing feelings of moral outrage towards this type of selection, or arguing that it devalues the child to the status of a commodity - a similar line of argument to concerns about the use of embryos as a means to a medical ends.

“I worry that each new step, even if taken for noble concerns such as preventing disease, will only stir up a chorus of voices demanding more and more frivolous treatments be available, such as sex selection. Children are a gift, and not something that should be available to custom-order.”

Individual, Other

While a relatively large number of respondents who oppose the techniques express concerns about the potential for reproductive cloning to become possible as a result of the ‘slippery slope’ little detail is given about this particular possibility. Other respondents raise the concept of eugenics, arguing that the techniques effectively ‘prevent’ the birth of individuals with particular genetic characteristics, in this case mitochondrial defects.

Aside from the potential outcomes, some respondents talk about the process by which these types of techniques might become acceptable, mentioning ‘desensitisation’ to genetic manipulation, or



the setting of a legal precedent which would allow further amendments to the law with less scrutiny. One respondent gives the example of the Abortion Act of 1967 which they believe demonstrate this principle, another discusses the increasing range of conditions for which pre-natal genetic diagnosis (PGD) is now available.

### **Altering the germline: safety and risk**

A total of 160 respondents who disagree with the introduction of the techniques in question 1 express concerns about whether they can be applied safely. Comment on Reproductive Ethics (CoRE) and the Church of Scotland are two of them. Some respondents make general statements about the impossibility of being certain about the consequences, while others specify that they are concerned about the perpetuation of (unknown) side-effects as a result of the germline modification. Views on risk differ between those participants who see the techniques as being likely to result in negative consequences, and those who feel that regardless of the likelihood of the consequences, the severity of side-effects introduced via the germline is so great that any risk is not acceptable. A few respondents give examples of techniques they believe are similar to those proposed and have resulted in negative consequences or side-effects when introduced in human or animal models, for example IVF and cloning.

Alongside the risk of side-effects being passed on, some respondents identify other potential consequences of altering the germline. Some cite the use of mitochondrial DNA to trace matrilineal relationships at the population level, either as a specific feature which would be lost, or as an indicator of the importance of the role mitochondrial DNA plays in maternal relationships.

“Mitochondrial DNA is identification for the human race. It was how the human race was traced back to Africa. Changing such a vital building block of human development in such a complex being may mean in the future, there may be some unforeseen complications or other disease prevailing as a result.”

Individual, Other

### **Social arguments: three genetic contributions**

While the social arguments raised in support of the introduction of the techniques focus on providing opportunities for parents to have healthy children, opponents are primarily concerned with the impact on the child of being conceived in this way. Many respondents who oppose the techniques, including the Anscombe Bioethics Centre, raise the involvement of DNA from a third party as a concern. Some respondents argue that involving the DNA of three people is fundamentally unethical - often citing their belief that Christianity specifies that all children should have one mother and one father. Other respondents believe there is potential for children conceived via these techniques to suffer psychological harm as a result of confusion about their identity. Some cite examples of adopted or donor-gamete born children seeking to contact their biological parents, others feel that the introduction of a third genetic contributor will leave children unable to resolve questions of their own identity. Arguments around whether there are implications for children's identity are covered in more detail in chapter 6.

#### **4.2.3 Other considerations**

While the majority of those responding to question 1 expressed their support for, or opposition to the techniques, many issues are raised which are not clearly for or against.

### **Safety, science, regulation and criteria for application**

The most common considerations cited in relation to the techniques overall are specific criteria which respondents think should be applied to decisions about either which technique/s to take forward and/or which to choose in specific cases, should they become available for clinical use, as

mentioned in section 4.2.1 above. Success rate, efficacy or efficiency of the technique is top of the list of criteria mentioned, closely followed by safety. Other criteria include patient choice or appropriateness, medical evidence and advice, cost or value, as well as others such as opening up the techniques to use for anyone or basing decisions around the use of either technique on scientific input or evidence.

A number of respondents stress that regulation would be needed, should the techniques come to fruition. More specifically, there are comments that regulation could or would help prevent the slippery slope, or that the regulator would have an important role in limiting the use of these techniques. Comments about the role of the regulator are analysed in more detail in Chapter 8, which deals specifically with regulation.

In relation to safety more specifically, some respondents are concerned that there is insufficient evidence to prove the safety of the two mitochondria replacement techniques, whilst others talk about the need to compare risks against benefits. Some express a view one way or the other that either the risks outweigh the benefits or vice versa. In addition, a few respondents point out that risks are always present with medical procedures. Many respondents talk about the need for further research, trials or evidence if or when the techniques are taken forward, including a few comments about the need for follow up studies with patients.

“If shown to be achievable, safe and effective, both techniques have potential to militate against mitochondrial disease. In principle, this is to be welcomed, but some caveats exist.

Current scientific consensus is that mitochondrial DNA (mtDNA) is unlikely to play a role in determining hereditary characteristics; however, understanding of the nature of the interaction between nuclear DNA (nDNA) and mtDNA is far from comprehensive. It has been suggested, for example, that a link exists between mtDNA and cognitive capabilities; caution is, therefore, appropriate.

Some nDNA has effects identical to mtDNA and, if defective, can cause similar illnesses. Mitochondrial replacement therapy will not address this problem. If techniques were developed to counteract these debilitating effects of mutant nDNA it might be assumed that the use of altered nDNA is acceptable, especially if such has already been the case with mtDNA. A separate and full debate on the use of altered nDNA is essential since we know that much nDNA directly affects hereditary characteristics. If mitochondrial replacement is permitted no inference ought to be drawn between it and nDNA manipulation.”

Organisation, Church of England: Mission and Public Affairs Council

“The monitoring of those involved in the first Clinical Trial must be exceptionally careful and long-term - and honest!”

Individual, Other

A number of respondents talk specifically about the function of mitochondria or other scientific aspects of the two techniques.

“... the mitochondria are the power plants of the cell. This is akin to changing a battery in a laptop for instance, the data does not change [sic], the layout does not change, the essence of the human is not altered, merely its power source.”

Individual, Family member/friend of someone affected by mitochondrial disease

"I would liken this to replacing faulty spark plugs in a car, it will look and perform the same but the engine will now run smoothly!"

Individual, Other

Others outline their understanding of the science or suggest an alternative approach. There are also a few comments from respondents who are concerned that science should remain at the heart of the decision making on this topic. Scientific considerations are discussed in more detail in the analysis of question 2 (chapter 5).

### **Ethical considerations**

Ethical considerations are covered in more detail in chapters 5 and 6, with the key points mentioned in response to question 1 outlined here.

Concerns over the use of embryos or eggs, and the difference in embryo usage between the two techniques or how others might feel about this, are mentioned by a number of respondents, with some expressing clear concern about the use of embryos or eggs without necessarily explicitly being opposed to techniques, and others saying they are not concerned about this issue. There are also several comments about ethics more generally, and a few on more specific issues such as the lack of consent or choice from the child's perspective.

Some respondents mull over the issue of where the line should or could be drawn with respect to this kind of technique, either around screening or genetic modification itself. Others mention more explicitly the need to consider the risk of a slippery slope occurring, either generally or more specifically with designer babies or commodification, or eugenics. There are also some respondents who point out that these techniques are different to those which would be involved in cloning or creating designer embryos.

### **Social considerations**

Social considerations are also covered in more detail in chapters 5 and 6, with the key points mentioned in response to question 1 outlined here.

In terms of social considerations, various potential legal or insurance issues are mentioned, along with the related issue of a third person's involvement in a child's conception. A number of respondents suggest considerations around the various actors in a potential mitochondria replacement procedure.

With regard to parents, considerations include primarily the need for information provision and close involvement, but also a desire that, should these techniques come to fruition, pressure is not placed on parents to use them. A small number of respondents discuss related issues around the worth society places on mitochondrial disease sufferers or disabled people. Some feel there is a risk that using these techniques would entail losing valuable individuals, respondents interpret the techniques as replacing an individual with mitochondrial disease with another, different individual..

With regard to donors, considerations include comments about the rights and responsibilities of donors, whether their identity should be known or not, and comparisons to gamete or organ donation, as well as a couple of comments about donor availability. These issues are covered in further detail in chapter 7. Considerations around the child include comments about the potential emotional or psychological impacts on a child resulting from these techniques, as well as a number of comments about implications for the child's identity. These issues are covered in more detail in chapter 6.

Other social considerations raised by respondents include considerations of the number of people mitochondria replacement would be applicable to, potential impacts on future generations (including the potential for resulting population increase) and a number of comments about costs

or funding; aside from general comments about who should pay, some people specifically say the NHS should not cover the cost of treatment and others that it should. A few respondents comment on the potential business interest or involvement in offering mitochondria replacement treatments. Others mention alternative treatments, including the suggestion that adoption could be made easier.

### Considerations for specific techniques

A number of respondents talk specifically about MST or PNT, or compare the two techniques, with some saying they see little or no difference between the two techniques, for example in terms of ethics. Several respondents say that they think MST could be more publicly or ethically acceptable than PNT, or that PNT is potentially the more controversial of the two because of the use of embryos. Other respondents talk about specific considerations for each of the two techniques, for example whether the use of spare embryos from PNT had been thought about. A few respondents believe that the way the techniques are described is misleading for various reasons.

“There has been a degree of misunderstanding among the public - these interventions are not a “genetic modification”. A genetic modification is when nuclear or mitochondrial DNA sequence is altered - mutated, deleted or inserted. Instead the use of wildtype DNA from a third party is in effect a donation and not a genetic modification.

In other words the human genome is not being modified.”

Individual, Researcher

“I think that it is deceptive to describe this technique as a therapy being offered to prospective parents. The therapy being offered is merely psychological: reassurance that they will not have a defective child. The person affected is the child him or herself.”

Individual, Other

“The term ‘mitochondria replacement’ is misleading as it is the pro-nuclei or spindles that are being replaced in the host cell rather than the mitochondria being replaced.”

Individual, Other

### Other references

Many respondents to question 1 make reference to specific supporting information. A large number of these references are personal to the participant, for example information about their knowledge or expertise, where they have a friend, relative or child with mitochondrial disease or similar, or where they themselves are a sufferer of mitochondrial disease. Several respondents make reference to religion or the Bible as part of their response, while others mention politics or the Government (for example the role – or not – of politics in these kinds of decisions), the HFEA, the views of other people generally, or of a specific group or individual. Current legislation on this topic, either in the UK or abroad, is mentioned by a number of respondents, as well as some references to learning from historical experience (for example the progression of scientific knowledge, Thalidomide, eugenics, and the development of IVF). Other specific supporting evidence is referred to by some respondents in the form of relevant research, documents, literature or discussions.

## Chapter 5      Question 2: changing the germ line

---

### 5.1      **Headline findings**

1,115 respondents answered question 2, which asked respondents:

**Q2: Do you think there are social and ethical implications to changing the germ line in the way the techniques do? If so, what are they?**

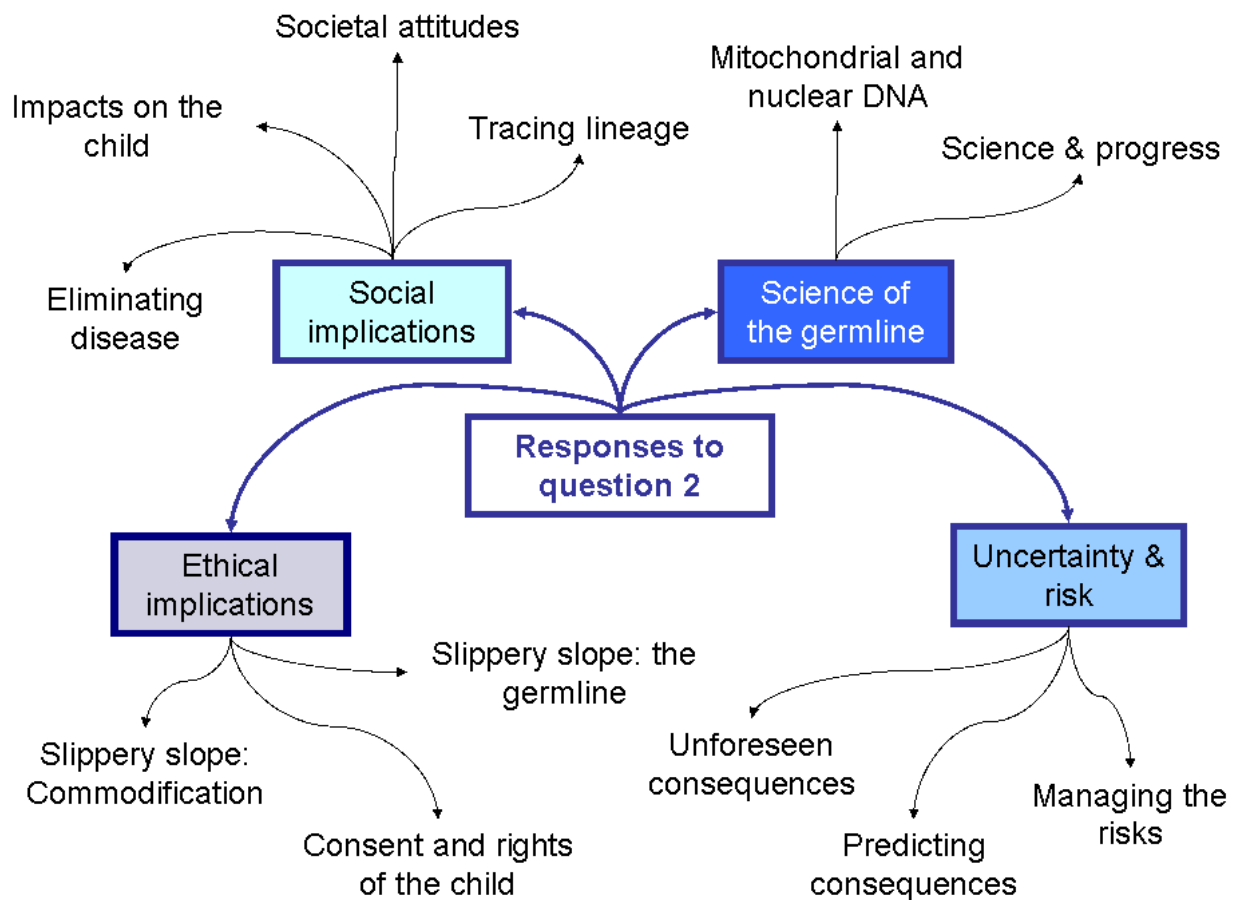
Most responses to this question outline potential implications of changes to the germ line including both negative and positive implications. Some respondents feel the severity of the impacts would outweigh the benefits they believe the techniques will bring; these respondents often cite similar ethical concerns to question 1, or social concerns about the introduction of a third genetic contributor. Others feel that the impacts could be adequately mitigated or are not serious enough to outweigh the benefits - these respondents tend to focus on the social impacts of reducing mitochondrial disease. The implication of changing the germ line is explored by many respondents in question 2, with concerns about the risks of a new scientific procedure, about genetic engineering more generally, and discussion of the role of mitochondrial DNA in the germ line. A number of respondents, including several who identify themselves as mitochondrial disease patients or friends/relatives of patients, state their belief that there are no social or ethical implications of the introduction of the two techniques into clinical practice, or that the only implication is the reduction of instances of mitochondrial disease.

#### **Non-questionnaire responses**

In some of the 503 non-questionnaire responses there is mention of changing the germ line. Overwhelmingly these comments are part of a range of similarly worded points which can be found in around 300 emails and letters. The point included about changing the germ line concentrates on uncertainty about the effects on future generations, which respondents consider a concern.

These arguments and others raised by respondents to question 2 are explored in more detail below under the following sub-headings:

**Figure 4 Responses to question 2**



## 5.2 Summary of comments

### 5.2.1 Uncertainty and risk

The paragraphs below describe the concerns of respondents who believe there are negative consequences of the techniques; in many cases respondents describe the scale and likelihood of the perceived consequences, while a few respondents argue on principle that any risk to future generations is unethical. They feel that the act of taking a decision which imposes these risks is unethical, as the choice is removed from the future individuals - this argument links closely to questions of consent explored under Ethical implications below (section 5.2.1).

#### Unforeseen consequences

The most common issue raised by respondents in relation to the germline is a concern that there may be unforeseen consequences of the proposed techniques, which would then be perpetuated in future generations. Often respondents are concerned with the scale of consequences - they see the potential consequences as too large or dangerous to be acceptable, even if they are very unlikely. Many refer to the idea that many generations would be affected, seeing this as frightening or inappropriate; others describe the potential germline change as being 'uncontrollable' suggesting that:

“... we simply do not know what harm we may be doing, and such harm may extend indefinitely to many generations.”

Organisation, Anscombe Bioethics Centre

Another variation on this theme is the idea that consequences may not be discovered until several generations have passed, by which time it may not be possible to contain the germline change, or even to identify all carriers.

While most respondents who comment on unforeseen consequences cite this as a general principle, a few respondents give examples of particular implications they see arising from use of these techniques, often describing these as unintended consequences. Some of these respondents believe there may be negative health impacts of the techniques, discussing issues such as the combination of mitochondrial and nuclear DNA when the two are inherited from different parents. Others talk in general terms about unpredictable psychological impacts on children born via the techniques and their families (discussed in more detail below).

### **Predicting consequences**

Other respondents discuss the level of risk - they are concerned that we are not able to adequately assess the potential consequences of using these techniques in clinical practice. For some of these respondents our inability to determine the consequences is seen as inherent, and they describe their feeling that the consequences of genetic modification are ‘unknowable’. Others argue that the consequences cannot be known until the techniques are implemented in humans, and even then not necessarily in the first generation, for example:

“The Council noted a number of ethical and social implications, including that using these techniques might create health risks to the resulting child and his or her descendants, particularly as it will not be possible to exhaustively assess the safety of the procedures until several generations have been born using them (paragraph 4.37).”

Organisation, Nuffield Council on Bioethics

A few respondents who believe that negative consequences may emerge in subsequent generations suggest that this would mean monitoring of both children born via the techniques, and their subsequent offspring for several generations.

### **Managing the risks**

Although most respondents who posit unforeseen consequences of the two techniques believe this should prevent them being authorised, some cite potential impacts and then suggest ways in which they can be mitigated. This includes procedural suggestions, such as ensuring that the mitochondrial donor has similar genetic heritage to the intended mother (i.e. has similar mitochondrial genes). Others give suggestions for managing the social consequences for the child, most often recommending that the child should be made aware of the circumstances of their birth, with information given in a considered and sensitive way.

One suggestion made by some respondents is that ongoing monitoring should include subsequent generations, however there are a number of respondents who express concern about the consequences of such monitoring. As described below, some feel it will lead to stigmatisation of the individuals concerned, or that they will feel ‘different’ because of the requirements of monitoring.

There are also a few respondents who discuss the concept of uncertainty and risk, suggesting that fears of the uncertain and unknown are common when novel technologies are posed, and should

not necessarily prohibit their progress. This debate is picked up again in the Science section 5.2.4 below.

### 5.2.2 Social implications

#### Eliminating disease

There are 68 respondents who specify that they believe the benefits of the techniques outweigh any social or ethical implications. The majority of these respondents, including a number of respondents who identify themselves as having personal experience of mitochondrial disease (patient or friend/relative), suggest that the elimination or reduction of instances of mitochondrial disease is a social benefit, offering benefits to children and families, or more generally as an improvement to health at a population level. As in several of the questions, a few respondents emphasise the severity of mitochondrial diseases, and the psychological impact of hereditary disease when weighing up potential benefits and disadvantages of introducing the techniques.

“If I can prevent the inheritance of mitochondrial disease by altering the gene line then this is far preferable than for the risk and fear of disease staying in my family forever.”

Individual, Family member/friend of someone affected by mitochondrial disease

A number of respondents to question 2 discuss benefits they perceive for future generations because of the modification of the germline. They argue that because the mitochondrial defect which causes disease is removed from the germline subsequent generations are also freed from the potential to inherit the disorder, and that this makes the techniques an ideal response to the problem of heritable disease.

#### Societal attitudes

A common issue mentioned in response to question 2 is how the introduction of the techniques to clinical practice might affect attitudes towards different groups, particularly those born as a result of the technique and sufferers of mitochondrial and other disorders. There are 56 comments on social attitudes towards those conceived via the techniques, with a range of views expressed. Some respondents, including the ProLife Alliance, suggest that those ‘treated’ could be ostracised or discriminated against for being ‘created in a lab’, or because of the third genetic contributor. Many of these respondents suggest that the requirements for those born via the techniques to take part in medical monitoring will contribute to them being treated as ‘guinea pigs’. This argument is often associated with ethical concerns about the motivations of parents, clinicians and scientists in implementing the techniques. In contrast, others note that such prejudices do not seem to have arisen in relation to artificial reproductive techniques such as IVF, and feel that it is not a major concern. A third point of view comes from those who feel that discrimination may be an issue in the short term, but will ultimately be overcome:

“Socially, there may be short-term issues with the interaction of treated with non-treated, and with those who opposed use of the techniques. However, that should not prevent us from moving forward with them. ‘Test tube babies’ do not appear to have met with any significant stigma over the long term, and I don't see why these babies would either.”

Individual, Other

A related issue raised by a similar number of respondents is whether making these techniques available will have an impact on attitudes towards those with disabilities (including mitochondrial disease). Some respondents argue that the techniques amount to preventing the births of people with mitochondrial disorders, effectively discriminating against them. A number of these respondents note a link to wider debate about perceptions of disability in society, and of disabled people themselves:



“My only concern about alterations in the germline is that it reifies genetic 'normality', and creates an anti-disability narrative that will encourage people to view themselves or others as 'abnormal'.”

Individual, Researcher

Respondents are concerned that there will be increased levels of intolerance for those with disabilities, especially mitochondrial disorders, with disabled people questioning why the proposed techniques were not used to prevent their disability, and by inference, their birth as disabled individuals. Others see a potential connection between the proposed techniques, decreased tolerance of genetic defects and increased acceptability of other genetic modification techniques and the ‘designer baby’ concept discussed in question 1.

A smaller number of respondents argue that rather than encouraging discrimination against those who are treated, introduction of the techniques will lead to negative attitudes towards those not treated. They argue that once the techniques are available:

“Parents who do not comply with such techniques will indubitably be made to feel irresponsible by scientists, medical personnel, society at large...”

Individual, Other

One or two specifically mention potential problems they see arising within families where some children have been conceived by the techniques, while others have not. Some respondents expand on this theme, suggesting that parents may be pressured into using the techniques either unnecessarily, or against their will, because of a perception that it would be irresponsible not to.

### Impacts on the child

As in most questions throughout the consultation, many respondents comment on the introduction of a third genetic contributor, expressing concern about the psychological impact of a third ‘parent’ to a child conceived via the techniques - these issues of identity are covered in detail under question 3 (Chapter 6). A number of respondents take the opportunity to express their concerns about the psychological or emotional impact on children conceived via these techniques, while a similar number express their belief that the wellbeing of any child would be improved.

A few respondents raise specific concerns about identity issues relating to the germline. In particular there are concerns that kinship and family may continue to be disrupted in subsequent generations.

“Families may not accept future generations as truly related if the germ line is changed, I would certainly be unsure if a child was truly my child if they had donor mitochondria.”

Individual, Other

### Tracing lineage

Mitochondrial DNA can be used to trace the genetic heritage of individuals, and of populations on an historical timescale - some respondents, including the National Gamete Donation Trust, make reference to this in question 2, noting that mitochondria replacement would confuse this genetic ‘family tree’. Most respondents who mention this issue describe it as a minor issue which should not prevent the techniques being used, and a few suggest that steps could be taken to record the identity of the mitochondrial donor in some way to mitigate the impact. One or two respondents raise the issue of criminal investigations using DNA evidence, and question whether mitochondria replacement could affect this.

### 5.2.3 Ethical implications

As in question 1 a number of respondents (158) express concerns about the use of embryos, particularly in the case of pro-nuclear transfer. These arguments are described above in section 4.2.1. Other arguments common to question 1 and explored in more detail there are those relating to 'playing God' and the ethical imperative to intervene.

#### Consent and the rights of the child

A number of respondents in question 2 discuss the concept of whether the modification of an embryo or egg (no distinction is made in this context between the two techniques) could be allowed to take place without the consent of the ensuing individual. There are two strands to this argument, firstly that in the case of the parents who use the technique to conceive, they have made that choice on behalf of the child. As one respondent puts it:

"I feel very uncomfortable with the prospect of making such decisions without the consent of the individual concerned. There's no 'going back' if someone finds the background to their conception difficult."

Individual, Other

Others refer to the importance of informed consent in scientific experimentation, and in medicine more generally - they argue that as it is impossible to gain the informed consent of the 'child' before the procedure is carried out, it is unethical. In contrast, a few respondents note that parents make decisions on behalf of their children as a matter of course, for example the Nuffield Council on Bioethics note that:

"The issue of consent has been raised in the context of germline therapies, given that no child born from such procedures can have consented to them. However, **this issue is common to all reproductive technologies, as well as other prenatal and childhood medical intervention** (paragraph 4.38)."

Organisation, Nuffield Council on Bioethics

The second strand of this argument is that once the change has been made to the germ line, it will be passed on - in effect the children conceived by the technique are not able to choose whether or not they pass on the technique to their children. Again, an opposing view is argued by a small number of participants who question whether this consent is relevant, given the impossibility of ever acquiring consent from future generations about any decisions taken on their behalf.

The argument as stated here focuses on the principle of consent of the individual to the changes; an alternative formulation focusing on the practicalities of making decisions for future generations is described above under uncertainty and risk, (section 5.2.1) where some respondents questioned whether individuals have the right to expose future individuals to particular risks.

#### Slippery slope: commodification

The 'slippery slope' by which the introduction of these techniques could lead to others is a common theme throughout the consultation, with respondents expressing a range of concerns about potential outcomes. There are 150 respondents to question 2 who raise concerns about the introduction of techniques which modify the germline opening the door to parents able to select for characteristics rather than medical need. While some respondents argue by comparison between 'selection' for medical purposes and selection for 'trivial' characteristics, others argue from the principle that any selection on the part of the parents crosses a line.

Once more the new techniques ignore the basic principle of what is meant by uniqueness in the individual. It opens the way to the normalisation of genetic modifications. In time it is inevitable that government will begin to interfere in the decision making process about what forms of offspring will / will not be acceptable. A dangerous threshold will have been crossed and the long term outlook is unknowable.

Organisation, Scottish Council on Human Bioethics

In contrast there are some respondents, including the Muscular Dystrophy Campaign, who state their disagreement with this argument, typically because they feel that sufficient steps will be put in place to prevent such a shift from one purpose to another. One or two suggest that because the proposed modification to the germline is limited to mitochondrial DNA, this argument is less applicable:

“Firstly, these techniques limit germline manipulation to genes of the mitochondria, which are involved solely in programming the functions of these organelles.”

Organisation: The Wellcome Trust

### **Slippery slope: the germline**

Another variation on the slippery slope argument common in question 2 focuses on a perceived relationship between germline modification and eugenics, suggested by 70 respondents. Many respondents who mention eugenics do so without giving detailed arguments, and may be using the term simply to denote all genetic modification or engineering. However others argue specifically that the process of ‘selecting’ against a particular genetic trait is the basis for their concern:

“We are also concerned that changing the germ line will result in the normalisation of genetic modification in humans. While it is admirable to seek to cure disease, we are concerned by the eugenic undertones of any technology that allows doctors and parents to ‘rank’ one embryo above another.”

Organisation, Christian Concern

Another discussion specific to question 2 is whether once germ line changes are introduced for mitochondrial DNA, it will gradually become possible for nuclear DNA changes to be introduced. This debate is brought forward by a small number of respondents, with a few arguing that the difference between the two types of DNA is clear, and one will not lead to the other, while a similar number argue that the difference will not prevent a move towards more techniques being available.

#### **5.2.4 The science of the germline**

There are a number of respondents who take the opportunity in question 2 to discuss aspects of the science around germ line modification which they feel are pertinent to the social and ethical implications of the techniques. Typically these points are made by smaller numbers of participants than the main ethical and social arguments described above, and are less commonly associated with an expressed preference for or against the introduction of the techniques into clinical practice.

### **Mitochondrial and nuclear DNA**

Several respondents talk about the role of mitochondrial and/or nuclear DNA, particularly in relation to the question of identity. The relationship between mitochondrial DNA and identity is covered in detail in chapter 6, dealing with question 3. The most common of these comments, made by the Academy of Medical Sciences and the British Fertility Society among other organisations and individuals, is that the nuclear DNA (and some respondents say the genome) is not affected by the two mitochondria replacement techniques, with some linking this to other comments such as the fact that they therefore have no ethical or social concerns. Other

respondents give conflicting views about mitochondrial DNA, with a number of respondents stating that it does not determine identity or traits and somewhat fewer stating that they think it does or might. The function of mitochondria is the subject of some responses, in particular from respondents who say that the mitochondria are just for energy production and that replacing them would be like changing batteries, although others believe they play a more important role or that we do not fully understand their role.

“I see this essentially as changing the batteries that power the fertilised egg, embryo and ultimately, person but without having the ethical impact of alteration of the expressed DNA.”

Individual, Other

“If mitochondria are so trivially put as powerhouses of the cell why are the consequences so dire when they do not work?”

Individual, Researcher

A number of respondents, including the Wellcome Trust, talk about the small amount of DNA involved in mitochondria replacement, whilst there are a couple of concerns that even this would be too much or have too much impact. There are also a small number of comments about the origin of mitochondrial DNA, specifically that they were originally symbiotic bacteria living in host cells.

“Mitochondria are best viewed as separate organisms living in cooperation with host cells. They are much like the gut bacteria without which we couldn't live a healthy life, there are increasingly numerous examples of organisms that cannot live without one another - plant roots and soil fungi for example.”

Individual, Other

Other comments about mitochondrial DNA are varied and include observations about the importance of mitochondrial DNA for sustaining life, the number of different lines of mitochondrial DNA and a range of other observations about the science surrounding mitochondrial DNA and the implications of mutations or replacement. In addition, there is a focus on the female or maternal line, with respondents saying either that the proposed techniques would only impact the female germ line, or that they would make tracing lineage through the female line more complicated. A few respondents talk about more technical aspects of mitochondria replacement; there are some suggestions about specific sources for the donation such as using the father's mitochondria, those of a close friend or relative, or mitochondria from the same haplogroup as the mother. There are also a small number of comments suggesting that the faulty mitochondrial DNA should be kept for posterity.

Respondents make a range of other comments about nuclear DNA. A few respondents say that DNA mutates naturally anyway over time, a process they see as analogous to the deliberate change introduced by mitochondrial transfer; in the main these comments focus on the argument that these techniques would be speeding up that natural process, although one respondent is concerned that evolution is based on abnormalities and that we should not “deny ourselves the chance to grow and show the best of ourselves”. Others discuss the natural mixing of DNA that occurs through reproduction, often accompanied by the view that this makes the process of mitochondria replacement less significant because it is seen as replicating a natural process.

“Changing the germ line is the very essence of sexual reproduction - the fact that mixing genes can result in a wider variety of characteristics is advantageous to a species. Essentially, it's a very natural thing.”

Individual, Student

There are also a small number of other comments about nuclear DNA, for example around its function, our current knowledge, and the influence of environmental factors on gene expression.

Many respondents talk about the germ line more generally, including the idea of altering it. There are equal numbers of respondents who say it is ok to alter the germ line (for example because this is a positive or purely functional alteration) and that it should not be altered (for example because of unknown consequences or the crossing of an ethical boundary). A few respondents comment that the germ line would not be significantly changed by these techniques. Others discuss specific outcomes they speculate could occur as a result of MST or PNT, for example that the germ line could reduce in diversity, or that the mixing of mitochondrial DNA could cause a genetic advantage or be beneficial, although others say that they think the germ line would simply be repaired rather than enhanced.

Other comments about the germ line include a variety of positive and negative comments about changing the germ line, the statement that we are all related if you go far enough back, that this would be a new step for science because it involves altering the germ line, and comments about the long-term (i.e. multi-generational) changes brought about by alterations to individuals through these techniques.

### **Science and progress**

The nature of science and scientific progress is commonly cited in response to question 2, either specifically in relation to mitochondria replacement techniques or more generally. By far the most popular comment in this respect is that reducing mitochondrial disease is a positive thing, with many of these respondents referencing some of the social benefits already cited in response to question 1. Other comments about scientific progress in relation to mitochondria replacement include: this is natural progress or that scientific progress overall is a function of being human; the possibility of doing something does not mean it should automatically happen or further progression of these techniques requires caution; and progress has gone too far to stop now. There are a few other observations on where these treatments sit in relation to overall scientific progress in this field.

“With the introduction of the treatment there may be a rise in research interests in this area, leading to safer, cheaper treatments, many targeting conditions which have not yet been treated. The treatment may even allow us to clear up any ethical/social concerns regarding germ line engineering of human nuclear DNA in germ line cells.”

Individual, Student

“Changing the germ line is a step change beyond other techniques currently used for infertility treatments.”

Individual, Non-questionnaire response

“This sort of gentic [sic] modification is merely an extension of medicine beyond most people's intuitive comfort zones when it comes to trusting and understanding science.”

Individual, Student

Some respondents comment specifically on the nature of these two techniques, including comments that this could or would be a one-off or single generation treatment, or that it could be restricted to male births. Other respondents express overall objections to fertility treatment, or in several cases talk about preferable priorities for investment such as other treatments or cures for mitochondrial disease.

Concerns that current scientific understanding is limited, for example about the function of mitochondrial DNA, are raised by some respondents, including Comment on Reproductive Ethics (CoRE), alongside other comments on the need for further evidence or research, for example specific suggestions for trials or follow-up studies.

“Should mitochondrial material, and the use of a donor cell wall, have greater purpose than is currently known, we are in danger of harming future generations unless there is a long and rigorous process of testing implemented.”

Individual, Student

There are some comments about the trust or lack of trust in scientists and scientists' motivations, for example concerns that scientists may not always undertake research for the right reasons or more overt expressions of mistrust (some respondents suggest scientists are 'arrogant'), as well as one respondent who says that they do trust scientists. Other respondents discuss the nature of medicine or science, for example stating that its purpose is to treat illness or to benefit humankind, although these statements are used in different ways to either support or oppose the two techniques, for example a number of respondents say that the use of embryos goes against the idea of benefitting humankind. A small number of suggestions for how science should balance with ethical, religious and scientific considerations are also made; some respondents would like to ensure that ethical considerations based on religious views have an important place in the debate, whilst others would like the debate to focus on science and ethics in purely secular terms.

Finally, there is a range of other comments about either the science of these techniques or overall science more generally. For example, some respondents question how effective these techniques would be and others talk about the need to weigh up all considerations for any new technique on a case-by-case basis.

## Chapter 6      Question 3: implications for identity

---

### 6.1      **Headline findings**

1,084 people responded to question 3 of the consultation which asked:

**Q3: Considering the possible impact of mitochondria replacement on a person's sense of identity, do you think there are social and ethical implications? If so, what are they?**

Most respondents make specific comments about how they think mitochondria replacement may have an impact on a person's sense of identity, or why they believe this impact will be limited.

Where respondents state that they believe there will be implications, most describe these. Their comments cover the genetic make-up of children born as a result of mitochondria replacement, the potential issues around children's relationship to their mitochondria donor, and the potential impact on these children's emotional or psychological well-being. A handful of respondents say they believe there will be implications but make no further comment.

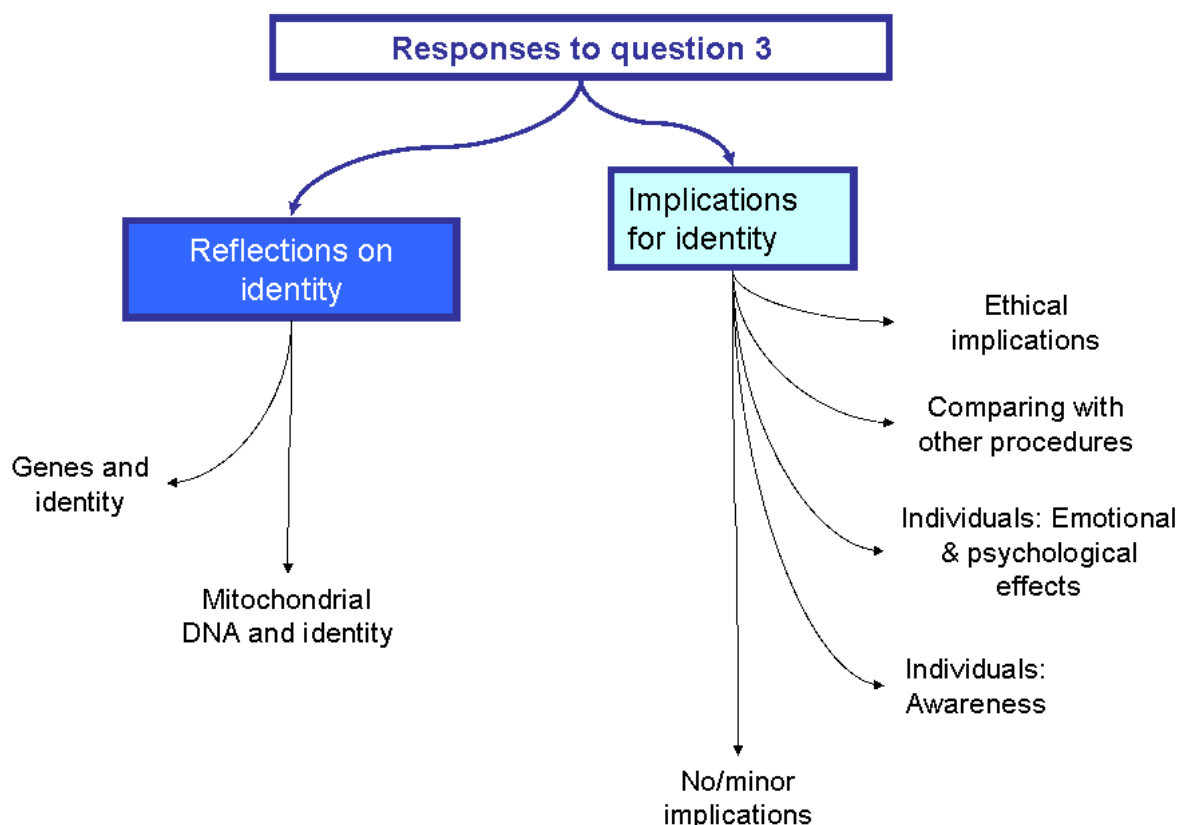
Where respondents indicate that they believe there will be no implications, they tend to argue that mitochondrial DNA does not determine a person's identity. Many suggest too that mitochondria replacement is unlikely to have greater implications than currently used procedures including egg and sperm donation. A total of 38 respondents merely state that they do not think there will be implications.

#### **Non-questionnaire responses**

Comments about possible implications on identity are also made in some of the 503 non-questionnaire responses. Most of these comments are made in letters and emails that follow a similar structure and make a series of similarly worded points. One of these points is a concern about the impact of mitochondria replacement on the well-being of children conceived in that way, who respondents believe may suffer psychological damage as a result of it. Also, the idea that three (or four) people would be involved in the conception process is often cited as a concern, although not always in relation to identity.

These arguments and others raised by respondents to question 3 are explored in more detail below under the following sub-headings:

**Figure 5 Responses to question 3**



## 6.2 Overview of comments

### 6.2.1 Reflections on identity

Question 3 inspires some respondents to reflect on the concept of identity and how personal identity relates to individual genetic make-up. Two broad themes characterise this discussion: whether or not mitochondrial DNA is significant to identity and whether or not a person's genes influence or determine identity at all. These two discussions are described in turn below.

#### The relationship between mitochondrial DNA and identity

When respondents comment on the relationship between mitochondrial DNA and identity, they often argue that this relationship is either negligible or absent. Some 100 respondents including several who identify themselves as mitochondrial disease patients, or friends/relatives of patients, say they believe that an individual's personal characteristics are not affected by their mitochondrial DNA, but rather depend on the genetic information in the nuclear DNA. This view is also expressed in responses of various stakeholder organisations including the Association of Clinical Embryologists (ACE) Executive Committee and the British Medical Association.

"Identity, if it rests anywhere in a person as an embryo, rests in the genetic inheritance in the parts of the DNA that affect personality, traits etc, not their mitochondria."

Individual, Family member/friend of someone affected by mitochondrial disease

The quantity of mitochondrial DNA relative to the quantity of nuclear DNA is discussed by 63 respondents. Most of these emphasise that mitochondria contain a very small part – some mention 1% and others cite smaller percentages – of a person's genetic information. Some respondents also reflect on the nature and function of mitochondria and mitochondrial DNA. Most of these say



that mitochondria are there to help cells produce energy, with several respondents likening mitochondria to batteries in cars or other tools. Respondents using these lines of argument generally think that the quantity and/or purpose of mitochondrial DNA suggest that it is unlikely that mitochondrial DNA has implications for identity.

“MtDNA, which is the only type of genetic material altered by these techniques, encodes just 37 of the 22,000 human genes, or less than 0.002 per cent of the total.”

Organisation, Wellcome Trust

A small number of respondents take a different view on the significance of mitochondrial DNA in the constitution of an individual's identity. Their comments emphasise that we do not know sufficient to be certain that mitochondria are relevant to energy generation alone and that the possibility remains that the genetic information in mitochondrial DNA does affect a person's traits.

“In reality our understanding of the amount, influence and purpose of mitochondria is still limited and conclusions such as this need to be treated with caution.”

Organisation, Christian Medical Fellowship

### **The relationship between genes and identity**

For some respondents a more fundamental question about identity needs to be addressed in relation to this discussion: to what extent is an individual's identity influenced or determined by their genes? Some respondents emphasise that identity is a complex concept which may have genetic as well as environmental and circumstantial components.

“Identity is a complex issue, and is based on a myriad of factors, of which a person's biological origin covers only a handful.”

Individual, Other

Several respondents argue that the extent to which individuals' sense of identity is affected by their genetic make-up, or their understanding thereof, is a personal matter and will vary between people. Some reflect on what they see as the struggle that many young people and adults experience trying to make sense of their identity in today's society, regardless of their family situation or genetic heritage.

“All people search to establish their sense of identity. All people struggle with whatever it is that has made them.”

Individual, Other

About 75 respondents discuss specifically whether it is one's genes (nature) or one's upbringing (nurture) that most influences their sense of identity. The majority of these respondents express the view that identity is predominantly formed during life, and many respondents highlight the role of parents in providing the environment in which a child grows up, saying this is a prime factor affecting their sense of identity. Organisations making this argument include the Humanist Society Scotland and PROGAR. A few respondents cite specific examples to underpin their arguments, such as two genetically identical twins growing up to be different individuals with their own distinct identities.

In contrast, a few respondents emphasise the role of genetic information in shaping a person's identity, stating it is this that makes them unique human beings. Others consider that neither genes nor upbringing are dominant by definition and that this uncertainty should be acknowledged.

“However, this brings us back to the long-debated Nature vs. Nurture argument. It is difficult to say how much of a person’s identity is influenced by their genetics, and how much is influenced by their upbringing.”

Individual, Student

### 6.2.2 Ethical implications

In responding to question 3 most respondents concentrate on social rather than ethical implications. Respondents who do comment on ethical implications often reflect on the proposed techniques in a general fashion. For instance, some argue that the techniques are interfering with nature and some suggest that they cross a boundary and set a precedent for other more controversial techniques. These and other discussions about ethical implications of mitochondria replacement in general are discussed in detail in the chapters on questions 1 and 2.

Several respondents raise an ethical implication specific to identity. These respondents emphasise that children born as a result of mitochondria replacement will not have been able to give their consent. This is generally followed by concerns that these children may experience this as a burden during their lives.

“This procedure also poses the ethical issue of changing a person's identity without his or her consent.”

Individual, Other

A different but related point is made in some of the 53 responses that cite the use of embryos in PNT as a particular ethical concern. Several respondents reflect on the impact of this on the resulting individuals' identity or well-being more generally. They are concerned that some people may feel a sense of guilt or unworthiness when they realise that their conception has been aided by a process that involves the creation and destruction of embryos. A few respondents speculate about the individuals that might have been born if the embryos used had been allowed to develop, and sometimes suggest that these could have become 'better' individuals, leaving the child with a greater than usual sense of having to make up for the potential achievements of those not born. They see this as an additional burden on children born as a result of PNT.

“So quite aside from the issue of parenthood, they will also have to battle with the idea that two distinct human lives were destroyed in the creation of their life.”

Individual, Other

A small number of respondents present views specifically on the ethical trade-off between health and identity, discussing whether one of these should prevail. A few argue that a non-compromised sense of identity should be favoured, whereas most of those reflecting on this trade-off prioritise the individual's health.

“I accept that some individuals will have a different view, but cannot see that such concerns would outweigh the benefits of being born healthy!”

Individual, Personal experience of egg, sperm or embryo donation or donor conception

### 6.2.3 Social implications

#### No implications or minor implications on identity

There are some 130 respondents, including the British Fertility Society, who specify their belief that mitochondria replacement will have little or no social or ethical implications for a person's sense of identity. Respondents who identify themselves either as being affected by mitochondrial disease or as being a friend or relative of someone affected by mitochondrial disease often take this view. Roughly half of those who do not foresee any implications explain their view with references to mitochondrial DNA, stating that this is considered to be insignificant compared to nuclear DNA. Some emphasise that the nuclear DNA of individuals conceived with the assistance of mitochondria replacement would be from both their parents, and that this is what will constitute their genetic make-up. Paragraph 6.2.1 above covers respondents' views on the significance of mitochondrial DNA in more detail.

"I think the implications of having mitochondrial DNA from a donor as well as nuclear DNA from two parents are interesting, but certainly not problematic."

Individual, Family member/friend of someone affected by mitochondrial disease

Several respondents explain that they have come to the view that there are no implications on identity by reflection on their own situation or sense of identity. Some comments concentrate on the respondent's genetic relationship with their parents, others attribute great importance to the family environment they grew up in. One comment is from a donor-conceived person, who states that from their personal perspective there are no implications for identity:

"I don't see any implications for identity, and I say this as a donor-conceived (DC) person who believes that genes help to make us who we are."

Individual, Personal experience of egg, sperm or embryo donation or donor conception

"From a personal perspective, I think if I knew I had different mitochondrial DNA I would see it as an additional part of my identity, rather than confusing my identity. I would still see the people who gave me my nucleic DNA as my biological parents, rather than the mitochondrial donor."

Individual, Other

Similarly a few respondents relate their response to question 3 to personal experiences with mitochondrial disease, generally arguing that they do not consider mitochondria replacement to greatly affect an individual's sense of identity. The Muscular Dystrophy Campaign engaged with families affected by a mitochondrial disease and found that they were not concerned that the proposed techniques would have identity implications:

"When families affected by a mitochondrial disease were asked this question none of them had any concerns that mitochondria replacement could have an impact on their future child's sense of identity."

Organisation, Muscular Dystrophy Campaign

Respondents sometimes emphasise that an individual's environment is important in mitigating the potentially negative implications on their sense of identity. One element of this, according to respondents, is the provision of accurate information to individuals conceived with the help of mitochondria replacement techniques. Some respondents specify that children should be told about the impact of mitochondrial disease as well as the process of mitochondria replacement.

This is usually seen as a task for the parents, and several respondents highlight that they believe children should be made aware of this from an early age.

Another element touched upon by multiple respondents is the quality of close family relationships. Respondents believe parents need to be loving, understanding and open, and that this should prevent children born with donor mitochondria from struggling with their sense of identity.

“As long as there is a loving family who are willing to explain and help the child understand [sic] and the child is disease free and can live a healthy life then there should not be an issue with a person sense of identity.”

Individual, Family member/friend of someone affected by mitochondrial disease

Many respondents who think there will be limited or zero social and ethical implications on identity make comparisons with other, existing procedures. Respondents make rather varied suggestions as to which procedures offer the most appropriate comparison, from blood donation to egg donation to adoption, but their overarching argument is often similar: that the identity implications of mitochondria replacement will be no different from those of the other procedure. For many respondents this equals a view that implications will be minimal, although some respondents feel different about this. Paragraph 6.2.4 below covers the detail of the comparisons respondents draw.

“The question of identity is often overinflated. It is the same argument as adoptive children, step-children, mixed-race children, donated sperm or egg children - it is about the individual and how this acceptance or rejection becomes part of who they are.”

Individual, Family member/friend of someone affected by mitochondrial disease

“Once the novelty of the technique itself has subsided, we do not believe properly informed recipients should have significant identity issues.”

Organisation, AMRC and Genetic Alliance UK

### **Implications for the individual: awareness**

A total of 105 respondents reflect on the need for individuals born after mitochondria replacement to be aware of this, and to understand it as fully as possible. There is not much debate about whether individuals should be told about their genetic make-up; virtually all comments are in favour of sharing this information with children. The topic of child awareness is addressed by several respondents who identify themselves as mitochondrial disease patients or friends/relatives of patients, as well as respondents who indicate that they have personal experience of gamete donation. It also features in responses from various stakeholder organisations including the National Gamete Donation Trust and PROGAR.

Many respondents believe that if parents are open with their children about the unusual way they have been conceived, children will not be troubled about their identity, or at least not more than children conceived in more traditional ways. Where respondents specify this, they generally believe that the information should be presented to children from a young age. Others specify that they believe parents should always be sensitive to their child’s ability to understand the information and pitch the message accordingly. A few respondents highlight the other side of the coin and say that children will be more likely to encounter identity issues if they do not receive clear information early in life.

"I can imagine that if it was not explained clearly to either the parents or the children it could produce issues later in life."

Individual, Other

A small number of respondents discuss the benefits of guidance and support available to parents of children conceived with the help of mitochondria replacement. They believe that this will help ensure that parents feel confident and sufficiently informed to talk to their child.

"The debate around these techniques should be informed by professional bodies so that any children born from these techniques understand that they are just as much their parents' child as if they had their mother's mitochondria."

Individual, Other

A few respondents express concern about parents' willingness or ability to inform their child of the process that led to their conception, with one respondent stating that this is a common problem in families with donor-conceived children. Another respondent raises the concern that individuals with mitochondria from a donor might not inform their future partners about this, which might have consequences for offspring further down the line. In the opinion of another respondent such situations are unlikely to arise, as the need for medical supervision will ensure that the individual is aware.

"Experience has shown that few donor conceived people have been told the truth about their conception by their heterosexual parents and doubtless fewer still will be told the exact nature of the preimplantation changes made to their embryo form at the laboratory stage."

Individual, Personal experience of egg, sperm or embryo donation or donor conception

### **Implications for the individual: emotional and psychological**

Many respondents, 228 in total, comment on the emotional and/or psychological implications mitochondria replacement could have on children resulting from the proposed techniques. Almost all of these respondents, including Comment on Reproductive Ethics (CoRE), think that there will be implications, and generally suggest that these would be detrimental to the individual. Most of these respondents, although not all, have stated their opposition to mitochondria replacement in response to question 1.

The most frequently cited reason for children to suffer emotional or psychological damage is confusion over their mitochondria donor, specified by many respondent as their 'third parent' (with numerous responses also citing a potential 'fourth parent' in relation to pro-nuclear transfer). Respondents highlight issues relating to uncertainty about who the mitochondrial donor is, but more often explore how the existence of the donor might complicate a child's relationship with its parents. There are, among others, some 25 responses using similar or identical words to describe how children conceived with the help of mitochondria replacement could be affected emotionally:

"Children born as a result of either of these processes may be confused or distressed in their understanding of who their parents really are."

Individual, Other

Another concern that many respondents mention is the likelihood that children will feel different because of their unusual genetic make-up. Respondents worry that children will experience difficulty fitting in, either within their family or among peers who have been conceived in more traditional ways. Some specify that children might perceive themselves as a 'freak' or a 'science

experiment' and that this may come with shame or low self-esteem. A few respondents emphasise that children have not been able to consent their conception through mitochondria replacement and suggest this can be an additional emotional burden. Several reflect on how they would personally feel and express their presumed disquiet in a variety of qualifications:

"I would feel disheartened and irreversibly dehumanised to realise that I am not biologically connected to my fellow humans around me in the same way that they all are to each other. My life would be heavily coloured by bitterness towards my parents and the doctors who had in part created me."

Individual, Other

To some respondents, an important component of children's potential emotional and psychological problems lies in the use and discarding of embryos as part of the pro-nuclear transfer technique. They are concerned that children will experience something they describe as 'survivor guilt' or 'survivor syndrome': a sense of guilt about the embryos destroyed in the process of their conception. Some respondents add that this may make the individual feel worthless, or that it will create pressure to live up to expectations of being the 'chosen one' among embryos that were not allowed to develop. A number of respondents qualify a child born through pro-nuclear transfer as a 'clone', stating that this will cause severe identity problems.

"There could also be guilt about any other embryos that have not survived the process and resentment of the fact that the person may not have been acceptable to his/her parents without the replacement."

Individual, Other

The potential impact of mitochondria replacement on an individual's sense of identity within their family, and vis-à-vis parents and siblings, is discussed in many responses. There are many aspects to this discussion, some of which only appear in a small number of responses.

As mentioned above, respondents often foresee emotional or psychological issues in the child's realisation that there is a mitochondria donor who contributed to their genetic identity. Although some respondents believe children will perceive the mitochondria donor as a (third) 'parent', others refrain from this assumption, or reflect on their uncertainty on the matter:

"Will they think of it as three parents? Or just two parents who went to the DNA store and bought some better DNA than their own DNA."

Individual, Other

Respondents believe that the involvement of a mitochondria donor will complicate the relationship between children and their parents. Some feel that family relationships depend on full genetic kinship, and are weakened if mitochondria are acquired from a donor. This, according to respondents, could make children feel inadequate or excluded from the rest of their family.

Another aspect mentioned in various comments is the potential for children to feel that their parents were not ready to accept them in their 'natural' capacity and preferred to artificially improve them through mitochondria replacement. In some comments, respondents conclude that this means parents were more concerned with their children's health or viability than with their 'innate' quality or identity. Another comment suggests that the interference with the child's conception may bring a child to sense that the parents were unhappy with their own identity:

"They could sense that the parents who wanted them did not want to conceive them naturally, as the parents themselves felt to be 'imperfect' and not happy with their own identity."

Individual, Student

There is also a suggestion in a few comments that tensions may evolve between the child and mother, since the mother has mitochondrial disease and the child does not.

Several respondents consider the trade-off between the parents' feelings and happiness and those of the child, sometimes arguing that parents are compromising the well-being of a child by allowing it to be conceived through mitochondria replacement. They believe that the complications around identity are a heavy burden to be imposed on a child.

"Whatever the unknown psychological or physical burdens that resulted, however, it has to be underlined that these would be borne not by the parents, but by the offspring."

Organisation, Comment on Reproductive Ethics [CoRE]

Respondents suggest a variety of other aspects that could disturb or confuse the relationship between the child and their family. Examples are that the child may be curious about 'siblings' it has through its mitochondria donor, and that any family difficulties or behavioural problems could be regarded as a consequence of the child's genetic relationship to its mitochondria donor.

"Despite the fact that it appears there will be no significant inherited characteristics from the procedure there may always be some doubt, particularly of relationships within the family become strained for any reason. The mitochondrial donation could then be blamed, albeit with little foundation."

Individual, Other

In a similar vein, several respondents emphasise that it is likely that the child will have a desire to know its mitochondria donor. Discussions about whether or not this should be possible are covered in chapters 7 and 8; here we focus on the possible impact of the donor's existence on the child's well-being. Respondents to question 3 suggest that children may consider their 'third' parent to be missing from the environment they grow up in. Some offer comparisons with children who were adopted or the product of gamete donation and assert that these children are known to develop a wish to find out about their biological or genetic parents.

"If a child gets DNA from 3 or more parents this will lead to desires to want to know the identity of the donor parent. Reasons could vary from thankfulness, curiosity, identity confusion, or desperate need to be loved."

Individual, Other

A few respondents describe potentially problematic aspects of the presence of a mitochondria donor. One respondent states that donor-conceived individuals are increasingly seeking psychological support, suggesting that this may also be the case for children born with the help of mitochondria replacement. Another believes that if the child's family is not a pleasant one to grow up in, the child may wonder about the family environment their mitochondria donor might offer.

Among many argued cases stating that there will be emotional or psychological consequences for the child, or that there will not, there are a few responses emphasising that the proposed techniques are fundamentally different from what we have knowledge about, and that as a consequence it is not possible to predict how resulting individuals will feel about them. Some respondents highlight the experimental nature of the techniques and the need to consider the long-

term psychological effects for individuals conceived in this way, as they may only encounter identity issues later in life. A few suggest that the potential implications on individuals' sense of identity are likely to decrease if mitochondria replacement would become more common.

"Yes, it is inevitable that the knowledge that they owe their genetic origins to three persons will affect those concerned, in ways that cannot now be predicted, since their situation would be entirely unprecedented."

Individual, Other

The impact of society's response to children conceived with the help of mitochondria replacement is mentioned in several responses to question 3. Some respondents who perceive the mitochondria donor as a 'third parent' worry that children may feel that they do not meet the norm of having two parents and that this could confuse them. Others highlight the risk of negative reactions children may be subject to from people who suffer from mitochondrial disease, or from people with strong views on reproductive ethics or genetic modification.

"Given that many people refuse to eat genetically engineered foods, how does one tell one's friends, family, potential mate that you are genetically engineered?"

Organisation, International Center for Technology Assessment

Another strand of argument broached in a small number of responses is around how public opinions are shaped. Respondents emphasise the risk that children conceived with the help of mitochondria replacement will carry a label that identifies them as a 'three-parent baby' or a 'GM baby' and that this may have a detrimental impact on their well-being. A few respondents specify the role of media in influencing public attitudes, and express concern that this may make children's lives more difficult.

"They fail to reckon with the power of our media which have already represented these techniques as creating 3-parent or 4-parent children. As these concepts are being increasingly embedded in the public consciousness, it will be virtually impossible to uproot them."

Individual, Other

Some respondents make other comments about the implications for wider society. A few discuss the legal status of the mitochondria donor, sometimes stating their belief this is important to consider in the light of kinship and identity. A few others posit a concern about the pressure that intending parents may feel when they would need to decide about the option of mitochondria replacement.

"[...] prospective parents who fear passing on the disease could ultimately be labelled irresponsible if they don't have the treatment, but, at the same time, they could sacrifice bonding with their child if they go ahead."

Individual, Other

Many comments include considerations about the current state of society and interpersonal relationships within it, in some cases to support a view that society will be ready to accept individuals conceived through mitochondria replacement, in other cases deploring that the techniques will further erode traditional structures.

"The multiple parent issue may become a catalyst [sic] to a very dangerous [sic] society change. We are confused enough already, and social studies have backed this up."

Individual, Other



#### 6.2.4 Comparing with other procedures

In considering the potential implications on children's sense of identity, many respondents propose comparisons with other procedures. There are great variations not only between the procedures that respondents liken to mitochondria replacement, but also between the conclusions they draw from this. The following set of quotations captures this very aptly: two respondents each citing both adoption and gamete donation, one as a satisfactory argument that identity implications will be manageable; the other to highlight additional complications specific to mitochondria replacement:

"There are many happy people raised with adoptive parents, surrogate mothers, or sperm-donor fathers; these don't have any bearing on the child's wellbeing."

Individual, Other

"A person who is adopted or born from the result of donor sperm or eggs might find themselves asking where they come from. At least in these situations the question has a definable answer."

Individual, Other

The most commonly cited procedure respondents to question 3 compare mitochondria replacement with is gamete donation. In most of these responses the comparison leads respondents to argue that the potential implications on a person's sense of identity are socially and ethically acceptable, sometimes highlighting that society already accepts the consequences of gamete donation. Many respondents feel that the impact of mitochondria replacement can be viewed as equal to that associated with gamete donation, while several others suggest that the proposed techniques will impact less, as no nuclear DNA is involved.

"We therefore consider that mitochondrial transfer techniques are likely to raise far fewer social and ethical issues surrounding offspring identity than are already raised by existing fertility techniques that are widely accepted, such as gamete donation and surrogacy."

Organisation, Wellcome Trust

A number of respondents are concerned about the implications of gamete donation on children's sense of identity, and emphasise that their concern extends to mitochondria replacement. Some cite publications containing examples of donor-conceived individuals struggling with identity questions.

"We do however have increasing anecdotal evidence about the importance of genetic heritage and parental bonds for those born from donated gametes and their desire to know about their full genetic heritage (3). Some have described anger at feeling like a medical experiment and cited problems with understanding identity for themselves and their own children" (4)"

Organisation, Christian Medical Fellowship

There are numerous comments considering a comparison of the implications of mitochondria replacement on an individual's sense of identity to those of organ, blood, or bone marrow transplantations. Several of these comments are from friends or relatives of people affected by mitochondrial disease. Most of the respondents drawing such comparisons do so to underline their argument that implications will be minor.

"A person can have an entire organ transplanted (heart, lung, liver, kidney, etc...) and not suffer any change to their identity [sic]. Indeed, transplants introduce foreign DNA into the recipient. I do not see this as being any different from using a donor's mitochondrial DNA"

Individual, Other

A small number of respondents specifically disagree with the suggestion that in this context mitochondria replacement can be compared to blood or bone marrow transplantations.

"The SCHB is of the opinion that the donation of an unfertilised or fertilised eggs can certainly not be thought similar to a bone marrow or blood donor. Biological elements partaking in the creation of life are completely different to biological elements that are used in the treatment of an already existing life."

Organisation, Scottish Council on Human Bioethics

Another procedure often referred to in responses to question 3 is adoption. The pattern of these responses is very similar to that referring to gamete donation, with a split of opinion between (more) respondents who believe both procedures have acceptable implications on identity and (fewer) respondents who think both procedures cause identity-related harm.

Some 130 respondents feel that the implications of the proposed techniques on an individual's sense of identity will be equal to other, existing procedures. While 15 respondents assert that the implications of mitochondria replacement will be greater, often identifying the mitochondria donor as the complicating factor; 42 respondents believe that there will be fewer implications, generally referring to the perceived insignificance of mitochondrial DNA. The latter group includes a number of respondents who identify themselves as friends or relatives of a person affected by mitochondrial disease and a few who indicate that they have personal experience of gamete donation.

"As an adoption worker myself I am very aware of the issues of identity and the impact on individuals of not knowing where they came from genetically. I spend much of my working life helping adopted adults find information and trace birth relatives. However, I believe this would be far less of an issue to a person born by the technique proposed and the relief from the anxiety for female children of passing on the disease to their children would be immense."

Individual, Family member/friend of someone affected by mitochondrial disease

The next chapter, chapter 7, discusses respondents' views on other procedures in more detail.

### 7.1      **Headline findings**

987 respondents answered question 4a, which asked:

**In your view how does the donation of mitochondria compare to existing types of donation? Please specify what you think this means for the status of a mitochondria donor.**

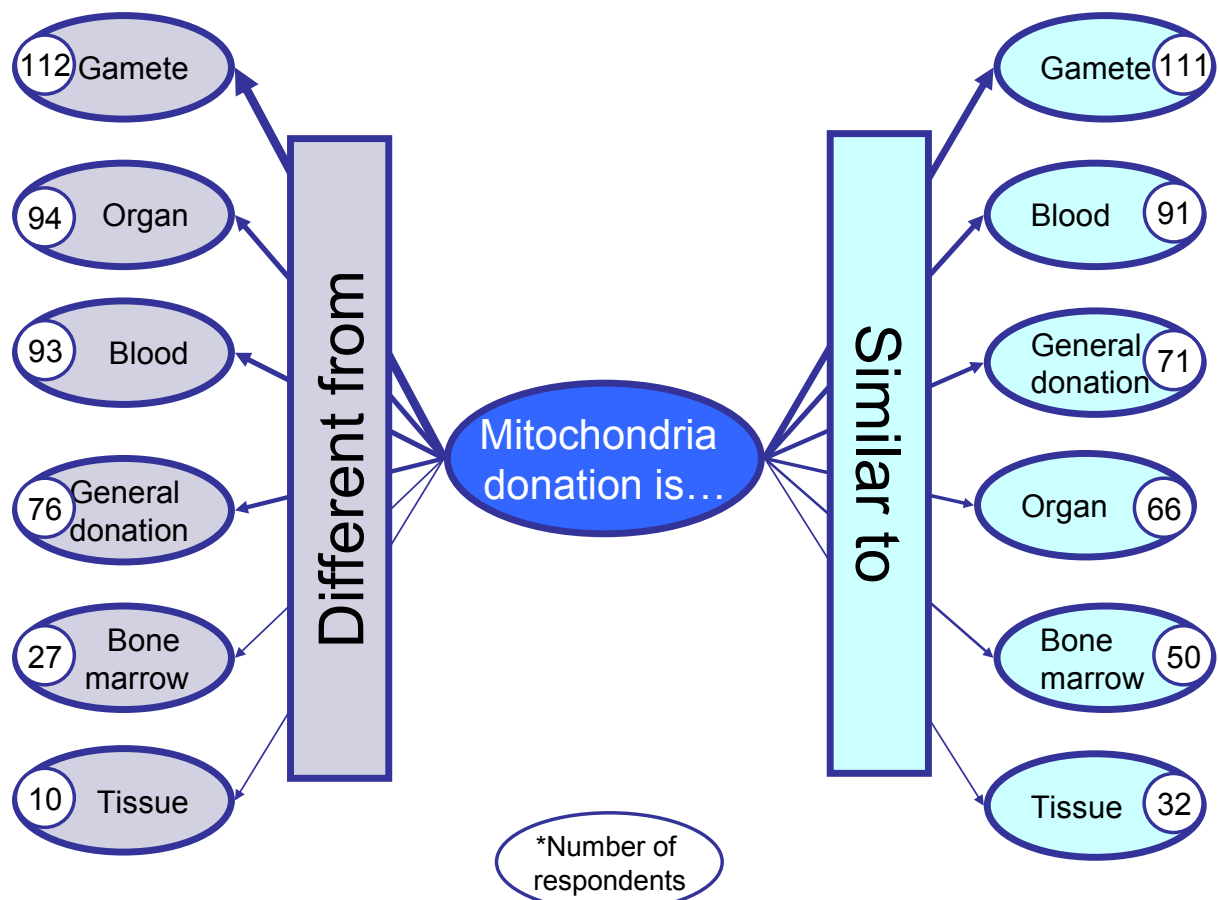
Responses to question 4a included a wide variety of views as to whether mitochondrial donation could be compared to existing types of donation, or represented an entirely different proposition. Typically respondents who believed the significance of mitochondrial donation to be similar to other non-reproductive donations supported its introduction, while those who regarded it as equivalent to donating sperm or eggs were more cautious.

### 7.2      **Summary of comments**

#### **7.2.1      Comparing mitochondrial donation**

The majority of respondents to question 4a suggest existing types of donation, with which to compare donation for mitochondria replacement and the most common are depicted in the diagram below. As the diagram shows, for most comparisons as many respondents thought mitochondrial donation was similar, as thought it was different to another type of donation. As the narrative below describes however, many different explanations were given for these comparisons, and often two respondents would conclude the same thing for entirely different reasons.

**Figure 6** Comparative views on mitochondria donation in responses to question 4a



As shown above, there are a number of respondents who suggest that mitochondria donation is similar, in general, to other kinds of donation without specifying further. These respondents were typically supportive of the techniques being introduced into clinical practice, often citing the perceived benefits of this for health:

"It is very similar. A donor would be increasing the chances [sic] of a more healthy, longer life for an individual. The organ being donated makes no difference."

Individual, Family member/friend of someone affected by mitochondrial disease

Similar sentiments however are expressed by some respondents who feel that mitochondria donation is totally different from other types of donation in a positive way:

"I think that mitochondrial donation is in a different category from other types and that the emphasis should be on its potentially remarkable role as a contribution to preventive medicine."

Individual, Other

A more common view among those arguing that mitochondrial donation is fundamentally different is that this difference warrants caution about introducing it to practice; either because it introduces new phenomena such as the genetic contribution of three parties, or because they believe it is unethical. These arguments are explored in more detail in the following sections. Others highlight that the donation differs fundamentally from other (non-reproductive) donations as the impacts persist through the germline rather than affecting one individual only.

Among respondents who indicate that they have personal experience of gamete donation or donor conception there is a divergence in views similar to respondents overall. While six respondents from this category state that they see mitochondria donation as different from gamete donation, five say they think it is similar. Within this category, several respondents suggest that mitochondria donation is similar to organ, blood or tissue donation, while very few emphasise a difference.

### Comparing with gamete donation

The most common comparison made by respondents in question 4a is between mitochondrial donation and the donation of gametes (eggs or sperm), with equal numbers arguing that the two types of donation are similar as argue that they are different. Organisations suggesting similarity include PROGAR and the National Gamete Donation Trust; organisations suggesting difference include the Wellcome Trust and the Nuffield Council on Bioethics as well as the Anscombe Bioethics Centre. Among those who believe that donating mitochondria is similar to donating gametes, some argue that the transfer of genetic material is the deciding factor, which differentiates these procedures from blood or organ donation. A few note that the proportion of genetic material contributed is much smaller than in full gamete donation, but still feel that it is significant.

“It is the same irrespective of the quantum & type of DNA donated. Hence, the status of the donor should be the same as with donated eggs or sperm.”

Individual, Other

For other respondents the key point is whether mitochondria affects identity; where respondents believe that there is no effect on traits or characteristics they suggest the donation can be seen as similar to blood donation, for example, but would be substantively different if such an effect did occur. There are some respondents who state their belief that mitochondrial DNA does not affect identity traits, often likening it to a ‘functional’ structure such as bone marrow. In contrast a few respondents suggest either that the role of mitochondria in identity may be discovered as the science of genetics evolves, or that it does contribute in some sense already, for example:

“The donation of mitochondrial DNA is very personal and individual reflecting a donation of an individual's personal characteristics even if this means how they function biochemically rather than their outward bodily characteristics.”

Individual, Other

An alternate focus for some respondents is the procedure for the donor, which they see as similar to that for egg donation. Some of these respondents suggest this comparison as evidence for the acceptability of the introduction of the techniques (i.e. it's no different than an already widely accepted process). However others express concerns about the existing process which they believe apply equally with the proposed techniques:

“The donation of mitochondria is going to involve egg donation. There are already more eggs wanted than donors ready to provide them. Egg donation is an unpleasant and risky business. It is in no way comparable with easy blood donation.”

Individual, Other

A third line of reasoning for the similarity between mitochondria and gamete donation for some respondents is that the donor in both cases is in some sense a ‘parent’ of the resulting child, either in a biological sense, or for a few respondents, in the sense of having a moral responsibility towards the child (explored more in section 7.2.2 below).

Respondents who state that mitochondria donation is different to donating gametes commonly suggest that the two are different because no nuclear DNA is transferred. Some specifically mention characteristics, arguing that because the donation will not impact on the child in this sense, the mitochondrial donor is not equivalent to an egg or sperm donor. Respondents arguing along these lines tend to support the introduction of the techniques, and feel that the donation of mitochondria is 'less' consequential than classic gamete donation.

In contrast several respondents who oppose the introduction of the techniques also argue that mitochondrial donation differs from egg donation because the procedure results in changes to the donated egg, altering the relationship between donor and child. Some of these respondents describe this change as affecting the extent to which the donor is the 'mother' of the child:

"The spindle is not an egg and without an egg there is no embryo. The egg donor is a kind of partial mother, just as the spindle donor is a kind of partial mother.

In the case of PNT the egg donor is not the mother directly of the final embryo created, but of an embryo who is destroyed to create that final embryo."

Organisation, LIFE Charity

Others argue that potential donors may not understand this apparent difference to typical egg donation, and that this lack of information would make them less informed and able to consent.

### **Comparing with embryo donation**

There are a number of respondents who make a specific comparison between donation for mitochondria replacement and the donation of embryos to research in which they may be destroyed and express ethical concerns about this process (153). The ethical argument made is that the donation of viable eggs which are used to create embryos which are not intended to be born results in the destruction or death of that embryo. Some respondents refer specifically to PNT, arguing that it amounts to the destruction of an embryo in order to create another, while others do not specify one or other of the techniques, and some specifically mention the donation of eggs rather than embryos. In addition to ethical concerns, some of these respondents suggest that the donor in such a situation may experience guilt or remorse after the donation:

"A mitochondrial donor is someone who is substantially risking her health and future fertility if she donates eggs: if she donates embryos, she is delivering her offspring up for destruction. A woman is in the position of one who is giving her embryos up for the purposes of research which is of no benefit to the embryo, and results in its eventual destruction. This is to ask women who donate embryos to treat their offspring as if they were commodities: which might be damaging to her relationship with subsequent or existing children (if one child is a commodity, why not all of them?)"

Individual, Other

Alongside concerns about the 'destructive' use of embryos and eggs in the techniques, often raised alongside concerns about the effect on the donor. Many of these respondents mention the procedures involved in donating eggs, particularly artificial stimulation. Others suggest that exploitation can occur when donors are offered financial reimbursement or access to fertility treatment in exchange - respondents typically note that these concerns exist for all techniques involving egg donation, but suggest they could be exacerbated by the introduction of the techniques into clinical practice. Others raise particular concerns about the availability of donors, either because they believe women will be less likely to donate given the perception of the techniques described above, or because of a general shortage of egg donors.

### **Comparing with organ, tissue and blood donation**

Although many respondents, including the Association of Clinical Embryologists (ACE) Executive Committee and the British Medical Association, specifically mention blood, organ or tissue donation they typically use the same arguments. Those who believe mitochondrial donation is different to these types of donation often refer to the genetic component of mitochondria, as described above. Others note that mitochondria replacement alters the germline, and thus the donation cannot be viewed in the same light as donations such as organs which affect only the individual involved. A small number of respondents argue that difference is based on the donor; they argue that the mitochondria are effectively donated by the egg or embryo (which they view as a separate person), rather than by the mother, and as such no informed consent is given. Others suggest that there are negative consequences of mitochondrial donation for the embryo or egg donated, where tissue donation has no significant effect on the donor:

“I think there is an enormous difference between donations that save lives (such as blood donation) and donations that result in the loss of (embryonic) life, such as egg or mitochondria donation.”

Individual, Other

Those who argue that blood, organ or tissue donation is similar to mitochondrial donation typically argue that there is no nuclear genetic contribution, and thus no impact on characteristics, as described above.

### **Comparisons: variations**

Some respondents specifically address differences they see in the status of donors to each technique. Of these most raise the arguments described above regarding the use of embryos in PNT, but tend still to oppose both techniques. A few respondents discuss their view that donation for MST is equivalent to blood or organ donation, as there is no genetic contribution, or to a sperm donation, in that it is likely to be accepted in a similar way.

There are two respondents who mention the sex of the resulting child - noting that as mitochondria are passed on only via the female line, the germline change is only passed on via female children. One suggests that this effectively makes a mitochondrial donation which results in a female child similar to gamete donation, but a donation resulting in a male child is more like an organ donation, where no change persists beyond the individual.

## **7.2.2 The mitochondrial donor**

### **Status of the donor**

Views on the status of the mitochondrial donor are strongly correlated with views on the status of the donation in relation to other types of donation; this section focuses specifically on the donor as an individual, with many arguments summarised above. The most common points raised by respondents in relation to the donor concern whether they are a ‘parent’ to a child conceived via the proposed techniques - with slightly more respondents supporting than opposing this concept. In responses from respondents who indicate that they have personal experience of gamete donation or donor conception few comments are made about the donor status. Three of these respondents suggest the donor is a parent to the child, one respondent states the donor is not, and two respondents say the donor has no rights or responsibilities towards the child.

"We find no distinction. s.47 of the Human Fertilisation and Embryology Act 2008 states: 'A woman is not to be treated as the parent of a child whom she is not carrying and has not carried'. The Humanist Society Scotland does not believe that the donor of mitochondria [sic] can have the same status as a reproductive egg or embryo donor, nor that mitochondrial [sic] donors should be legally pressured to be identified to the adults born from the donation."

Organisation, Humanist Society Scotland

Those who believe that the mitochondria donor is in some sense a 'parent' to the resulting child tend to focus either on the genetic contribution of the donor, arguing that the fact that their DNA is passed on qualifies them as a 'parent'. Others refer to the essential role of the donor in the conception of the child.

"The person could not exist without this mitochondrial DNA and therefore I feel this makes the mitochondria donor a parent of the child in a very real sense as they have been integral to the process of conception."

Individual, Other

Many of those who state their belief that the donor is a 'parent' qualify this, suggesting that the role is shared with the intended parents (who contribute their nuclear DNA) - a smaller number state specifically that all three genetic contributors have an equal role as parents.

Despite the number of respondents who argue that the donor has a role as a parent, far fewer suggest that they have particular rights or responsibilities towards the child - which may be because many of those who believe the donor is a parent do not believe the techniques should be permitted. Statements about responsibilities of the donor tend to identify that these responsibilities exist without going into detail about what they entail.

"I think that the mitochondria [sic] donor is a third parent. I think that any techniques which use genetic material from three people has this problem."

Individual, Other

In contrast those who argue that the mitochondrial donor should not be considered a parent often suggest that the genetic contribution is not significant enough, or is purely functional, and so does not bestow a parental relationship. Others focus on the social role of parenting, arguing that the donor contributes genetically, but has no role raising the child, and as such is not a parent.

Those who do not believe there should be a parental relationship between donor and child also tend to believe that the donor should not have rights or responsibilities over the child, with several returning to comparisons with other donation scenarios:

"Mitochondrial donation is more akin to giving blood than it is to surrogate parentage. The Mitochondrial donor and child should not have any contact with the child and has no rights over the child's upbringing."

Individual: Student

A number of respondents (24) specifically mention the legal status of the donor, with the majority arguing that there should be no binding legal requirement on the donor with regards to contact or obligation towards the child. This is seen as a potentially challenging issue by some, who suggest that the complexities of the relationship between intended parents, donor and child may result in legal challenge, or cumbersome legislation. The theme of confusion is echoed by others, who



express the view that the status of the donor in general is unclear, with some suggesting that this is symptomatic of overall problems with the techniques.

“We simply cannot predict the meaning that the mitochondrial donor (and the donation itself) will have to those directly affected – and neither is that meaning likely to be (i) static over their lifetimes or (ii) standard either within or across the different ‘groups’ concerned.”

Organisation, PROGAR

Many respondents make comments in question 4a on the extent to which information should be available to a child conceived as a result of the techniques; these arguments are explored in the following chapter. However a number of respondents express more generally their view that the donor should have the right to anonymity, either as a blanket policy or as an option they could choose. Concerns for the right of the donor to anonymity are often associated with the view that the donation is an altruistic act, which should not have harmful implications for the donor. Many of these respondents associate the act of mitochondrial donation with ‘helping’ a child, rather than ‘creating’ one:

“In the same way that organ, egg and sperm donors consent to helping another life, a mitochondrial donor would be doing the same-not wanting a child etc but wanting to help another human being “

Individual, Personally affected by mitochondrial disease

However there are some respondents who take the opposing view, and feel that something about the nature of mitochondrial donation, either its genetic aspect, or the fact that life is ‘created’ as a result, is a significant enough contribution to the resulting child that they must have the right to information about the donor.

### 8.1      **Headline findings**

A total of 1,039 respondents answered question 4b, which asks:

**Q4: b) Thinking about your response to 4a, what information about the mitochondria donor do you think a child should have? (Choose one response only)**

- 1) The child should get no information**
  - 2) The child should be able to get medical and personal information about the mitochondria donor, but never know their identity**
  - 3) The child should be able to get medical and personal information about the mitochondria donor and be able to contact them once the child reaches the age of 18**
  - 4) Other**
  - 5) I do not think mitochondria replacement should be permitted in treatment at all.**
- Please explain your choice.**

As summarised in the figure 7 below, the largest number of respondents chose option 5, implying that the other options are not relevant to them as they would rather not see the techniques permitted. Looking at the different respondent types, the only group where a majority selected option 5 are respondents describing themselves as 'other' (see chapter 2). Among specified respondent types (e.g. patients, relatives, students) the opinion is divided between all five options.

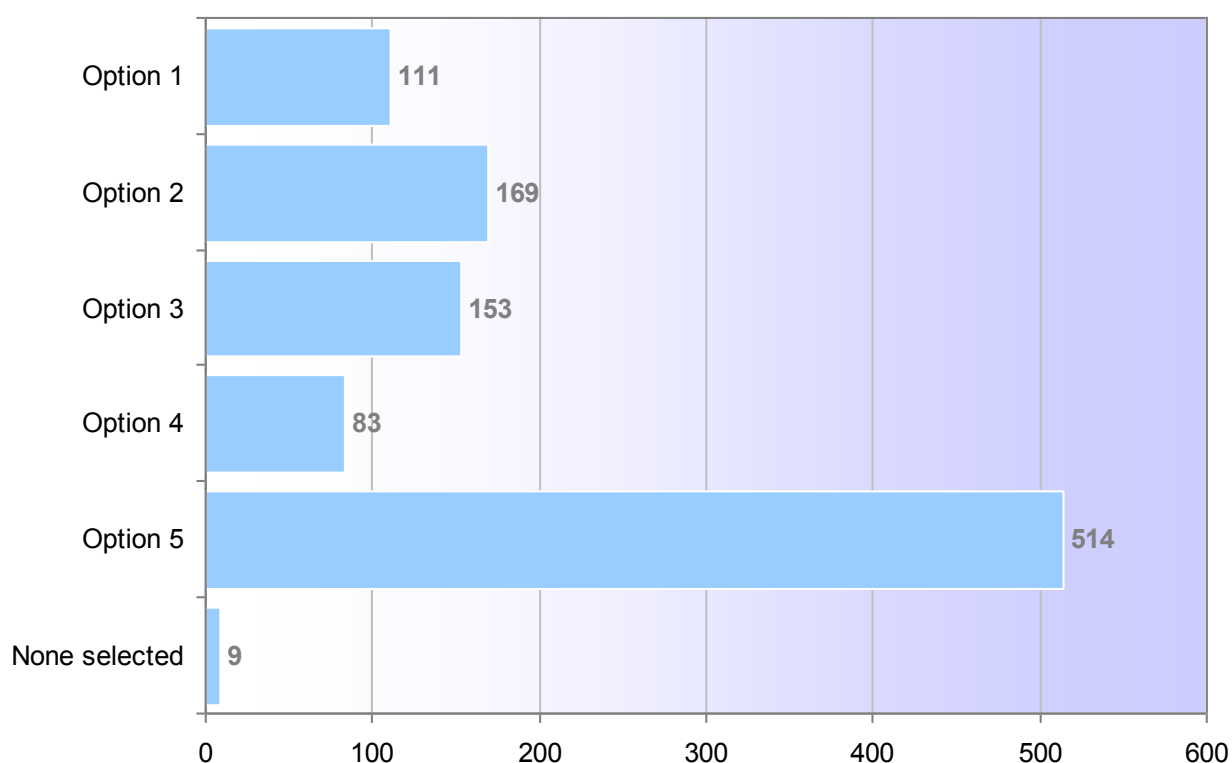
Respondents' choices divided fairly evenly between options 1, 2 and 3, with option 1 receiving the fewest selections and option 2 the most among them. A smaller number of respondents selected option 4, 'other', and suggest different approaches or variations to what is proposed in options 1, 2 and 3.

Though most respondents selected one of the 5 options presented, nine respondents made further comments without selecting any of the options presented.

Looking at the options selected by different types of respondents, there is a relatively clear preference for option 2 among those who indicate they are personally affected by mitochondrial disease and/or a friend or relative of someone affected by mitochondrial disease. Among the (few) respondents who indicate that they have personal experience of gamete donation or donor conception, options 2, 3 and 4 are selected more often than option 1. Very few respondents from the categories mentioned here have selected option 5.

Among stakeholder organisations options 1 and 3 are more often selected than option 2. Proponents of option 1 include the British Medical Association and the Nuffield Council on Bioethics; option 3 is supported by the Church of England (Mission and Public Affairs Council) and PROGAR, among others. Human Genetics Alert, the Church of Scotland as well as some other organisations state a preference for option 5.

**Figure 7 Preferred option in responses to question 4b**

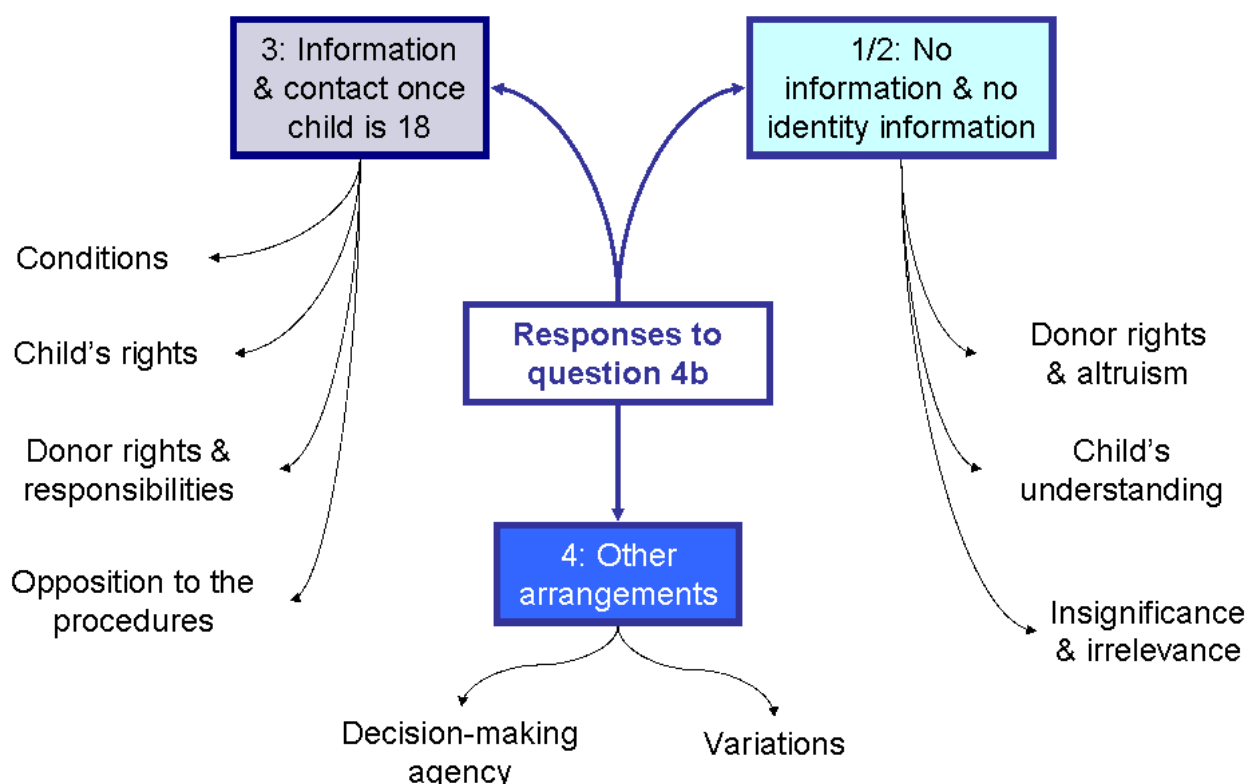


Respondents selecting options 1 and 2 express some similar views in explanation of their perspectives, frequently focusing on the ethical status of the donation and the rights and responsibilities thought to be contingent. A few choosing option 1 state explicitly that option 2 would be their next preference, and vice versa. Similarly, the explanations of respondents selecting options 2 and 3 display some similarities, often anticipating future medical needs and identifying concerns of offspring of the techniques.

Respondents who comment that they oppose the techniques generally selected option 5, although a smaller number selected option 3, in order to express their preference about disclosure of information in the event that the techniques are to be permitted. Their views are explored further in the section on option 3, below.

This chapter examines in turn the explanations of respondents, grouped according to the options they preferred for donor information disclosure. Their explanations are explored in more detail below under the following sub-headings:

**Figure 8 Responses to question 4b**



## 8.2 Summary of comments

### 8.2.1 Option 1 (no information) & option 2 (some information but not identity)

Respondents selecting options 1 or 2 agree that the identity of a donor involved in the techniques should at no point be disclosed to the child, although those who chose option 2 think that medical or personal information should be available to them. Explaining their choices, these respondents raise many similar considerations. Further, three respondents selecting option 1 said option 2 would be their second choice, and three selecting option 2 said option 1 would be their alternative preference.

#### Insignificance and irrelevance

A number of respondents selecting options 1 or 2, including several who are personally affected by mitochondrial disease, or a patient/relative of someone who is, argue that no more information should be disclosed on the grounds that the donation has the same status as a blood or organ donation. They say that as those donations guarantee anonymity, so should the donation involved in these techniques. A smaller number of respondents selecting either option compare the donation to that of eggs or sperm, arguing that its lesser significance for the genetic identity of the child indicates that less donor information should need to be disclosed. A few make similar arguments based on comparison with adoption or surrogacy. A few respondents selecting option 2 suggest the procedure is similar to egg or sperm donation, but suggest disclosing the donor's identity is complicated, or should be conditional on consent.

"The reason children born following donor conception require information about the donor is because the information relates to them, as a person, and the donor's genes have

contributed to their physical appearance and personal characteristics. The same does not apply to donated mitochondrial DNA. The closest analogy is to blood or bone-marrow donation which is carried out anonymously with the recipient receiving no information about the donor.”

Organisation, British Medical Association

Some respondents who refute the need to disclose the donor’s identity based on the comparative status of the donation go on to explain that their views are informed by the function of mitochondrial DNA. They say that as mtDNA does not determine the identity or the traits of the child, the donor’s identity can have no significance. Others say they can’t see circumstances in which it would be necessary or important for the child to access more information about the donor.

“I believe that children conceived by this technique should not need any information on the identity of the mitochondrial donor. As the conceived child will not inherit any personal characteristics or traits from the mitochondrial donor, they will have no legitimate interest in their identity.”

Individual, Member of staff at a licensed HFEA centre, Researcher

Some respondents selecting either option 1 or 2 explain their view that certain circumstances might influence what donor information should be disclosed. A small number of respondents selecting option 1 comment that in case of new medical evidence or other unforeseen developments, the relevant information should be confidentially stored, or the rules about its disclosure might need to be reconsidered. Comment on the circumstances of disclosure is significantly more common among respondents selecting option 2, some of whom mention the possibility of medical developments that might justify more information. Most frequently, they describe these circumstances as likely to be connected to the health of the child, other medical developments in the field, or unforeseen consequences of the techniques.

### **Child’s understanding**

Respondents sometimes link the way children are informed about the techniques to the significance of information about the donor. Some say they believe children should be given no or limited donor information, but do have a right to understand the process that has taken place. Others state concern that making available too much information about the donor could lead the child to an inaccurate understanding of its medical or personal significance to them.

A small number of respondents reflect on the motivation of the child in seeking information about their donor. Some of the respondents favouring option 1 note that a child’s curiosity would be understandable, but that it need not require the disclosure of more information than is fitting for the donor. This view is connected to their feeling that the significance of the mtDNA is limited, and it is vital that children understand this.

“...The child should have the right to know how they were conceived and why, but have it explained that their genetic characteristics such as physical traits, personality traits, intelligence etc come from the parents they are growing up with. I think it would confuse the issue if they were to have the right to know who the donor was given the minimal input from the donor mitochondria to the person's make-up.”

Individual, Family member/friend of someone affected by mitochondrial disease

### **Donor rights and altruism**

Other views common to respondents selecting options 1 or 2 focus on the rights of the donor, or considerations about the experience of donating and about privacy. Some express concerns about

the possibility of intrusion into the donor's life if their identity were to be disclosed. Others note that knowing a child might seek them out later in life would be a disincentive to donate, or note that guaranteeing donor anonymity would likely encourage altruistic donors. Some describe the relationship between the donor and the parents as altruistic or as offering a simple medical 'repair', and so part of a dispassionate and impersonal act of generosity that need not imply future contact or association.

"I feel that using a mitochondria donor would be a gift. A way to erase the spelling mistake within my gene pool. My child would be made up of myself & my partner & very little of the donor. I think having access to medical conditions & personal information would feed any interest but that person isn't the main gene donor & I feel there's enough reassurance there for a child as its still made up of mum& dad genetically with some help from a kind person..."

Individual, Personally affected by mitochondrial disease

### Comments specific to option 2

Though most comments made by respondents favouring either option 1 or option 2 are similar, some comments made by respondents selecting option 2 weren't reflected in comments of those who chose option 1.

Specifically, nine respondents select option 2 and mention specific reasons why personal information should be made available to the child. In most cases respondents say this disclosure should be subject to the relevance or utility of personal information, although one respondent suggests any criminal history of the donor should be available to the child.

"In case of any medical complications in the child, the knowledge of the medical and personal information could be useful to reduce the certain complication. However the donor identity may be unknown as only a small percentage of the donor is a part of the child."

Individual, Student

Four respondents selecting option 2 say that option 3 would be their second choice, usually suggesting that the two differ little, and that the donor's consent for the disclosure of their identity should be the critical factor.

### 8.2.2 Option 3 (information and ability to contact once child is 18)

Respondents selecting option 3 tend to attach greater significance to the results of the technique for the child, and often consider these outcomes at length in their explanations.

A number of these respondents echo explanations given by respondents selecting other options on information disclosure. For instance, some respondents state relatively straightforwardly that they regard option 3 as the appropriate arrangement since they see mitochondria replacement as equivalent to egg or sperm donation.

#### Child's rights

Of respondents choosing option 3, several explain that they feel it is the child's right to know the identity of the donor. Many of these accept the curiosity or the emotional or medical needs of the child, and a number give their explanations in terms of parenthood or origins, connecting the disclosure of the donor's identity with the child's ability to understand their own background. Some respondents who select option 3 cite the child's general right to information about their biological make-up, and others mention that they may wish to thank the donor.

Eight respondents frame the child's rights differently, focusing on the right to understand the process that took place. For most of these respondents this is the responsibility of the child's parents, and they anticipate that if done properly, there would be no need to withhold any information from the child, who may be content not to act on any information they could access.

For nine respondents, the decision on how important knowledge of the donor's identity is must rest with the child. For this reason, they consider option 3 the best arrangement, so that the information should be available when needed.

"Paternalistic and/or culturally discriminatory assumptions about whether or not such offspring will need information to meet their identity (or future medical) needs have no place in the modern world and we should not be risking the future well-being of those offspring for whom it may prove important..."

Organisation, PROGAR

A number of respondents selecting option 3 state in their explanations their support for the provision for disclosure of information when the child reaches adulthood or the age of 18. Some respondents reaffirm this age conditionality, but six suggest that the disclosure might be appropriate or helpful earlier in the child's life, or simply that the age limit ought to be fixed elsewhere.

### **Donor rights and responsibilities**

A smaller number of respondents stress that the child's rights must be balanced against the rights of the donor. Though only four respondents who select this option state that disclosure of the donor's identity should be subject to their explicit consent, a number of other respondents draw attention to the rights of the donor to decline to enter into a relationship with the child, for instance, or to maintain their distance from the child.

"This option seems to provide the maximum freedom to obtain information if the child wishes it on reaching adulthood, without infringing the donor's right to anonymity."

Individual, Other

Eight respondents who select option 3 explain their view that it would be justified to disclose the information and identity of the donor because they regard it as part of the donor's responsibility. Specifically, they suggest the donor should take account of the possibility of future contact before the donation takes place.

Other option 3 respondents, though, feel greater flexibility would be appropriate. Some suggest that the disclosure of donor identities should be flexible to a degree, dependent of the will of some combination of the parties, or else different case-by-case depending on the needs of the child. A few respondents selecting option 3 suggest that disclosing the identity of the donor would be less problematic if the donor were likely to be someone known to the family benefitting.

### **Conditionality**

Many respondents who select option 3 impose conditions on the disclosure of information outlined. A few respondents specify that the rules on donor identity should reflect the technique used: so, a child born using MST should have the right to know the identity of the egg donor, while one born by PNT should know the identities of both the egg and sperm donors involved in the process. Another suggests that since male children will not pass on the donor mitochondria, they need only receive the information implied in option 2, while female children should know the donor's identity too, as in option 3. Others refer to the significance of this transmission through a female child, without asserting the possibility of different rules.

Some respondents selecting option 3 suggest further medical evidence or outcomes as conditions on the disclosure of donor information. Similar to arguments made by respondents selecting option 2, these respondents consider the possibility that information about the donor might be important in future medical research or treatment. A couple suggest that if the techniques were shown to transmit some characteristics to the child, the donor's identity would be important to disclose.

"...as the replacement of mitochondria is a new technique without the benefit of years of results it is possible that unforeseen [sic] problems may arise. I would therefore be in favour of allowing the child to obtain medical and personal information that may help in this case. That said, this should in no way lead to the situation where a mitochondrial donor could be found responsible for the future health and well-being of the child."

Individual, Family member/friend of someone affected by mitochondrial disease, Other

## Opposition to the procedures

Although most respondents opposed to the techniques select option 5 as their preferred model for managing donor information, seven select option 3, and go on to explain their choice. Most explain that they would prefer it if the techniques were not permitted, but in the event that they are, that option 3 would be appropriate because of the biological significance of the procedure for the child.

### 8.2.3 Option 4

Respondents who selected option 4, signifying some other arrangement for disclosure of information, sometimes propose a specific variation on options 1 to 3. Their focus also tends to be on a more flexible approach, depending on circumstance and often based on mutual agreement between the parties involved. A few respondents, for instance, again suggest the need for different arrangements according to whether MST or PNT is used, or depending on future understanding of the functions of mtDNA or the medical consequences for the child.

"This one-off tick box does not allow those opposed to these techniques to say how to accurately consider the implications of these techniques. If MST is legalised, such children should not be deprived of knowing their egg donor mother.

If PNT is legalised, such children should be fully informed of the procedure and have full knowledge of the woman who donated the second egg and the man whose sperm was used to create the donor embryo with that second egg."

Individual, Other

## Decision-making agency

While some of these respondents repeat the view found above that the decision on disclosure of their identity should rest with the donor, a number of others suggest that the donor should enjoy some discretion in what other information is shared with the child, or even, in one instance, that the decision should be reversible. A few respondents note the possibility that discretion might encourage more donors to come forward.

A few other respondents suggest that the parents should have greatest agency in decisions about what information is shared with the child. One suggests the need for input from medical professionals too, while others say the parents should hold on to the information until the child is better able to understand it.

A number of respondents repeat views described above that attribute a responsibility to the parents for ensuring the child's appropriate understanding of the procedure and whatever information is disclosed to them, and when. In a variation on this perspective, three respondents



believe that protecting or ensuring the welfare and independence of the child is paramount in considering the disclosure of information.

For many respondents, though, the decision on disclosure of information to the child must be shared. Some say it should be negotiated according to the wishes of the child and the donor, while others suggest that the donor and the parents should be the key agents. As seen above, many more respondents than these hint at these possibilities of joint responsibility in describing varied conditions and circumstances of consent and disclosure.

“It should be the choice of each donor as to what information is provided, along with any other conditions of their donation, and the choice of the parents as to whether to accept these conditions. There is no need for blanket conditions; donors can be matched up with compatible parents.”

Individual, Other

## Variations

Some respondents defer in their explanations to established rules governing the disclosure of information in other donation procedures. A few say it should be the same as for organ, blood or bone marrow donation, while one identifies egg or sperm donation as the appropriate model.

A number of respondents selecting option 4 describe an alternative variation on options 1 to 3. A few respondents suggest that only medical information should be disclosed. One respondent argues that as well sharing medical information from birth, personal information about the donor - falling short of identification - could be positive if disclosed once the child reaches 18. A small number of respondents support option 3, but disagree that it should be age-limited. A few others stress that the information shared need only be minimal. A number also distinguish between MST and PNT in exploring these variations.

“That the status of mt donors depends on whether MST or PNT transfer has been undertaken

(a) With MST, the mt donor is in a similar position to a blood donor. If an individual needed blood to save their life and then subsequently went on to conceive a child, it could be said that the child born was as a result of the life-saving blood donation. But the donation is not an integral part of the child's identity. In the case of MST, the healthy egg has been deliberately extracted for this purpose with the donor knowing it would be used in this way without her nuclear DNA, but with the tiny amount of mt DNA being preserved in a future life...

(b) With PNT, it is felt that the donor's identity is stronger (despite it still only being the same tiny amount of mtDNA that is preserved), because of the deliberate creation of the embryo rather than the donation of an egg, perhaps in a similar way to those who have received heart or face transplants where the recipient may question identity. Here there is a donor embryo made up of two people's DNA and whilst the mt is only connected to the maternal line, this healthy mt from the donor embryo is only available because DNA from two people has come together to make the embryo. If we're thinking in a social context, it is possible that the donor conceived person might also want to know the fourth 'donor' involved in this process.”

Organisation, National Gamete Donation Trust

In addition to these views focused on the range of options presented, some respondents comment more broadly on the information proposals. Three respondents criticise the wording of option 5 as apparently precluding a view on the appropriate information arrangements from those opposed to

the techniques. A few others argue in general that transparency around the procedure is important due to its newness and complexity, or that information provision should go beyond any of these options and include information on other parties involved.

“The institutions making the plan, the society approving it, the parents requesting it, the donors participating must all be transparent to the offspring (and their descendants) who will have a social right to criticize their production. Social responsibility amounts to that kind openness.”

Individual, Other

#### 8.2.4 Option 5

The majority of the very large number of respondents selecting option 5 revisit in their explanations the arguments against the introduction of the techniques they have made in response to earlier questions. 128 refer directly to another question. An additional 96 respondents selecting this option give no further explanation.

Some of those selecting option 5 go on to echo the criticism made by some selecting option 4, that only one option expressing opposition to the techniques limits the ability of those opposed to propose mitigating arrangements. Also, a small number of respondents criticise the label ‘mitochondria replacement’ as a misrepresentation of the MST and PNT techniques.

#### 8.2.5 Other comments

There are a few other comments about information management made in responses to question 4b. Eight respondents who select various information disclosure options comment on the importance of donor screening. For most, the screening process, ensuring mitochondrial health and checking other potential problems, reduces the importance of keeping or sharing much information or the identity of the donor. In contrast, one respondent suggests there should be age and health restrictions on potential donors.

Some respondents simply note that retaining donor records would be important, mostly in anticipation of future health problems or in case of some other need to follow-up. A few comments are made about the legal implications of the procedures, one calling for more clarity before information rules are set, another suggesting the law could be altered to fit when the personal effects of the techniques on the child are clearer, and one querying how the donor’s role will be legally recorded through the child’s life.

## Chapter 9      Question 5: regulation of mitochondria replacement

### 9.1      **Headline findings**

Question 5 asks:

**If the law changed to allow mitochondria replacement to take place in a specialist clinic regulated by the HFEA, how should decisions be made on who can access this treatment?**

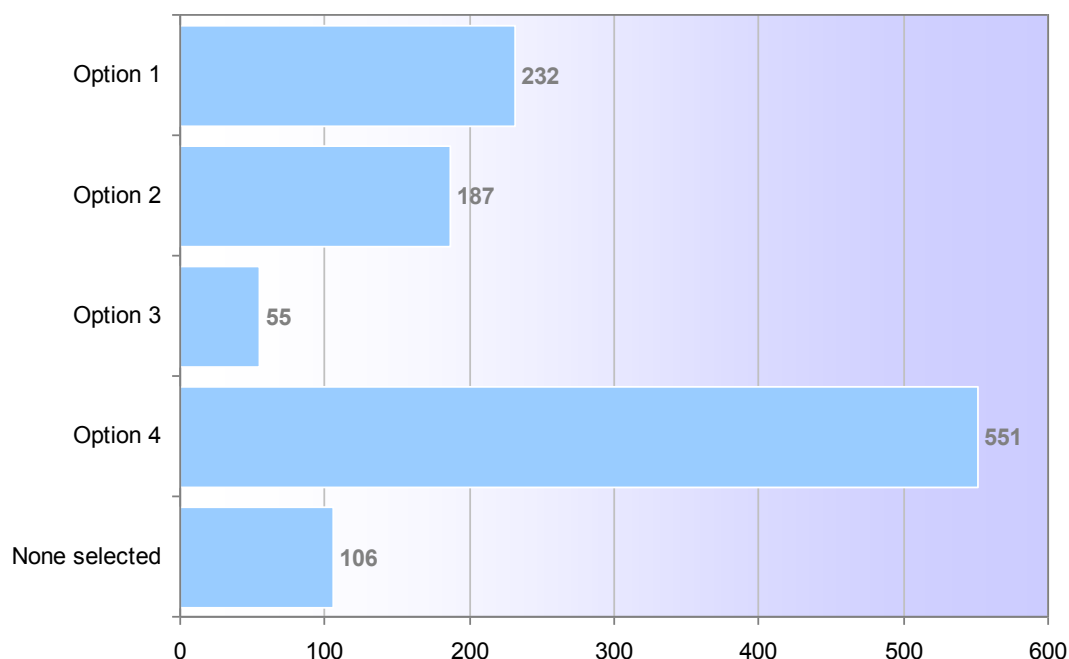
A total of 1,143 respondents answered this question. Respondents were given four options to choose from, and were asked to select one response only:

- 1) Clinics and their patients should decide when mitochondria replacement is appropriate in individual cases.**
- 2) The regulator should decide which mitochondrial diseases are serious enough to require mitochondria replacement and, just for these diseases, permit clinics and patients to decide when it is appropriate in individual cases.**
- 3) The regulator should decide which mitochondrial diseases are serious enough to require mitochondria replacement and also decide, just for these diseases, when it is appropriate in individual cases.**
- 4) I do not think mitochondria replacement should be permitted in treatment at all.**

Respondents were then asked to explain their choice.

A division can be made between options 1-3, which all propose a change in the law to allow mitochondria replacement treatment to take place with differing levels of regulation, and option 4, which states that the law should not be changed at all.

**Figure 9      Options selected in responses to question 5**



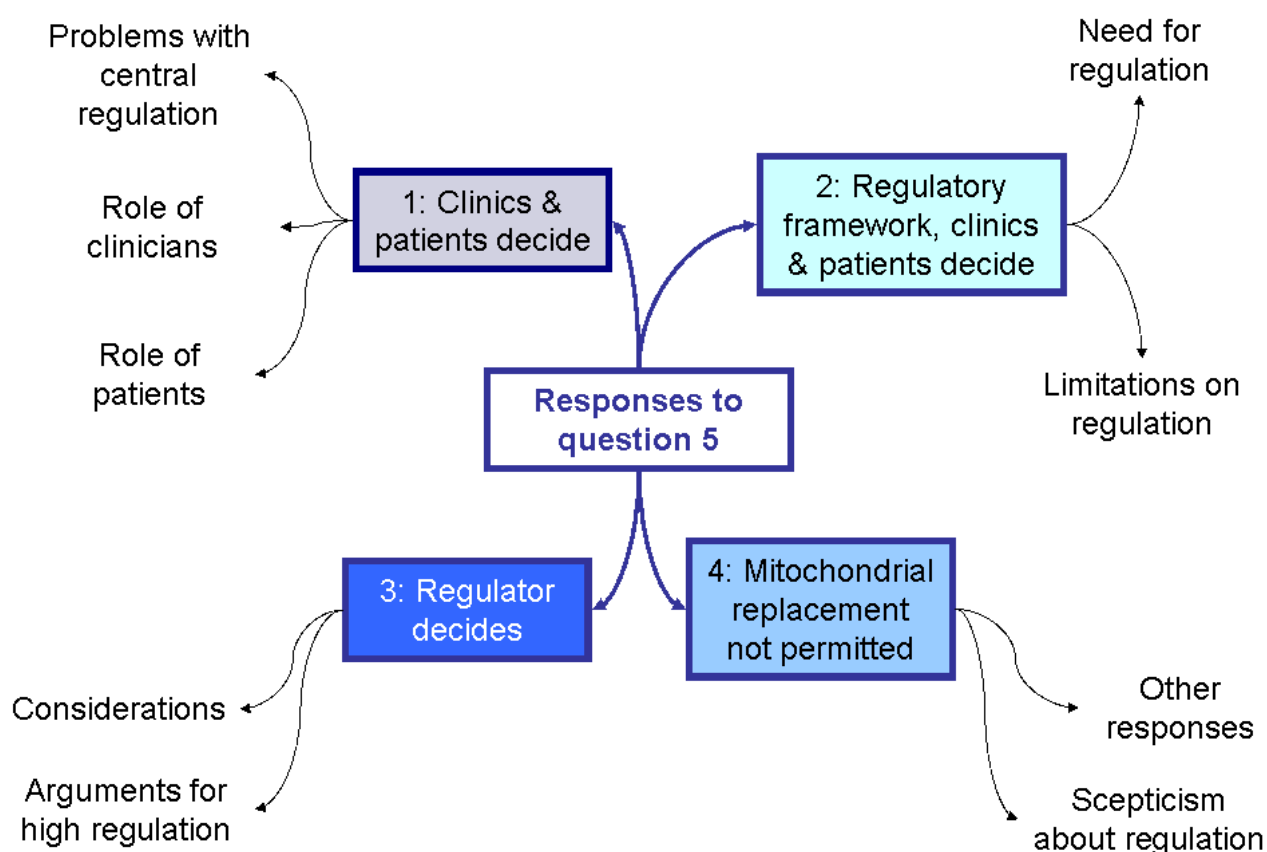
Of the respondents who selected options 1-3, the majority (232) selected option 1 (clinics and patients should decide when mitochondria replacement is appropriate in individual cases). Slightly fewer people (187) selected option 2 (a regulatory framework of diseases deemed serious enough to warrant mitochondria replacement, with clinicians and patients able to make decisions within this framework). Significantly fewer respondents (55) selected option 3, which calls for the highest level of regulation - an external regulatory framework with the regulator also responsible for making individual decisions within this. Just under half of the overall respondents (551) chose option 4, stating that they did not think mitochondria replacement should be permitted at all. The remainder of the respondents did not select an option, most leaving the question blank altogether, and a minority (11) writing general comments. People who left comments but did not select a response commonly said that they did not know, were unsure or had no strong opinion; several offered other suggestions for regulation, for example regulation by Parliament; and others simply reiterated their opposition to mitochondria replacement.

Among respondents who identify themselves as 'personally affected by mitochondrial disease' or 'family member or friend of a person affected by mitochondrial disease' option 1 is by far the most frequently selected option. Among respondents who identify themselves as 'student' or 'researcher' opinions are split between options 1, 2 and 4. Of the very few respondents who indicate that they are a member of staff of an HFEA licensed centre, three select option 1 and three select option 2. Among respondents who identify themselves as 'other' the great majority selected option 4 (see chapter 2 for an overview of respondent types).

There are a few stakeholder organisations in support of each of the options: option 1 is selected by the Association of Clinical Embryologists (ACE) Executive Committee among others; option 2 receives support from the Wellcome Trust, the Muscular Dystrophy Campaign and the Humanist Society Scotland; option 3 is favoured by the National Gamete Donation Trust and others; option 4 is selected by Comment on Reproductive Ethics (CoRE), the Anscombe Bioethics Centre and others.

In the second part of the question, respondents were asked to explain their choice. The reasons for these choices and the arguments surrounding them are explored in detail in this chapter under the following sub-headings:

**Figure 10 Responses to question 5**



## 9.2 Overview of comments

### 9.2.1 Responses to option 1 (clinics and patients to decide)

Option 1 states that ‘Clinics and their patients should decide when mitochondria replacement is appropriate in individual cases’. This option proposes the lowest level of centralised regulation, with decision-making power devolved to the individual clinic level. Of the three options which allow for mitochondria replacement to take place (options 1-3), option 1 proved the most popular with 232 respondents indicating it as their preference. When respondents were asked to explain their choice, typical comments and arguments centred on issues of personalisation and the right to individual choice. Many respondents state their faith in the judgement of clinicians, while others focus on the rights of patients to play a central role in the decision-making process.

#### Problems with centralised regulation

Many respondents raise potential problems with centralised regulation to explain their preference for decision-making at the individual clinic level. The most common concern cited is that a central regulatory board would be rigid, inflexible and generalist, and would not be sensitive to individual circumstances. Many respondents feel that patients and clinicians are better placed to make decisions about the appropriateness of treatment, as they have a deeper understanding of individual circumstances and medical history.

“ACE believes that clinics and their patients should decide when mitochondria replacement is appropriate in individual cases. This allows the expertise of specialist scientists and clinicians to be used to make these decisions rather than relying on a regulator who is unlikely to have the knowledge required to make the decision in an efficient or even appropriate manner.”

Organisation, Association of Clinical Embryologists (ACE) Executive Committee

Another concern respondents mention is that decision-making by a regulatory board would make the process too bureaucratic, expensive, or time-consuming. There are concerns around that centralised regulation would involve onerous levels of red tape and about the effect this would have on patients, particularly the level of distress that may be caused by added bureaucracy and time delays.

“I would feel more comfortable with the decision being taken on a wider scale than just lying in the hands of one regulator.”

Organisation, The Lily Foundation

A number of respondents suggest that the nature of mitochondrial disease means that a ‘list’ of diseases qualifying for mitochondria replacement treatment would not be appropriate. Some point out that mitochondrial disease is extremely varied, and not all variations have been discovered and categorised. Even within established diseases, it is noted, symptoms can vary widely, and can be more or less serious in different cases. Some respondents therefore feel that maintaining a list of qualifying diseases would not be effective or useful, as the following quote illustrates:

“As I understand it, mitochondrial disorders do not all fall into conveniently identifiable syndromes, and the same genetic fault might manifest in different ways. By their very nature, these diseases are inseparable from the distinct individual family stories of patients, and I believe that only they and their doctors can chart the right course.”

Individual, Family member/friend of someone affected by mitochondrial disease

In relation to this point, some respondents raise concerns about the status of new or rare diseases, and suggest that a centralised list of diseases might delay treatment for diseases which had not yet been assessed or categorised by the regulator. One respondent described personal experience of this situation to argue against a regulated list of treatable mitochondrial diseases, which might deny sufferers of unidentified variants the chance of a child free of the disease.

Most of the respondents who chose option 1 feel that central regulation would not be sufficiently effective, efficient or sensitive to individual circumstances, and that clinicians would be better placed to make decisions on a case-by-case basis.

### **The role of clinicians**

Many respondents argue that clinicians have the most familiarity with the individual circumstances and medical history of their patients, and are therefore best placed to make decisions about their treatment. The varied nature of mitochondrial disease, some respondents note, means that it is necessary to take into account the medical history of the individual and their family in establishing the best course of treatment.

Other respondents add that if practitioners are sufficiently well-trained and qualified there should be no need for external regulation.

### **The role of patients**

Many respondents feel that it would be important for the patients themselves to have a central role in the decision-making process. The majority of respondents who selected option 1 feel that a joint decision, made between patients and their doctors, would be the most appropriate. Many argue that individual patients know their own circumstances better than anyone else, and are therefore best placed to make decisions about what is right for themselves and their families.

An argument put forward by several respondents is that it is impossible to set an objective measure on what constitutes a serious disease. The experience of disease, it is argued, is subjective and personal – disease may be experienced as ‘severe’ to different degrees depending on the circumstances of the individual. The following personal vignette illustrates this point:

“Only the patient can identify the severity of their symptoms... I have a disfiguring disease in my family that has led three members to avoid having children. Some might say the condition wouldn't warrant them refusing to have children with a 50/50 chance of contracting the condition, but they have lived it, they have had the operations to attempt to correct it, they've suffered the bullying in school and feeling different as a child. Only the parents can say how severe their condition is to them.”

Individual, Student

It is therefore problematic, some respondents argue, to set an external, objective regulatory standard of what constitutes sufficient severity for treatment, and instead necessary to maintain a more flexible system which allows for individual circumstances.

Similarly, some respondents argue that treatment should be widely available and not restricted to patients with the most serious illnesses only. They argue that everybody has the right to a life free from disease, and that it should not be left to a regulatory board to decide which diseases are serious enough to qualify for treatment. A number of respondents invoke an equality principle, arguing that if the treatment were made available to some patients it should be available to all.

Four respondents who chose option 1 cited personal experience of mitochondrial disease, stating that either they, or a family member, had suffered from the disease. Of these respondents, two argue that all mitochondrial disease was serious for those affected, and they do not believe that treatment should be restricted only to diseases deemed to be most severe. The other two respondents explain their choice on the grounds that the disease of which they have experience is rare and may not be covered by regulatory guidelines.

### **9.2.2 Responses to option 2 (regulatory framework; clinics and patients decide)**

Option 2 states that: ‘The regulator should decide which mitochondrial diseases are serious enough to require mitochondria replacement and, just for these diseases, permit clinics and patients to decide when it is appropriate in individual cases.’ Slightly fewer respondents (187) selected this option than option 1. Most respondents who chose option 2 emphasise that they believe clinicians and patients should have an important role in the decision-making process, but also feel that there is a need for some level of external regulatory framework. Some respondents specify that they think more regulatory oversight will be needed when the techniques are first used.

#### **The need for regulation**

A number of arguments are made for the need for a level of central regulation. Many of these arguments are based on the need to prevent abuse or overuse of mitochondria replacement treatment, and ensure that it is used only when medically appropriate and necessary. The ‘slippery slope’ argument, familiar from previous questions, resurfaces in response to this question. Some respondents argue that allowing mitochondria replacement could potentially open the gates for the rise of eugenics or ‘designer babies’, and that regulation is necessary to ensure that the treatment

is used responsibly and appropriately. Others suggest that regulation is necessary to guard against profiteering on the part of private clinics, who might be inclined to offer the treatment when not strictly necessary. Some respondents feel that the treatment, particularly in the early stages, should be used to treat those most severely affected by mitochondrial disease only, and that regulation is necessary to limit the application of the treatment:

“The technique should be regulated so it is only permitted for certain serious diseases. This would avoid it being labeled [sic] the 'slippery start of the slope' and also protect families from inappropriate/unnecessary treatment if there is no good clinical benefit to outweigh the risks.”

Individual, Other

Another set of arguments is based on the need for centralisation to ensure fairness and equity in the provision of treatment. Some respondents feel that a central regulator is the fairest way of distributing treatment, and making sure all applications for treatment are judged according to the same criteria. Some respondents raise concerns about the possibility of a ‘postcode lottery’, and argue that central regulation is necessary to ensure fairness.

A small number of respondents argue for central arbitration on the ethical questions raised by mitochondria replacement. They suggest that the complexity of the ethical questions involved means that different individuals are likely to have very different views on to what extent and when treatment is appropriate. Central regulation is therefore necessary, it is suggested, to mitigate against the subjectivity of individuals, and to ensure the same ethical standards, for example definitions of the rights and moral status of unborn children, are applied in all cases.

Several respondents draw a parallel between the regulation of mitochondria replacement treatment and Pre-implantation Genetic Diagnosis (PGD). The British Fertility Society calls for regulation of mitochondria replacement treatment to follow the model of regulation of PGD, with a regulator responsible for deciding which diseases are serious enough to warrant the treatment:

“The BFS is of the opinion that the regulator should decide which mitochondrial diseases are serious enough to require mitochondria replacement in line with current approvals for Pre-implantation Genetic Diagnosis, and permit clinics and patients to decide when it is appropriate to treat for these disorders in individual cases.”

Organisation, British Fertility Society

The Association of Medical Research Charities (AMRC) and Genetic Alliance UK echo the views of the BFS on the need for centralised regulation on which diseases should receive treatment, and also offer some suggestions for how these diseases should be identified:

“In reaching a decision on the severity of mitochondrial diseases we believe the regulator should follow the principles used in the regulation of PGD, such as peer review, use of an experienced standing committee, and of stakeholder input.”

Organisation, AMRC and Genetic Alliance UK

## Limitations on regulation

A number of issues and suggestions are raised regarding the role of the regulator, and the limitations which should be placed on centralised regulation. Many respondents emphasise that while they feel that some centralised regulation is necessary, they do not believe that a regulatory board should be responsible for making individual decisions (as proposed in option 3). The reasons for this tend to be similar to those cited in option 1. These respondents argue that it would be too bureaucratic, impersonal and time-consuming for the regulator to be involved in decisions



about individual cases. As in option 1, many respondents state that clinicians are best placed to make decisions in individual cases, and that the individual patient should have an important role in the decision-making process. It is frequently emphasised that clinics and patients should be given the freedom to make decisions about treatment within the parameters set by the regulator:

“It seems unnecessarily bureaucratic and intrusive for a regulator to review individual cases but equally some central, disinterested guidance in what diseases should be treated seems sensible.”

Individual, Family member/friend of someone affected by mitochondrial disease

A number of respondents feel that higher levels of regulation would be necessary in the early stages due to the uncharted nature of the treatment, but suggest that central regulation could be relaxed once the procedures were more established if they proved to be safe and effective.

Several respondents call attention to the need to keep regulation up to date as new diseases are discovered and new scientific developments occur. These respondents argue that the regulatory body should also be subject to monitoring and review to ensure that it keeps step with evolving knowledge of mitochondrial disease.

### 9.2.3 Responses to option 3 (regulator decides)

Option 3 proposes that: ‘The regulator should decide which mitochondrial diseases are serious enough to require mitochondria replacement and also decide, just for these diseases, when it is appropriate in individual cases’. This option proposes the highest level of centralised regulation, suggesting that an external regulator should be responsible not only for providing a regulatory framework, but also for adjudicating in individual cases. This was the least popular option, with significantly fewer (55) respondents choosing it than options 1, 2 or 4. Of the respondents who did choose option 3, many said that they did not think that the law should be changed to allow mitochondria replacement treatment, but that if it were they would choose option 3, as it offered the most intensive regulation of the treatment.

#### Arguments for high regulation

A number of arguments for high levels of regulation are put forward by respondents to this question. Many of these are similar to those addressed in option 2. As in option 2, a number of respondents argue that because of the nature of the treatment it should only be offered in the most serious cases, and that it is necessary for an external body to determine what these cases are. Many respondents report concern about the treatment being overused, and argue that central regulation is necessary to ensure that the treatment is used only when medically necessary and appropriate. As in option 2, many respondents raise concerns about private clinics being driven by a profit motive to offer the treatment in inappropriate cases, and argue that high levels of regulation are necessary to guard against this. The issue of bias or partisanship on the part of clinicians is also raised. Some people suggested that individual doctors might be biased by a personal relationship with a patient, or pressured by patients and their families, into offering treatment which was not appropriate:

“I think this area needs strict regulation to maintain public confidence, and that this extends to individual cases. I am in favour of the use of the technique and would not like to see it potentially mis-used due to pressure from patients or clinics.”

Individual, Other

It is therefore necessary, some respondents argue, for decisions about individual cases to take place at a centralised level, to ensure impartiality and guard against partisanship.

As in option 2, several respondents suggest that high levels of centralised regulation are necessary to safeguard equity and fairness. Concerns about a ‘post code lottery’ resurfaced, with a number of respondents expressing unease about differential access to treatment. Respondents suggested frequently that a centralised decision-making body would be a fairer and more effective mechanism for allocating treatment.

## Considerations

Some respondents add further comments and suggestions about the role of the regulator. Several suggest a flexible model of regulation in which treatment would be highly restricted and monitored at first, but could be relaxed over time, with more decision-making power devolved to clinicians, if the treatment proved to be safe and effective.

A number of respondents mention the need for the regulator to conduct long-term follow-up on the effects of the treatment. Some respondents cite the need for long-term review of the medical consequences of the treatment, suggesting that changes to the germ line could create unpredicted effects on future generations, which would require careful monitoring. Others cite the need for follow-up research to monitor the social and psychological consequences of the treatment for the patients and their families. The Project Group of Assisted Reproduction (PROGAR) offers some suggestions for how this follow-up research should be carried out:

“Regulation and associated research must, in our view, include central attention to psycho-social as well as medical, scientific and developmental psychology aspects. Research must include social science qualitative research, including longitudinal, to capture nuance, ambiguity and meaning to the parties directly concerned.”

Organisation, PROGAR

The role of the regulator, it is suggested, is not only to make decisions about which diseases qualify for treatment, but also to research the broader and more long-term implications of mitochondria replacement.

### 9.2.4 Responses to option 4 (mitochondria replacement should not be permitted)

Option 4 states: ‘I do not think mitochondria replacement should be permitted in treatment at all’. It differs from options 1-3, allowing respondents to register their opposition to mitochondria replacement, particularly if this meant that the other options are not relevant to them. About half of those responding to the question (551) selected option 4. Respondents tend to reiterate arguments made in response to earlier questions, particularly question 1. Many simply direct the reader to refer to their previous responses; others reiterate or elaborate on their opposition to mitochondria replacement treatment. This section will discuss responses directly related to regulation only – wider arguments against mitochondria replacement can be found in other chapters.

#### Scepticism about regulation

Many respondents who selected option 4 are sceptical about either the relevance or the effectiveness of regulation. A substantial proportion of respondents (38) state that no level of regulation could make mitochondria replacement acceptable because it is fundamentally unethical:

“I do not think mitochondria replacement should be permitted in treatment at all because regulating or licensing unethical action does not make it right.”

Individual, Other

These respondents often go on to reiterate ethical arguments against mitochondria treatment, or direct the reader to refer to their previous answers.

Others respondents raise concerns about the effectiveness of regulation, or state their scepticism that strict regulation would be maintained in the long term. Some specifically cite their lack of trust in the HFEA. There is a concern that regulation tends to relax over time, and some respondents feel that even if treatment were strictly regulated at first, regulation would gradually become less stringent and treatment more widely available. Some respondents referred to historical precedents of regulations which have become less stringent over time. Several used the regulation of abortion as a comparative example, as the following quote illustrates:

“Political safeguards are as reliable as chocolate teapots. When abortion was first legalised we were told that strong safeguards would be put in place in order to eliminate abuse. These so-called safeguards were watered down, or totally ignored, as the years went by. What we now have, in effect, is abortion on demand. The same would happen with the procedures under discussion. Any safeguards would, over the years, be watered down and then ultimately ignored.”

Individual, Student

Most respondents who selected option 4 feel that regulation would be inappropriate or ineffective and therefore feel that the law should not be changed to allow mitochondria replacement at all.

### **Other responses**

A small number of respondents who selected option 4 on the grounds that they did not want the law to be changed also indicate what kind of regulation they would choose if the law were to change. Of these respondents the majority say that they would choose option 3, on the grounds that this proposes the strictest level of centralised regulation. Four respondents say that they would choose option 2.

A number of respondents suggest that if the law were to be changed, regulation should take place at a parliamentary level. Many of these respondents cited a lack of trust in other regulatory safeguards, and raised concerns about the slackening of regulation and expanding use of techniques over time. The following quote illustrates this perspective:

“I have no confidence in regulatory bodies, as their recent history has been lamentable. Should such techniques be approved at all, I think their [sic] should be a clear set of laws limiting them, saying both what is allowed and what is not, debated and passed in parliament, with no room for ambiguity, interpretation or other erosion. The regulator's role should be to enforce the law, not interpret or soften it, or campaign for its creative reinterpretation etc.”

Individual, Student

Respondents who advocate for parliamentary regulation tend to feel that regulation enshrined in law and overseen by Parliament would be more stringent and effective, and therefore preferable to other forms of regulation.

## Chapter 10      Question 6: should the law be changed?

---

### 10.1      **Headline findings**

Question 6 asks:

**In Question 1, we asked for your views on the mitochondria replacement techniques MST and PNT. Please could you now tell us if you think the law should be changed to allow (one or both of) these techniques to be made available to people who are at risk of passing on mitochondrial disease to their child?**

1,055 people responded to this question.

The overall views of respondents in response to this question broadly reflect the views about acceptability expressed in response to question 1. Overall, 558 respondents commenting on question 6 oppose a change of law. A further 316 of respondents indicate that they support a change in the law, and 82 say that they would if their caveats are addressed. A few respondents think the law should only change for one of the proposed techniques. Only 7 respondents do not express an explicit opinion either way on whether or not the law should change, instead discussing related issues and considerations.

That the numbers reported above are not completely equal to those of respondents arguing in favour or against the techniques in their responses to question 1 is mainly a consequence of the fact that not all respondents answered all consultation questions. There are fewer than a handful of respondents each way whose comments about changing the law (question 6) are seemingly conflicting with their comments about the acceptability of mitochondria replacement techniques (question 1). Additionally, six respondents who say in response to question 1 that the techniques are acceptable if certain conditions are met subsequently argue against a change in the law when responding to question 6.

Respondents who indicate that they are personally affected by mitochondrial disease are overwhelmingly in favour of a change in the law. The same is true for respondents who indicate that they are a friend or relative of someone affected by mitochondrial disease. All in all around 95 respondents from these categories make comments in favour of a change in the law, with a dozen saying they are in favour subject to caveats.

Of respondents who indicate they have personal experience with gamete donation or donor conception, 13 say they are in favour of changing the law and three state the opposite.

Organisations in favour of changing the law include the Wellcome Trust, the Muscular Dystrophy Campaign and the Humanist Society Scotland. The British Medical Association, the Academy of Medical Sciences, the Association of Medical Research Charities and the Genetic Alliance UK, and the British Fertility Society support a change in the law in principle, but make caveats. Human Genetics Alert, the ProLife Alliance and others are against a change in the law.

## Non-questionnaire responses

A number of the 503 non-questionnaire responses contain comments about changing the law. Many of these comments are made in responses that follow a similar structure and make a range of similarly worded points. More than 200 emails and letters include a statement against a change of the law. In many cases these comments are accompanied by references to legislation in other (EU) countries, with respondents expressing concern that the UK would be the first country to cross a boundary and allow techniques that are illegal elsewhere. There are a few letters and emails with comments endorsing a change of the law.

Those respondents opposing a change in law tend, as with question 1, to focus largely on ethical concerns such as the use of embryos, and interference with the natural or spiritual aspect of reproduction.

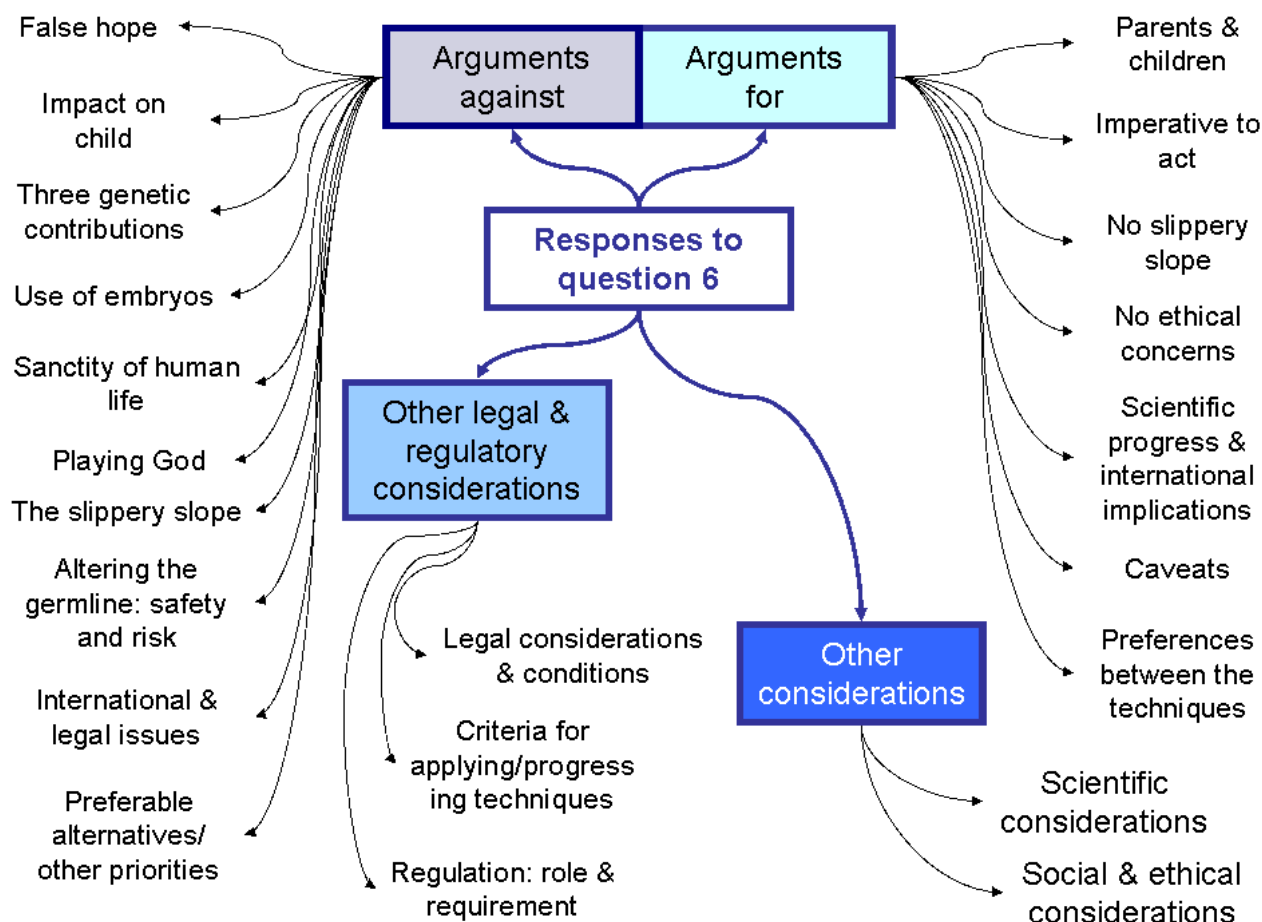
Several respondents mention a preference for other alternative approaches to addressing mitochondrial disease; others express concerns about unknown consequences. There are also concerns expressed about the slippery slope, as well as references to these techniques not currently being legal in other countries.

Those respondents supporting a change in law tend to focus primarily on the benefits the treatments could provide, particularly disease avoidance and the opportunity for parents to have a healthy child, with several discussing the impacts of mitochondrial disease on sufferers and their families. Others talk about the ethical imperative to intervene, again as in previous questions.

Where a preference is expressed for one technique in particular, this again tends to be for MST over PNT, as respondents note that this technique uses eggs rather than embryos. In total, 21 respondents state that the law should be changed to permit MST, and a further 10 agree with a caveat, compared to just one arguing for the law to change to permit PNT. Meanwhile 22 respondents argue that the law should not change to permit PNT, while none make the same case against MST.

These arguments and others raised by respondents to question 6 are explored in more detail under the subheadings reviewed below:

**Figure 11 Responses to question 6**



## 10.2 Overview of comments

### 10.2.1 Arguments against a change in law

A total of 244 respondents say that they oppose a change in law to allow one or both of the two techniques but do not explain their opposition. A number of respondents refer back to supporting arguments made in response to previous questions and some give a fuller explanation in of their opposition to a change in law in response to question 6, as summarised here. Some of these respondents make it clear that they have sympathy for those affected by mitochondrial disease but still oppose a change in law for many of the reasons outlined below.

#### Use of embryos, sanctity of human life, playing God, overall ethical issues

As with question 1, the most commonly cited argument against a change in law is that the creation and destruction of human embryos involved in these techniques (often specifically in PNT) is unethical (75). A number of comments relate to this point. These include points about the sanctity or dignity of human life being jeopardised by these techniques, as well as concerns that these techniques interfere with natural reproductive processes or would involve humans playing God.

“I object to the techniques themselves, since they involve the discarding of embryos. Human life should be respected and yet these techniques are promoting the destruction of life.”

Individual, Other

Other respondents say there are simply too many ethical or moral concerns, with a small number of comments that the end does not justify the means.

“The very fact that there are strong ethical arguments against these procedures and a large lobby against them should make the government very cautious indeed about permitting research to advance in this direction.”

Individual, Other

### **Preferable alternatives and other priorities**

Several respondents, many using similar wording, state that there are other preferable alternatives for the treatment or cure of mitochondrial disease, which should be pursued instead of these techniques (63).

“Other methods (such as repairing faulty mitochondria) are already being developed by scientists and should be examined further instead of considering PNT and MST.”

Individual, Other

Other respondents comment that people do not have an automatic right to a healthy and/or genetically related child; in relation to this, a number of other preferred options for at-risk parents are cited, including adoption, a decision not to conceive, counselling or support, and use of donor eggs.

A few respondents suggest (and these suggestions tend to be general rather than specific) that there are more pressing issues that should receive focus and/or funding over and above the progression of these kinds of techniques.

### **Altering the germ line: safety and risk**

The unknown future risks, impacts or unintended consequences of these techniques are also cited as arguments against their legalisation (57). Many of the comments made are general, for example mentioning ‘potential problems’, ‘complications’, ‘serious risks’, ‘impacts on future generations’ and so on; they also focus on both individual (e.g. health risks) and overall societal risks or impacts.

“As the risks are unknown & the potential for harm in various parameters (social etc) is high, the law should not be changed.”

Individual, Other

Some respondents say explicitly that the costs or risks of these techniques would outweigh the benefits; others talk about the impact of altering mitochondrial DNA on the germ line or genetic lineage or say that altering DNA is simply not acceptable, with some offering the view that these techniques involve cloning or hybridisation as a supporting argument for not changing the law.

### **International and legal issues**

A number of respondents, many using similar wording, note that outside the UK these techniques are not legal or can incur prison sentences. The UK would thus be the first country to cross this particular ethical boundary. Others state that the legalisation of these techniques would contravene international (for example EU or UN) law. A small number of respondents add that the UK should not be allowed to make a decision which could have a global impact.

“No, the law should not be changed. If it were, the UK would become the only country in the world to legalise such procedures and this is one area where there seems to be no benefit in being out on a limb.”

Individual, Other

A few respondents go further in saying that they think the law should be made stricter, for example by restricting the application of existing techniques involving embryos or to further discourage research into or development of any potential new techniques.

### **The slippery slope**

As in their responses to previous questions, respondents raise both general and specific concerns about the introduction of these techniques. Some see them as the start of a slippery slope with negative consequences at its end. Others mention designer babies or commodification of the human, eugenics, cloning, and the normalisation of genetic modification as specific concerns.

“If we permit these procedures which manipulate genetic information, it is possible that future genetic ‘treatments’ for cosmetic reasons will become acceptable.”

Individual, Other

### **Three genetic contributions, impact on child, false hope**

Again, as with previous questions, respondents raise concerns about these techniques involving genetic material from three people. Many of these are related to worries about interfering with natural reproductive processes or playing God by creating ‘three parent families’; others mention concern for the child’s sense of identity, and for their general or psychological wellbeing, as well as the potential for valuable individuals to be lost as a result of these techniques.

“We do not know what the psychological effects will be on a child when they learn they have three or four parents...”

...The sanctity of human life is upheld throughout the Bible. It is very clear that God intends human beings to have two parents – a mother and a father.”

Individual, Other

Some respondents question whether the techniques would actually work, suggesting that they would present ‘false hope’ to parents at risk of passing on mitochondrial disease, while others comment that these techniques are not a cure or will not necessarily eradicate mitochondrial disease.

### **10.2.2 Arguments in favour of a change in law**

A total of 170 respondents say that they would like the law to change to allow one or both of the two techniques without explaining their view. A few of respondents refer back to supporting arguments in response to previous questions and some respondents give a fuller explanation of their support in their response to question 3, as summarised here.

#### **Parents and children**

As with question 1, the most frequent argument in favour of legalising these techniques cites the importance of the health of the child, with the avoidance of mitochondrial disease being passed on, or even its eradication, being seen as a positive step.

Some respondents talk about the impact of mitochondrial disease not only on the sufferers themselves, but also on the parents and families of sufferers, several making reference to personal experience. A number of related comments refer to the benefits of these techniques for potential parents and families overall, for example through offering parents an opportunity to have a child without the worry of mitochondrial disease being passed on. A few respondents state that they think parents have a right to a healthy and/or genetically related child, which these techniques would enable.



"I believe mitochondria replacement to be the human right of the unborn children of women whose damaged mitochondria are likely to manifest in their serious ill health. The progressive and often terminal course of the conditions linked to these mitochondrial abnormalities have a devastating impact on the person and those who love and care for them.

I have watched my oldest friend deteriorate from a fun loving, happy child and teenager to an often angry, frightened and confused 30 year old who experiences drop-seizures daily and is now entirely dependent on her parents. The multi-systemic difficulties associated with mitochondrial conditions are often of late onset and families embark on a harrowing journey where they must try to adapt to each new stage of the disease before the next progression..."

Individual, Family member/friend of someone affected by mitochondrial disease

### **Ethical imperative to act, not a slippery slope, no concerns**

The imperative to intervene if the ability to do so exists is again given as a supporting argument for allowing these techniques.

"Both of these techniques should be made available to all who have need for them. It is unethical to have the technology and not to use it."

Individual, Student, Researcher

Some respondents state that they think the techniques are safe, have an acceptable level of risk, or that the benefits outweigh the risks. A few state explicitly that they have no ethical concerns or, more specifically, no concerns about these techniques representing the start of slippery slope with a negative end. In support of these statements, a small number of respondents point out that these techniques are different to those required for designer embryos or cloning (for example because nuclear DNA is not altered) or that regulation should prevent this from setting the precedent for other techniques they might find unacceptable.

### **Scientific progress and international implications**

A few respondents talk about the development of these techniques being a positive or important scientific advance or natural progress.

"These procedures are hope. They would be a dream come true. They signify years of research & the new ability to overcome genetic disease with amazing technology."

Individual, Other

Related to this are comments about the need to change the law quickly to enable the benefits of these techniques to be felt as soon as possible, and the potential for the UK to be a leader in this new area of science. A small number of respondents talk about the international aspects of these techniques, for example the suggestion that other countries would introduce these techniques if the UK did not and that UK patients or expertise may end up overseas.

### **Caveats for changing the law**

A number of respondents expressing support for a change of law either for both techniques or for MST do so only under the condition that certain caveats are met. These caveats tend to focus on specific criteria for the application of the techniques, the need for regulation, and specific legal considerations or conditions – these are covered in section 10.2.3 below. Other caveats include the need for further research, trials or evidence should these techniques progress, and the expression of a preference for MST over PNT should both techniques be found to be equally

viable. Indeed, the most common caveat for those supporting a change in law for MST only is that PNT be explicitly disallowed.

“Yes both techniques should be available initially, until such data is available to either favour one technique or establish that neither is a worthwhile avenue of treatment. This may necessitate all treatments being part of a national surveillance/tracking project to collect this data as part of a trial period.”

Individual, Researcher

### Preferences between the techniques

As discussed above, where there is a preference for one technique to be legalised over the other, the preference falls with MST over PNT. The arguments in favour of MST over PNT tend to focus on the respondent having fewer ethical concerns about MST because of the use made of embryos in PNT.

“I am in favour of MST because what I have read leads me to believe that the underlying genetic makeup or essence of a person would not be changed i.e. they would be the same person they would always have been except for the sole exception that their cells would work properly. Thus they would have an improved quality of life (as may their families) and no real identify confusion. The procedure would be equivalent to a transplant.

At the moment I am uncomfortable with PNT because two embryos are created meaning two lives could be viewed to have started yet one of them is given no chance to live and is sacrificed for the other. While others would argue an embryo is not really a life until it is several weeks old (the thinking that makes aborting permissible) I have never been comfortable with it.”

Individual, Other

### 10.2.3 Other legal and regulatory considerations

#### Other legal considerations and conditions

The Human Fertilisation and Embryology Act is mentioned a number of times in responses to this question. These response include remarks on individual respondents’ understanding of what the Act does or does not provide for in relation to this particular issue; for example that these kinds of techniques were banned under the original Act, that the Act is ambiguous, or that it does indeed provide for the development of such techniques.

Some respondents have other comments or queries about the law in relation to this topic, or the legal system more generally. These include: whether a change in law is needed; the difficulty of creating a law with no loopholes; the relationship to Scottish law; and the need for the law to protect human rights or human embryos.

Others provide suggestions for specific details, should the law be changed. These include: suggestions that the law should show a preference for a particular technique (e.g. MST in the first instance) or that the law should not specify particular techniques; comments on which diseases or types of diseases should be written into law; a comment on specifying the origin of donor DNA by law; comments on the need for careful drafting and specification of boundaries (for example specify the techniques are to be used for the treatment of mitochondrial disease only) to prevent abuse; the need for a central database of donor information; and suggestions for other changes in law in related areas of fertility and embryology.

A few respondents suggest specific legal conditions, including: only allow PNT in specific circumstances, only allow testing or trials in the first instance, allow one technique only (either,

depending on the evidence). Others say that further exploration is needed, either generally or of PNT specifically, before any change in the law is considered. These conditions or requirements are often given as caveats to support for a change in the law.

Other comments on the legal system include various comparisons with other procedures or donation types, the suggestion that the law could be re-visited after a set period if needed, and a couple of comments stressing that the law does not have a place in these decisions ahead of patient or professional choice.

### **Criteria for applying or progressing techniques**

When it comes to deciding which technique/s should be progressed to clinical use and made available to potential parents, respondents suggest a number of criteria for deciding whether to progress a specific technique, to help choose between the two techniques or to help with a decision about which cases they should be used for. The most commonly mentioned criterion is safety, closely followed by the efficacy or efficiency of the technique. Other criteria include medical evidence or advice, cost or value, patient need or appropriateness, as well as a number of other suggestions.

“PNT raises more problems for me, considering that it involves the destruction of potentially viable embryos. However, on the assumption that this would be performed at a very early stage, it might well be that the benefits are worth the worry if it becomes evident that PNT is safer and/or dramatically cheaper than MST.”

Individual, Student

Several respondents talk about criteria for who decides rather than on what basis the decision is made. For example: it should be down to the parents or the parents and clinician together to decide which technique if any to use; the decision should be down to ‘scientists’; to the regulator, or to parliament. A small number of respondents suggest that there should be no criteria or that the technique should be open to anyone who wants it.

In relation to the point about availability, there is also a small number of comments about the need for equitable provision or ease of access should these techniques become publicly available. A few respondents comment on funding and between them offer opposite arguments: that the NHS should cover these techniques, or that it should not and they should be funded privately by individuals.

### **Regulation: role and requirement**

A small number of respondents note a distinction between regulation and ethical acceptability, stating that the former does not entail the latter. One respondent notes a general lack of trust in the regulators. Aside from these comments, most of those discussing regulation in response to question 6 focus on two areas: the need for regulation and the specific roles of the regulator.

Comments on the need for regulation tend to be at a general level, i.e. regulation is needed should these techniques become legal; several respondents here use words such as ‘suitable’, ‘strict’, ‘close’ and ‘careful’ to stress the level of regulation which they feel would be required. Suggestions of specific roles for the regulator include the following: enabling provision to high-risk patients; monitoring safety; setting boundaries, producing guidelines and preventing abuse such as non-medical usage; assessing and licensing clinics; and maintaining a register of applicable diseases.

“As I stated, all these techniques have come about as a result of our ability to improve and advance ourselves. An old saying about ‘once the genie is out of the bottle...’ comes to mind. In that light I feel all of these options should be legalised and available but again under strict control from the regulator.”

Individual, Other

#### 10.2.4 Other considerations

##### Scientific considerations

Aside from the comments about scientific progress and further research outlined in 9.2.2 above, there are relatively few comments on the scientific aspects of MST and PNT compared to responses to other questions, perhaps because respondents tend to focus on the wider social and ethical arguments for or against progressing these techniques. A few respondents mention mitochondrial function and other procedures such as IVF; others talk about progress in either a cautious (for example, that there is a lack of understanding, proceed with caution) or a positive (for example expand this type of research to other diseases) light, with a small number suggesting that science should prevail or take precedence in decision making.

##### Social and ethical considerations

The number of respondents to question 6 commenting on social and ethical considerations in a more neutral manner tends to be relatively low, with most using ethical and social arguments to support their views about whether or not the law should be changed. Those respondents who do mention social and ethical issues in a more neutral manner tend to reflect on issues already covered in response to other questions. These include reflections on the rights of embryos or eggs, availability of donors, follow-up studies or monitoring, information provision and support to parents and donors, and consideration of the number of people who would benefit from these treatments.

## Chapter 11      Question 7: further considerations

---

### 11.1      **Headline findings**

A total of 883 respondents answered question 7 which asks:

**Q7: Are there any other considerations you think decision makers should take into account when deciding whether or not to permit mitochondria replacement?**

Respondents answering question 7 tend to use their response as an opportunity to do one or more of the following: reiterate arguments for or against taking forward the two techniques; discuss additional considerations they would like decision makers to take into account; or consider the wider context and overall decision-making process.

Arguments for and against the further progression of MST and/or PNT largely echo those expressed previously in response to other questions, with arguments against tending to concentrate on crossing boundaries or the creation and destruction of embryos, and arguments in favour focusing on the benefits to those at risk of passing on mitochondrial disease.

A number of the additional considerations raised by respondents in response to question 7 are also familiar from responses to previous questions, for example those focusing on social or ethical dilemmas and implications. However, there are some specific areas that receive more attention here. These include more detailed comments about the practicalities of taking forward these techniques, for example questions of regulation and criteria for application, as well as other comments about the nature of science and the need for further research and monitoring.

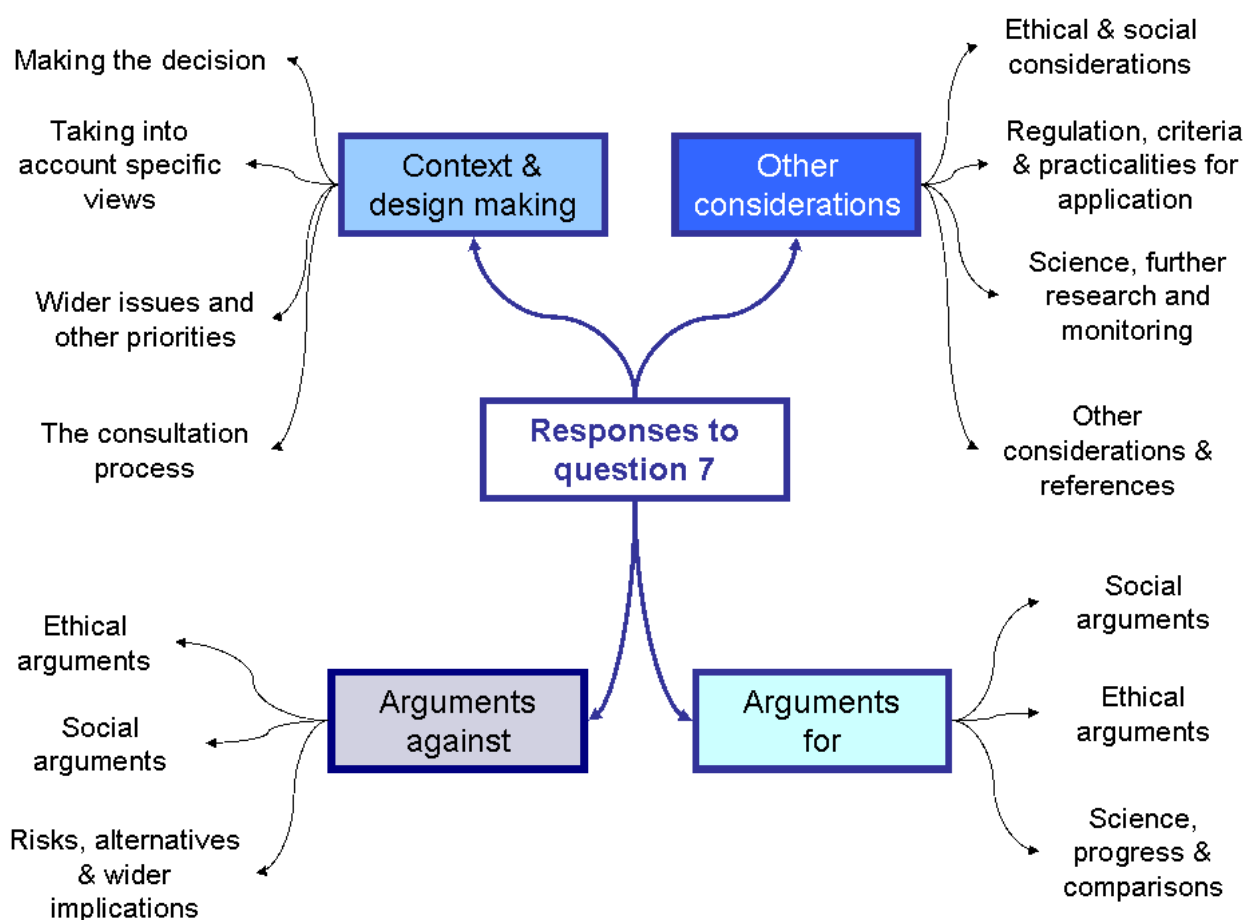
Those respondents who talk about the wider context or the decision making process in response to question 7 cover a range of issues. Some talk about the nature of the decision and the basis on which it should be made, for example with ethics at the centre, or with science at the centre. Others point out that there are wider issues that would benefit from discussion, or other priorities that require focus. A number of respondents ask that decision makers specifically consider the views of certain groups, or do not give undue weight to others. There are also some comments about the consultation itself, both positive and negative.

#### **Non-questionnaire responses**

In some of the 503 non-questionnaire responses there is mention of other treatments of mitochondrial disease, which respondents say are emerging. Overwhelmingly these comments are part of a range of similarly worded points which can be found in around 300 emails and letters. The point respondents make about other treatments is that (research into) these should be prioritised over mitochondria replacement. No specific reference is made as to what these other treatments are, or where they are being developed.

Responses to question 7 are explored in more detail in this chapter under the subheadings summarised below:

**Figure 12 Responses to question 7**



## 11.2 Overview of comments

### 11.2.1 Arguments against the introduction of the techniques

In response to this question some respondents simply state their opposition to the techniques or for a change in law, while others focus on outlining their reasons for opposition in more detail. The majority of these arguments against the two techniques reflect those appearing in response to other questions, and there are also a number of responses to question 7 containing similar text and which gives consistent sets of arguments against the techniques.

#### Ethical arguments

The most common argument given against the two techniques is the involvement of the creation and destruction of embryos, with related concerns about the sanctity of life and interfering with the natural or sacred processes of reproduction. A number of respondents talk about general concerns regarding the slippery slope argument, with others again specifying specific concerns about cloning, designer babies or commodification, and eugenics. A few respondents say that regulation would not necessarily prevent a descent along the slippery slope. Others say that the end simply does not justify the means or that there are too many ethical or moral issues to justify taking these techniques forward.

“Broadly speaking, all the currently proposed techniques involve the instrumentalisation of human life; irreversible changes to the human germ line; destruction and/or manipulation of individual human embryos; radical challenges to our understanding of individual identity.”

Organisation, LIFE Charity

### **Social arguments**

The related issues of a third person as a parent or donor (which itself is related to concerns about playing God) and the impact on the child and its identity are again the most common social arguments against MST and PNT. A few respondents add that there are just too many social issues, or that the impact on the donor (including the risk of exploitation) or on family relationships is of concern.

“The Church of Scotland welcomes the opportunity to comment on these proposed technologies. As indicated above, we are concerned not only about the specifics of these techniques, but also about the general direction in which this will drive society, and also the effective downgrading of the special status of the early human embryo.”

Organisation, Church of Scotland

“It has to be stressed that egg harvesting is not a risk-free procedure. In the process of MST, it is not clear whether the proposals would require the cycle of the donor woman to be timed to coordinate with the cycle of the woman carrying the mitochondrial disease. This would make the whole process fairly precarious in terms of timing. This would once again show how the donor is being used as an object of exploitation.”

Organisation, ProLife Alliance

There is also a common argument which arises in a number of responses to question 7: the concern that historical experience shows embryo research has consistently failed to deliver results and that these techniques would therefore be offering false hope to a vulnerable group of people, and/or that mitochondrial disease would not be eradicated.

### **Risks, alternatives and wider implications**

Another very common response to question 7 is that scientists are already working on other techniques for addressing mitochondrial disease and that these should be pursued instead of MST or PNT. As with previous questions, some respondents state that people have no right to a healthy and/or genetically related child, and a number of preferred alternatives are cited; these include use of donor eggs and adoption.

Unintended or unknown future risks, consequences and impacts are again a concern for a number of respondents. This includes the risks of altering the germ line, with some respondents stating that these techniques involve cloning, and others highlighting the unacceptability of altering DNA at all. There are also concerns that, just because a technique is possible, this does not automatically mean it should be used, and that our current scientific understanding here is limited. The role and motivation of scientists is also of concern to a number of respondents.

As with previous questions, concern is expressed that these techniques are not legal anywhere else (and indeed could result in a prison sentence) and that the UK would be the first to cross this boundary. Some respondents say this is not the UK's decision to make without considering worldwide consequences, or that they are concerned regulation would not be consistent should these techniques become widely available.

Finally, other respondents touch on the cost of these techniques; either specifically that they are too expensive to be justified, or more broadly that there are other issues which should be prioritised. There are also comments expressing concern that the techniques would lead to an increase in population.

### **11.2.2 Arguments for the introduction of the techniques**

In response to this question some respondents simply state their support for the techniques or for a change in law, while others outline their reasons for support in more detail. The majority of these arguments in support of the two techniques again reflect those appearing in response to other questions, and are summarised below.

#### **Social arguments**

The most common argument in favour of the two techniques in response to question 7 is the degree to which mitochondrial disease causes suffering and affects both sufferers and their families, with many citing personal experience. Related to this are a number of other common responses about the benefits to the health of the child and to potential parents or families, as well as the avoidance or eradication of the disease being a good thing. The potential for these techniques to reduce the overall burden on services, including the NHS, is also mentioned by some respondents.

#### **Ethical arguments**

As with previous questions, the imperative to 'help if we can' is the most common ethical argument in favour of MST and PNT. A few respondents state that people have a right to a healthy and/or genetically related child. There are also some more general comments from respondents who have no concerns about the slippery slope specifically, or about ethics more widely, with a couple of comments again favouring MST over PNT because of less involvement of embryos in the former.

#### **Science, progress and comparisons**

Again, some respondents talk about the positive aspect of the two techniques either in terms of general scientific progress or their potential to lay the foundations for other new treatments (either for mitochondrial disease or other conditions). A few respondents suggest that the UK could be the leader in these new techniques, that it is natural progress, or that the underlying science should be allowed to progress as far as it can.

In terms of risks and benefits, some respondents explicitly state they are satisfied that the techniques are safe, that the risks are acceptable or that the benefits would outweigh the costs or other considerations. In addition, a few respondents suggest that these techniques would be preferable to other existing options, or simply that there is no reason not to allow them to progress.

"Objections have been raised against these techniques on the grounds that mitochondrial donation, and germline alterations to DNA, are "unnatural". However, all medical interventions, including transplants, antibiotics, vaccines and even setting of broken bones, are to a greater or lesser extent unnatural. What these procedures, and mitochondrial donation, have in common, is that they offer the potential for humanity to overcome the cruelties of nature, and to offer people affected by disease the chance of a healthier life.

When new medical treatments are given to human beings for the first time, it is never possible to be certain that these will be 100 per cent safe or effective. Even the most exhaustive research can establish only that a technique is sufficiently likely to be safe to justify first-in-man clinical use in a research setting. If medicine is to progress, however, doctors must be permitted to use new techniques when evidence suggests these are



indeed sufficiently safe and effective to use on patients for the first time. In the case of mitochondrial donation, there will be much more evidence for safety and effectiveness available before the first clinical use than was available for many other techniques, such as organ transplants and IVF.”

Organisation, Wellcome Trust

### 11.2.3 Other considerations

Aside from those respondents who do not give any response to question 7, a number explicitly state there are no further considerations beyond what they have already said, while a few say they do not know. Some respondents compare the considerations for mitochondria replacement to those for other existing treatments or techniques, for example IVF. Other considerations and wider issues raised by respondents are summarised here and in section 11.2.4.

#### **Ethical and social considerations**

A number of ethical and social considerations appear in response to question 7, all of which have also appeared in response to previous questions. The most common ethical considerations in response to this question are around consideration of the slippery slope argument (including comments that these techniques are different from those which would be required for cloning or designer babies) and equity of provision. The most common social considerations in response to this question include consideration of overall societal impact, impacts on future generations, the number of people for whom the techniques would be relevant, and the effect these techniques might have on society’s attitudes towards disabled people in general or sufferers of mitochondrial disease in particular.

#### **Regulation, criteria and practicalities for application**

Several respondents discuss regulation in response to this question. Other than saying it is needed (although there is one respondent who says this kind of research should not be subject to government regulation), there are a number of specific suggestions for regulation. These include the role of the regulator in limiting the application of the techniques and ensuring practitioners do not overstep certain boundaries, as well as other roles such as building in a review process (e.g. for newly classified diseases), prescribing the list of diseases, balancing control with flexibility, regulating clinics and physicians, ensuring provision of counselling, and providing guidelines or a code of practice.

“If these techniques are introduced, we wish to see protection and promotion of the autonomy of the various parties that may be affected. This may require additional stipulations beyond current safeguards on matters such as counselling and information for couples and donors. At present, those seeking licensed assisted reproduction treatments in the UK are offered, under the HFEA act, “proper” information and a “suitable opportunity to receive proper counselling about the implications” of the treatment. If introduced, the provision of cell reconstruction treatments should follow this model. Furthermore, given the complex nature of mitochondrial inheritance and the issues of novelty around reconstructing embryos, we suggest that while the initial discussions about the procedure could be within a routine setting, there should be further opportunity offered for prospective parents to speak to a specialist with appropriate training and up to date information in a dedicated unit accustomed to dealing with mitochondrial disorders (paragraphs 5.9-5.10).

We believe that in the first instance that PNT and MST (or any comparable future treatment) should only be offered as part of a research trial in centres specialising in mitochondrial disorders. Consent to follow up would need to be included as a mandatory part of parental consent to participating in the trial (paragraph 5.6).…”

A few respondents talk specifically about international regulation, for example concerns that if the UK does not take these techniques forward then other countries with less rigorous controls in place may do so and that UK patients may go abroad for treatment, or that it might be difficult to follow up patients coming from abroad to receive treatment in the UK.

As with question 6, some respondents suggest a number of criteria for deciding whether to progress a specific technique, to help choose between them or to help decide on which cases they should be used for. Safety and success rate/efficacy/efficiency of the technique are again the most commonly mentioned criteria, with the addition of seriousness of disease or risk to the child, cost or value, medical evidence or advice, family situation or ability to provide, patient need or appropriateness, and others. The parents or the parents and clinician together, and the regulator, are again mentioned as potential decision makers for who is eligible and for which technique. Others mention the need for a national screening programme to determine eligibility for treatment.

“How do we know whether or not we have mitochondrial disease? There needs to be a national screening programme. My family only found out that this disease existed, and that others in the family are at risk, after losing a family member to it. Screening in pregnancy should be mandatory in order to eradicate this disease.”

Individual, Family member/friend of someone affected by mitochondrial disease

In terms of practicalities, the question of who would pay for the treatments is raised by a number of respondents, some of whom say explicitly that the NHS should or should not fund treatment. The need to explore the question of commercial benefits to clinics in offering these techniques is also mentioned by a few respondents. The requirement for patients to receive a good level of information and involvement in the decision, as well as the availability of support and counselling, is a common suggestion. In addition, a small number of respondents discuss donor considerations, such as recruiting and screening donors, storing records of donations and whether or not to pay donors.

### Science, further research and monitoring

A number of respondents discuss the need either for further research, trials or evidence if or as the techniques progress further, or for follow-up studies and monitoring of patients who undergo the procedure/s. There are also some more disparate comments about science in general or in relation to this particular decision.

“Our economy could benefit from a stronger more proactive scientific and technological sector. This could benefit everyone - present and future.”

Individual, Other

“The more information which comes to light about the physical and emotional outcomes from all forms of assisted reproduction, the more it becomes apparent that it is a branch of medicine which seriously conflicts with the Hippocratic oath: “First do no harm”. Scientists are proposing a new and convoluted form of IVF procedure when finally, after 30 years, emerging studies are showing what some of us have worked out for ourselves, despite regular denials from the industry, that babies born through standard IVF are 25% more likely to have birth defects. The use of IVF, with or without the use of donor gametes, should be discouraged.”

Individual, Personal experience of egg, sperm or embryo donation or donor conception

“Decision makers should consider that they will have significant power to influence the course of science in this field.

If allowed, we should make all effort to succeed in the trials (while not obscuring good science) as a simple lack of diligence can cause the door to shut on all therapies of this kind.”

Individual, Student, Researcher

Others mull on the motivations of scientists and the progress made so far, as highlighted by the range of comments below:

“The drive to research these problems that a handful of members of our society face is caring. The possibility that dark forces are at work attempting to subvert society should be rejected as the silly work of over active imaginations.”

Individual, Other

“Those in the medical profession must be humble and seeking the benefit of patients and not personal glory.”

Individual, Other

“I think that the decision makers should take into account that this is not a cure in the traditional sense but should be viewed as preventative medicine at its most advanced.”

Individual, Family member/friend of someone affected by mitochondrial disease, Other

### Other considerations and references

A small number of respondents reflect back on previous responses about donation status and the nature of information received by the child who is produced as a result of this treatment. Others discuss scientific aspects of the techniques, for example: the nature of mitochondria and mitochondrial DNA; other procedures; and the variety of forms of mitochondrial disease.

Similar to responses to previous questions, many respondents make reference to the views of other people generally or other specific individuals and groups, religious views, government and the HFEA. Others comment on the role of the media, either in reference to specific coverage of this issue they have seen or heard, or to the way the issue tends to be framed. The need for a clear, neutral coverage of the facts is suggested by some; and there is also the suggestion from a few respondents that reporting of the techniques so far has been misleading in one way or another:

“The decision makers must consider the significant benefit to the lives of the parents and the child that avoid mitochondrial diseases whilst rising above the sloppy journalism citing 3 parents. The techniques being discussed here DO NOT create 3 parents...”

Individual, Other

Other respondents cite relevant research, documents or websites in support of their responses, as with responses to other questions.

## 11.2.4 Context and decision making

### Making the decision

As well as some questions about who will be making the decision and on what grounds, there are a number of comments on the nature of overall decision to be made in response to question 7, with some respondents recognising that this is a complex decision covering new or difficult territory. Others call for rational and objective consideration of the issue, the need to weigh up the overall risks with benefits or net gain, and the need to humanise the issue away from “cold ethical debate”. On a similar note, the question of whether science or ethics should be central to the decision making process is raised by some respondents:

“The ethical questions should take precedence over the scientific considerations.”

Individual, Other

“I hope that the decision will be taken on consequentialist grounds, following the consensus of the scientific community.”

Individual, Other

The speed of implementation, should a decision to proceed be made, also elicits varied views from those few respondents who comment on it, with some calling for a speedy progression and others for caution:

“It is not urgent in the scheme of things to proceed now, there are many benefits from waiting.”

Individual, Other

“It would be a shame to see one such as this, which has so many benefits andrew [sic] if any drawbacks, not be put into effect as soon as possible.”

Individual, Other

### Taking into account specific views

Primarily in support of their views in support of or opposition to the two mitochondria replacement techniques, a number of respondents suggest that decision makers should talk to or take into account the views of particular groups or people, or that undue weight should not be given to particular views. Illustrating a similar tension as the science/ethics question outlined above, some respondents would like the views of different religious groups or of people with firsthand experience of mitochondrial disease to be specifically listened to; some are also concerned that vocal objections, for example based on ethics or religion, should not overshadow the views or needs of those who would benefit from these treatments.

Examples of specific viewpoints some respondents would like decision makers to take into account:

“The decision makers should talk to people who actually suffer from mitochondrial disease. So little is known about it that even when you talk to some doctors about it, they have never heard of it. The people who make the decision cannot make a proper decision without knowing all the facts, it is a rare disorder most people haven’t got a clue what it does to you and how it makes you feel, they need to know.”

Individual, Personally affected by mitochondrial disease

"People who know more about the treatments should visit people with different religious views and they should take note on their views. The older generations should be questioned too."

Individual, Student

"I think that if everyone was made to talk to and interact with parents of disabled children they will find out a lot more than just thinking they know from seeing it from a distance."

Individual, Other

"The views of the wider population should be considered and upheld at all times."

Individual, Other

"I would want consultation with disabled people and stakeholders to ask what they think of this as well - not just 'normal' people who see disability as a terrible dark thing to be avoided."

Individual, Personally affected by mitochondrial disease, Family member/friend of someone affected by mitochondrial disease

Examples of specific viewpoints some respondents would like decision makers not to give undue weight to:

"Many people will have philosophical objections to these procedures; based on abstract ideas of what it means to be human, religious concerns about 'playing god', worries about what may possibly lie in the future if we take a step in this direction. While these are all relevant considerations, and issues for society to discuss honestly, these concerns of the majority should not be given undue weight against the real needs of the minority who actually suffer from this disease, those who will suffer the consequences of a decision to deny this treatment. Similar issues surround the introduction of other medical advancements, from medicines to transplants, but the health and quality of life of the vulnerable and the individual is more important than the abstract concerns of others - the same approach should be taken here."

Individual, Other

"If individual families have objections they will not have the treatment. Those who object should not be allowed to deny access to others who could benefit."

Individual, Other

Other observations:

"I believe that there is a high correlation between those who do not approve of Mitochondrial Replacement [sic] and those who do not understand either the science behind it or the impact of Mitochondrial Disease upon individuals and their families.

Interestingly, a handful of people commenting on this topic on the BBC website today revealed that they themselves suffered from genetic disorders, including Mitochondrial Disease.

Perhaps surprisingly, all but one stated that they were very much in favour of Mitochondrial Replacement with only one commenting that they found the idea of eradicating genetic disorders to be personally insulting to them.”

Individual, Family member/friend of someone affected by mitochondrial disease

### **Wider issues and other priorities**

Aside from those respondents who focus on other issues or alternatives as part of their opposition to the two techniques, there are also some more neutral comments about wider issues which would be useful topics for further debate or consultation, as well as other societal priorities which respondents feel might be worth looking at either alongside or in preference to mitochondria replacement.

The wider issues mentioned as potential topics for further consultation are fertility treatments, genetic disease more generally, pre-implantation techniques and the use of animals in research. Other priorities suggested as being worth consideration are other health or research priorities more generally, the concept of family, mitochondrial disease diagnosis and/or other treatment avenues, poverty, and psychological or psychiatric care.

### **The consultation process**

Several respondents comment on the consultation process in response to this question. Whilst some say they welcome the consultation and the chance to input or provide other positive comment, others question the neutrality of the consultation or provide other negative comments (for example about poor publicity, bad timing, cost or lack of information). There are also a few specific comments and suggestions about the questions and response form.

“This consultation is extremely premature, since the experiments on safety are years away from being completed. A 10 week consultation period accompanied by as little overall public discussion as other HFEA consultations usually attract is radically inadequate to dealing with the seriousness of the issues posed by human germ line modification.”

Organisation, Human Genetics Alert

Finally, there are a number of comments about follow-up to the consultation. Aside from requests for specific information, these primarily focus on the need for further communication and public education about mitochondria replacement and surrounding issues, including comments on the need for wider debate of the issue (for example utilising more social media) and the ongoing role for the media.

“There needs to be very clear explanations of the technique itself and explanations of the role of mitochondrial DNA made available to the press to help to combat sensationalist reporting. Examples of the significant value of the technique to families carrying mitochondrial diseases [sic] which can be dealt with by the technique also should be well publicised.”

Individual, Other

# Appendix

---

## A.1 Consultation questions

### 1. Permissibility of new techniques

Having read the information on this website about the two mitochondria replacement techniques – maternal spindle transfer and pro-nuclear transfer, what are your views on offering (one or both of) these techniques to people at risk of passing on mitochondrial disease to their child? You may wish to address the two techniques separately.

### 2. Changing the germ line

Do you think there are social and ethical implications to changing the germ line in the way the techniques do? If so, what are they?

### 3. Implications for identity

Considering the possible impact of mitochondria replacement on a person's sense of identity, do you think there are social and ethical implications? If so, what are they?

### 4. The status of the mitochondria donor

a) In your view how does the donation of mitochondria compare to existing types of donation? Please specify what you think this means for the status of a mitochondria donor.

b) Thinking about your response to 4a, what information about the mitochondria donor do you think a child should have? (Choose one response only)

- The child should get no information
- The child should be able to get medical and personal information about the mitochondria donor, but never know their identity
- The child should be able to get medical and personal information about the mitochondria donor and be able to contact them once the child reaches the age of 18
- Other
- I do not think mitochondria replacement should be permitted in treatment at all

Please explain your choice.

### 5. Regulation of mitochondria replacement

If the law changed to allow mitochondria replacement to take place in a specialist clinic regulated by the HFEA, how should decisions be made on who can access this treatment? (Choose one response only)

- Clinics and their patients should decide when mitochondria replacement is appropriate in individual cases
- The regulator should decide which mitochondrial diseases are serious enough to require mitochondria replacement and, just for these diseases, permit clinics and patients to decide when it is appropriate in individual cases

- The regulator should decide which mitochondrial diseases are serious enough to require mitochondria replacement and also decide, just for these diseases, when it is appropriate in individual cases
- I do not think mitochondria replacement should be permitted in treatment at all

Please explain your choice.

## **6. Should the law be changed?**

In Question 1, we asked for your views on the mitochondria replacement techniques MST and PNT. Please could you now tell us if you think the law should be changed to allow (one or both of) these techniques to be made available to people who are at risk of passing on mitochondrial disease to their child?

## **7. Further considerations**

Are there any other considerations you think decision makers should take into account when deciding whether or not to permit mitochondria replacement?



## A.2 Responding organisations

List of responding organisations
Affinity
Alliance for Humane Biotechnology
AMRC and Genetic Alliance UK
Anscombe Bioethics Centre
Association of Clinical Embryologists (ACE) Executive Committee
British Federation of Women Graduates - Northern Region
British Fertility Society
British Heart Foundation
British Medical Association
Cardiff Sixth Form College
CARE
Cathedral School Llandaff
Catholic Parliamentary Office
Centre for Genetics and Society
Christian Concern
Christian Concern & The Christian Legal Centre
Christian Medical Fellowship
Church of England: Mission and Public Affairs Council
Church of Scotland
Clinical Ethics Committee, University Hospitals of Leicester NHS
Comment on Reproductive Ethics (CORE)
Cornwall's Community Standards Association
East Hampshire District Councillor
Escher Fund for Autism
Fareham Community Church
Free Church of Scotland
Friends of the Earth United States and Friends of the Earth England, Wales and Northern Ireland
Galway for life
HEAL UoS (Health Ethics and Law, University of Southampton).
Horsley Evangelical Church
Howell's School Llandaff
Human Genetics Alert

<b>List of responding organisations</b>
Humanist Society Scotland
International Center for Technology Assessment
Islamic Medical Association/UK and on behalf of the Society of Muslim scholars
Justice et Solidarite Mondiales
LIFE Charity
Morality Forum
Muscular Dystrophy Campaign
National Council of Women
National Gamete Donation Trust
Newcastle University
No Less Human
North East Scotland Youth For Christ
Nuffield Council on Bioethics
Our Bodies Ourselves
Porter Dodson Solicitors &Advisors
Pro Life Alliance
Pro-Choice Alliance for Responsible Research
PROGAR
Progress Educational Trust
ProLife Alliance
RedBridge People First
Resident Community of Pilgrims Hall Christian Centre
Retired
Right To Life
Royal College of Obstetricians and Gynaecologists
Royal College of Physicians
Scottish Council on Human Bioethics
Scottish Council on Human Bioethics
Society for the Protection of Unborn Children
Spring Road Evangelical Church
St Bernadette's Catholic Church, Larbert, Stirlingshire
The Academy of Medical Sciences
The Christian Institute

<b>List of responding organisations</b>
The Lily Foundation
Trinity Grace Church, Ramsbottom
University Hospitals of Leicester NHS Trust (Clinical Ethics Committee)
Wellcome Trust
Women and Medical Technologies

### A.3 Analysis: List of themes

Theme	Acronym
Acceptability	AC
Arguments against	AG
Arguments in favour	FA
Considerations	CO
Consultation process	CP
Decision making	DM
Donation status	DS
Information	IN
Legal Status	LS
Other	O
References	RF
Science	SC
Social and ethical	SE

## A.4 Analysis: List of codes applied per question

The tables below list the themes and codes applied to the text of responses to each question of the consultation and the number of times that each code was used.

### 1. Permissibility of new techniques

Having read the information on this website about the two mitochondria replacement techniques – maternal spindle transfer and pro-nuclear transfer, what are your views on offering (one or both of) these techniques to people at risk of passing on mitochondrial disease to their child? You may wish to address the two techniques separately.

Code	Count
AC - Acceptable - MST	20
AC - Acceptable - MST and PNT/general	349
AC - Acceptable with caveat - MST	3
AC - Acceptable with caveat - MST and PNT/general	106
AC - Acceptable with caveat - PNT	3
AC - Not acceptable - MST	2
AC - Not acceptable - MST and PNT/general	502
AC - Not acceptable - PNT	24
AC - Not sure - MST and PNT/general	3
AC - Not sure - PNT	2
AC - Overall - not for me to decide	4
AC - Overall - unable/not qualified to answer	5
AC - Overall - understand issue/have sympathy	32
AC - Overall - unsure/no strong view	4
AC - Preference - MST over PNT	72
AC - Preference - no preference	12
AC - Preference - PNT over MST	11
AG - Altering DNA - cloning/hybridisation	46
AG - Altering DNA - impact on germ line/lineage	109
AG - Altering DNA - not acceptable	41
AG - Costs/risks - outweigh benefits	42
AG - Disease - will not be eradicated/not a cure	9
AG - Donation - risk/exploitation	31
AG - Ethics - egg (mainly MST) creation/destruction	22
AG - Ethics - embryo (mainly PNT) creation/destruction	232
AG - Ethics - end does not justify means	23
AG - Ethics - general/too many ethical issues	56

Code	Count
AG - Ethics - interfering with evolution/playing god	70
AG - Ethics - judging value/worth of life (particularly PNT)	13
AG - Ethics - lack of consent/choice	16
AG - Ethics - no right to healthy/genetically related child	20
AG - Ethics - other comment	18
AG - Ethics - sanctity/dignity of human life	101
AG - Ethics - UK first in crossing ethical boundary	21
AG - Future - risks/impacts/unintended consequences	160
AG - MST - could be more emotionally difficult	2
AG - MST & PNT - both involve IVF/embryo destruction	68
AG - PNT - ethically worse	30
AG - PNT - riskier/no guarantee of survival	4
AG - Population - artificially selected/GM	7
AG - Population - too big/would increase	4
AG - Preferable alternative - adoption	26
AG - Preferable alternative - counselling/support	1
AG - Preferable alternative - decide not to conceive	10
AG - Preferable alternative - donor eggs	12
AG - Preferable alternative - education	1
AG - Preferable alternative - other treatment/cure of MD	79
AG - Preferable alternative - other/general	19
AG - Preferable alternative - screening eggs/embryos	5
AG - Regulation - may not be consistent across the board	1
AG - Science - false hope/may not work	24
AG - Science - just because it is possible does not mean it should be done	13
AG - Science - role/motivation of scientists	10
AG - Science - understanding is limited	33
AG - Slippery slope - attitudes to euthanasia	2
AG - Slippery slope - cloning	35
AG - Slippery slope - concerns	34
AG - Slippery slope - designer babies/commoditisation	71
AG - Slippery slope - eugenics	49
AG - Social - general/too many social issues	6
AG - Social - hardship is natural/contributes to strength of society	3
AG - Social - impact on child/identity/psychology	85

Code	Count
AG - Social - impact on donor/donor considerations	14
AG - Social - impact on family relationships	13
AG - Social - impact on parents	8
AG - Social - legal implications/scenarios	7
AG - Social - other comment	7
AG - Social - prioritise other issues/solutions	10
AG - Social - third person as parent/donor	129
AG - Social - worth of MD sufferers/disabled people	17
AG - Wider issue - against artificial fertilisation	10
CO - Alternatives - encourage/make adoption easier	3
CO - Alternatives - other comment	9
CO - Availability - NHS cover	4
CO - Availability - NHS should not cover/fund privately	5
CO - Business interest/involvement	4
CO - Cost/funding - general/who pays	11
CO - Criteria - cost/value	12
CO - Criteria - medical evidence/advice	16
CO - Criteria - other	6
CO - Criteria - parent/patient choice	30
CO - Criteria - patient need/appropriateness	17
CO - Criteria - safety	57
CO - Criteria - success rate/efficacy/efficiency	66
CO - Donation - availability/origin	2
CO - Donation - like organ/blood	1
CO - Donation - like sperm/egg/IVF	4
CO - Donor status - record identity	3
CO - Donor status - rights/responsibilities	8
CO - Embryo or egg rights/life - concern	23
CO - Embryo or egg rights/life - general/other	26
CO - Embryo or egg rights/life - not a concern	10
CO - Ethics - different to designer embryos/cloning	11
CO - Ethics - interfering with evolution/playing god	3
CO - Ethics - lack of consent/choice	4
CO - Ethics - other comment	20
CO - Ethics - where to draw the line with screening/modification	8

Code	Count
CO - Identity - child access to information	5
CO - Identity - child should know about conception	2
CO - Identity - concerns	6
CO - Identity - no concerns	2
CO - Labelling of techniques - misleading/misunderstood	6
CO - MST - could be more publically/ethically acceptable	27
CO - MST - other consideration	4
CO - MST & PNT - other comparative comment	11
CO - MST & PNT - see no/little difference	20
CO - Patients - follow up studies/monitoring	5
CO - Patients - information provision/involvement	25
CO - Patients - may go elsewhere/abroad	1
CO - Patients - rights/responsibilities	1
CO - Patients - support/counselling	1
CO - PNT - other consideration	5
CO - PNT - potentially controversial	10
CO - PNT - use of spare embryos	5
CO - Population - could increase	1
CO - Regulation - limitation of use	3
CO - Regulation - needed	18
CO - Regulation - other comment	5
CO - Regulation - would prevent slippery slope	7
CO - Safety - evidence insufficient	14
CO - Safety - risks is always present with medical procedures	6
CO - Safety - risks vs benefits	14
CO - Science - alternative/additional suggestion	5
CO - Science - further research/trials/evidence	56
CO - Science - mitochondrial function	12
CO - Science - other comment	19
CO - Science - participant understanding	12
CO - Science - should prevail	10
CO - Slippery slope - designer babies/commoditisation	14
CO - Slippery slope - eugenics	1
CO - Slippery slope - general	9
CO - Social - child emotional/psychological impact	7



Code	Count
CO - Social - impact on future generations	4
CO - Social - insurance considerations	2
CO - Social - legal considerations	14
CO - Social - number of cases	14
CO - Social - parents should not be pressurised	6
CO - Social - risk losing valuable individuals	2
CO - Social - third person as parent/donor	10
CO - Social - worth of MD sufferers/disabled people	2
CP - Consultation - challenge information/data	4
CP - Consultation - comment on question	5
CP - Consultation - lack of information	4
CP - Consultation - outcomes	1
CP - Consultation - participants not qualified	2
CP - Consultation - question motivations/bias	4
CP - Consultation - specific information	3
CP - Follow-up - further consultation	6
CP - Follow-up - further info on specific topic/s	1
CP - Follow-up - further info would help form opinion	6
CP - Follow-up - please keep informed	1
CP - Follow-up - public communication/education	2
CP - Website - difficulty	1
CP - Website - general	8
CP - Website - lack of information	2
CP - Website - positive comment	1
CP - Website - video	3
FA - Benefits - outweigh cost/other considerations	25
FA - Cost - no concerns	1
FA - Disease - avoidance important/positive	69
FA - Disease - eradicate	35
FA - Disease - impact on families/sufferers	15
FA - Disease - risks of passing on	11
FA - Disease - scale of suffering underestimated	3
FA - Donation - like organ/blood	8
FA - Donation - like sperm/egg/IVF	2
FA - Ethics - ethical imperative to intervene	30

Code	Count
FA - Ethics - no concerns	40
FA - Ethics - right to healthy/genetically related child	25
FA - Identity - compare to sperm/egg donation	3
FA - Identity - no concerns	10
FA - MST - destroying eggs no concern	10
FA - MST - does not destroy embryos	35
FA - MST - fewer ethical concerns	10
FA - MST - less wastage of genetic material/does not involve father	2
FA - MST - like organ donation	2
FA - MST - might be easier/more efficient	7
FA - MST - other comment in favour	5
FA - MST and PNT - better/alternative to current options	11
FA - MST and PNT - not different from existing practices	7
FA - PNT - fewer ethical concerns	2
FA - PNT - involves the father/normal inheritance better	4
FA - PNT - less risky	2
FA - PNT - more robust/better success rate/economic sense	6
FA - PNT/general - similar to IVF/donation ethically	8
FA - Safety - techniques are safe/risks acceptable	3
FA - Science - could lead to new treatments (MD or other diseases)	4
FA - Science - important/positive	30
FA - Science - natural progress	8
FA - Science - no concerns	3
FA - Science - no genetic traits are passed on	10
FA - Science - nuclear DNA not altered	7
FA - Science - origin of mitochondria/not human	3
FA - Science - other comment	5
FA - Science - UK as a leader in new techniques	3
FA - Slippery slope - not a concern	21
FA - Social - benefits to potential parents/families	80
FA - Social - general benefit to society/public health	13
FA - Social - genetic parentage/no third parent issues	11
FA - Social - health/wellbeing of the child	97
FA - Social - poor provision of care for sufferers	1
FA - Social - reduces burden on services/NHS	4

Code	Count
O - Blank response/no comment	2
O - Refer to other question	6
RF - Culture/literature	2
RF - Current legislation	20
RF - Current legislation - non UK	36
RF - External document	6
RF - External event/discussion	2
RF - HFEA	14
RF - Historical experience	14
RF - Media coverage	3
RF - Participant - friend/relative/child with MD/similar disease	40
RF - Participant - has MD/similar disease	20
RF - Participant - info about	51
RF - Participant - other medical details	12
RF - Participant - personal details	4
RF - Politics/government	19
RF - Relevant research	14
RF - Religion	43
RF - Scientific review panel	3
RF - Specific individual/organisation/group	8
RF - Views of other people/participants	30

## 2. Changing the germ line

Do you think there are social and ethical implications to changing the germ line in the way the techniques do? If so, what are they?

Code	Count
AC - Acceptable - MST and PNT/general	1
AC - Not acceptable - MST and PNT/general	4
AC - Overall - unsure/no strong view	1
CP - Consultation - challenge information/data	2
CP - Consultation - comment on question	3
CP - Consultation - lack of information	1
CP - Consultation - other comment	1
CP - Consultation - other positive comment	1
CP - Consultation - participants not qualified	2
CP - Consultation - question motivations/bias	2

Code	Count
CP - Consultation - specific information	1
CP - Consultation - welcomed	2
CP - Follow-up - further consultation	7
CP - Follow-up - further info on specific topic/s	2
CP - Follow-up - other comments	1
CP - Follow-up - public communication/education	9
CP - Website - video	2
O - Blank response/no comment	3
O - Other/general comment	2
O - Refer to other question	34
RF - Current legislation	5
RF - Current legislation - non UK	55
RF - External document	2
RF - External website	4
RF - HFEA	7
RF - HFEA - website	3
RF - Historical experience	19
RF - Media coverage	3
RF - Other evidence/examples	3
RF - Participant - friend/relative/child with MD/similar disease	9
RF - Participant - has MD/similar disease	6
RF - Participant - info about	11
RF - Participant - other medical details	4
RF - Participant - personal details	1
RF - Politics/government	6
RF - Relevant research	6
RF - Religion	40
RF - Specific individual/organisation/group	10
RF - Views of other people/participants	50
SC - DNA - mutates anyway over time	7
SC - DNA - natural mixing	7
SC - DNA - nuclear DNA/genome not affected	39
SC - DNA - other comment	5
SC - Germ line - could reduce in diversity	4
SC - Germ line - diversity/mixing is beneficial/genetic advantage	4

Code	Count
SC - Germ line - not significantly changed	7
SC - Germ line - ok to alter	22
SC - Germ line - other comment	39
SC - Germ line - should not be altered	22
SC - Germ line - will be repaired/not enhanced	5
SC - Mitochondria - function/form	18
SC - Mt DNA - does not determine identity/traits	38
SC - Mt DNA - keep faulty DNA for posterity	2
SC - Mt DNA - maternal/female line	19
SC - Mt DNA - may affect identity/traits	10
SC - Mt DNA - origin/not human	3
SC - Mt DNA - other comment	24
SC - Mt DNA - quantity/impact too much	2
SC - Mt DNA - small quantity/impact	30
SC - Mt DNA - suggested source for donation	7
SC - Other procedures - abortion/termination	5
SC - Other procedures - adoption	16
SC - Other procedures - genetic techniques/gene therapy	6
SC - Other procedures - IVF/egg or sperm donation/surrogacy	46
SC - Other procedures - not conceiving	4
SC - Other procedures - organ/tissue/blood donation	21
SC - Other procedures - other/general	5
SC - Other procedures - stem cell donation	4
SC - Other procedures - vaccination	4
SC - Overall - addition/alternative suggestions	3
SC - Overall - balancing science/ethics/religion/society	5
SC - Overall - further research/trials/evidence	14
SC - Overall - invest in other priorities/solutions	18
SC - Overall - motivation of scientists	5
SC - Overall - nature of medicine/science	17
SC - Overall - object to infertility treatment	4
SC - Overall - one-off/single generation treatment	3
SC - Overall - other comment	21
SC - Overall - restricting to male births	4
SC - Overall - trust/mistrust of scientists	18

Code	Count
SC - Overall - understanding is limited	19
SC - Progress - has gone too far to stop now	2
SC - Progress - natural consequence/function of humanity	10
SC - Progress - other comment	5
SC - Progress - possibility does not mean it should happen automatically	6
SC - Progress - reducing MD is good/positive	91
SC - Progress - requires caution	6
SC - Regulation - can't guarantee limits	1
SC - Regulation - international considerations	6
SC - Regulation - needed	10
SC - Regulation - other comment	8
SC - Regulation - specifics	3
SC - Regulation - would prevent slippery slope	4
SC - Safety - other comment	13
SE - Ethical - benefits small number	4
SE - Ethical - consent/choice concern	38
SE - Ethical - consent/choice no concern	4
SE - Ethical - consent/choice other	8
SE - Ethical - embryo rights/usage concern	158
SE - Ethical - embryo rights/usage no concern	4
SE - Ethical - embryo rights/usage other	16
SE - Ethical - end does not justify means	2
SE - Ethical - equity of provision	6
SE - Ethical - ethical imperative to intervene	39
SE - Ethical - genetic modification of human embryos	10
SE - Ethical - implications	8
SE - Ethical - implications minimal/insignificant	1
SE - Ethical - interfering with evolution/playing god	73
SE - Ethical - interfering/playing god already happens	17
SE - Ethical - interfering/playing god is ok	8
SE - Ethical - judging value/worth of life	3
SE - Ethical - limitation of use	13
SE - Ethical - no implications/concerns	29
SE - Ethical - no right to healthy/genetically related child	10
SE - Ethical - no slippery slope/not crossing boundary	29

Code	Count
SE - Ethical - not genetic modification	2
SE - Ethical - other comment	15
SE - Ethical - right to healthy/genetically related child	4
SE - Ethical - sanctity/dignity of human life	67
SE - Ethical - slippery slope generally/crossing boundary	141
SE - Ethical - slippery slope other comment	30
SE - Ethical - slippery slope to designer babies/commoditisation	150
SE - Ethical - slippery slope to eugenics	70
SE - Ethical - slippery slope/similar to cloning	72
SE - Ethical - UK first in crossing ethical boundary	4
SE - Ethical tradeoffs - MST vs PNT	7
SE - Ethical tradeoffs - society vs individual	1
SE - General - benefits outweigh issues	68
SE - General - comment on MST specifically	6
SE - General - comment on PNT specifically	14
SE - General - current social/ethical expectations	4
SE - General - implications (Yes)	301
SE - General - implications all/largely positive	10
SE - General - implications based on personal beliefs	8
SE - General - implications minimal/insignificant	13
SE - General - issues outweigh benefits	8
SE - General - no different to current breeding habits	5
SE - General - no implications/concerns (No)	158
SE - General - not sure	2
SE - General - other comment on implications	27
SE - General - other procedures acceptable/better	12
SE - General - preferable to other procedures	12
SE - General - similar to other procedures	29
SE - General - unforeseen problems/impacts/health issues	232
SE - Social - attitudes towards disabled people/MD sufferers	53
SE - Social - attitudes towards those not treated/and their parents	27
SE - Social - attitudes towards those treated	56
SE - Social - availability of counselling/testing/support	2
SE - Social - benefit to future generations	30
SE - Social - benefits to potential parents/families/relationships	25

Code	Count
SE - Social - child awareness not necessary	1
SE - Social - child awareness/understanding	19
SE - Social - child emotional/psychological impact	74
SE - Social - child health/wellbeing improved	59
SE - Social - child health/wellbeing other	7
SE - Social - child ID/mixed genetic make-up	87
SE - Social - child impacts/damage (other/general)	30
SE - Social - child rights	22
SE - Social - cost/resources	6
SE - Social - donor considerations	31
SE - Social - hardship is natural/contributes to strength of society	3
SE - Social - impact on family relationships (not third parent)	24
SE - Social - impact on future generations	175
SE - Social - impact on lineage/traceability	30
SE - Social - implications	4
SE - Social - implications all/largely positive	1
SE - Social - implications minimal/insignificant	3
SE - Social - implications subjective/time-bound	2
SE - Social - increased burden on NHS	5
SE - Social - issues from having MD/disability	7
SE - Social - legal implications/issues	17
SE - Social - minimal family/relationship impacts	2
SE - Social - no ID issues/implications foreseen	7
SE - Social - no implications/concerns	12
SE - Social - no lineage/traceability concerns	2
SE - Social - no third party parentage issues	11
SE - Social - not sure	2
SE - Social - ongoing monitoring/follow-up	29
SE - Social - overall societal benefit/not harmful	11
SE - Social - overall societal impact	10
SE - Social - overpopulation	9
SE - Social - parent awareness/understanding	4
SE - Social - parent psychological impact	10
SE - Social - parent rights/responsibilities	14
SE - Social - parents should not be pressurised	16



Code	Count
SE - Social - public/societal response/fear	17
SE - Social - reduced burden on services/NHS	11
SE - Social - risk losing valuable individuals	7
SE - Social - third party parentage issues	119

### 3. Implications for identity

Considering the possible impact of mitochondria replacement on a person's sense of identity, do you think there are social and ethical implications? If so, what are they?

Code	Count
AC - Not acceptable - MST and PNT/general	11
CO - Criteria - parent/patient choice	2
CO - Labelling of techniques - misleading/misunderstood	7
CO - Patients - information provision/involvement	5
CP - Consultation - comment on question	6
CP - Consultation - comment on response form	1
CP - Consultation - lack of information	1
CP - Consultation - question motivations/bias	2
CP - Consultation - specific information	2
CP - Follow-up - public communication/education	8
CP - Website - general	1
CP - Website - video	4
DS - Donor - responsibility for actions/know what they are getting into	2
DS - Donor function - providing medical solution/repair	10
DS - Donor motivation - other	1
DS - Donor status - is not parent/relation to child	7
DS - Donor status - is parent/relation to child	4
DS - Donor status - is unclear/ambiguous	4
DS - Donor status - no rights/responsibilities to child	4
IN - Age - other comment	1
IN - Child identity - should not be known by donor	1
IN - Child rights - no right/reason to access any information	2
IN - Child rights - to information generally	2
IN - Child rights - to know origins/donor/parents	36
IN - Donor identity - not relevant/necessary	3
IN - Donor identity - other comment	8
IN - Donor identity - should be available (general)	4

Code	Count
IN - Donor identity - should be optional/not mandatory	1
IN - Donor rights - to anonymity/lack of intrusion	1
IN - Donor status - same as blood/tissue/organ donor	7
IN - Donor status - same as egg/sperm donor	2
IN - Logistics - database/infrastructure resourcing	1
IN - Medical info - available for specific reasons/circumstances	1
IN - Medical info - should be available (general)	6
IN - Overall - depends on MtDNA function	1
IN - Overall - other comment	1
IN - Overall decision - flexible/mutual/depends	1
O - potential quote	1
O - Refer to other question	42
RF - Current legislation	1
RF - Current legislation - non UK	6
RF - External document	2
RF - HFEA	5
RF - Historical experience	14
RF - Media coverage	6
RF - Other evidence/examples	8
RF - Participant - friend/relative/child with MD/similar disease	5
RF - Participant - has MD/similar disease	3
RF - Participant - info about	23
RF - Participant - other medical details	5
RF - Politics/government	3
RF - Relevant research	5
RF - Religion	13
RF - Specific individual/organisation/group	5
RF - Views of other people/participants	17
SC - DNA - natural mixing	4
SC - DNA - nuclear DNA/genome not affected	36
SC - DNA - other comment	3
SC - Germ line - other comment	2
SC - Germ line - should not be altered	2
SC - Mitochondria - function/form	31
SC - Mt DNA - does not determine identity/traits	97

Code	Count
SC - Mt DNA - limited amount/types	2
SC - Mt DNA - maternal/female line	4
SC - Mt DNA - may affect identity/traits	19
SC - Mt DNA - origin/not human	3
SC - Mt DNA - other comment	9
SC - Mt DNA - small quantity/impact	63
SC - Other procedures - abortion/termination	3
SC - Other procedures - adoption	68
SC - Other procedures - genetic techniques/gene therapy	2
SC - Other procedures - IVF/egg or sperm donation/surrogacy	112
SC - Other procedures - not conceiving	1
SC - Other procedures - organ/tissue/blood donation	75
SC - Other procedures - other/general	4
SC - Other procedures - stem cell donation	1
SC - Other procedures - timing is different	1
SC - Other procedures - vaccination	1
SC - Overall - addition/alternative suggestions	1
SC - Overall - assessing/managing risk	1
SC - Overall - further research/trials/evidence	7
SC - Overall - invest in other priorities/solutions	8
SC - Overall - motivation of scientists	1
SC - Overall - nature of medicine/science	2
SC - Overall - object to infertility treatment	1
SC - Overall - other comment	8
SC - Overall - question about application	2
SC - Overall - trust/mistrust of scientists	6
SC - Overall - understanding is limited	6
SC - Progress - natural consequence/function of humanity	1
SC - Progress - possibility does not mean it should happen automatically	1
SC - Progress - reducing MD is good/positive	12
SC - Regulation - other comment	3
SC - Regulation - specifics	1
SC - Regulation - would prevent slippery slope	1
SC - Safety - other comment	1
SE - Ethical - benefits small number	1

Code	Count
SE - Ethical - consent/choice concern	11
SE - Ethical - consent/choice no concern	4
SE - Ethical - consent/choice other	1
SE - Ethical - embryo rights/usage concern	53
SE - Ethical - end does not justify means	2
SE - Ethical - ethical imperative to intervene	7
SE - Ethical - implications	4
SE - Ethical - interfering with evolution/playing god	37
SE - Ethical - interfering/playing god is ok	3
SE - Ethical - judging value/worth of life	2
SE - Ethical - no implications/concerns	3
SE - Ethical - no right to healthy/genetically related child	3
SE - Ethical - no slippery slope/not crossing boundary	2
SE - Ethical - other comment	5
SE - Ethical - right to healthy/genetically related child	2
SE - Ethical - sanctity/dignity of human life	8
SE - Ethical - slippery slope generally/crossing boundary	22
SE - Ethical - slippery slope to designer babies/commoditisation	11
SE - Ethical - slippery slope to eugenics	7
SE - Ethical - slippery slope/similar to cloning	10
SE - Ethical - UK first in crossing ethical boundary	1
SE - Ethical tradeoffs - health vs identity	18
SE - Ethical tradeoffs - society vs individual	1
SE - General - benefits outweigh issues	53
SE - General - comment on MST specifically	25
SE - General - comment on PNT specifically	35
SE - General - current social/ethical expectations	6
SE - General - implications (Yes)	174
SE - General - implications all/largely positive	1
SE - General - implications based on personal beliefs	2
SE - General - implications cannot be understood	4
SE - General - implications minimal/insignificant	6
SE - General - issues outweigh benefits	3
SE - General - no different to current breeding habits	1
SE - General - no implications/concerns (No)	134

Code	Count
SE - General - not sure	3
SE - General - other comment on implications	7
SE - General - other procedures acceptable/better	1
SE - General - similar to other procedures	11
SE - General - unforeseen problems/impacts/health issues	68
SE - Social - attitudes towards disabled people/MD sufferers	4
SE - Social - attitudes towards those not treated	3
SE - Social - attitudes towards those treated	41
SE - Social - availability of counselling/testing/support	10
SE - Social - benefit to future generations	6
SE - Social - benefits to potential parents/families/relationships	6
SE - Social - child awareness not necessary	2
SE - Social - child awareness/understanding	105
SE - Social - child emotional/psychological impact	228
SE - Social - child health/wellbeing improved	37
SE - Social - child health/wellbeing other	4
SE - Social - child ID/mixed genetic make-up	368
SE - Social - child impacts/damage (other/general)	13
SE - Social - child may want to meet donor	3
SE - Social - child rights (non-information related)	5
SE - Social - cost/resources	2
SE - Social - donor considerations (other)	16
SE - Social - donor/child bond OR lack of bond	39
SE - Social - donor/child relationship difficulties	21
SE - Social - ethnic/historical ID issues	3
SE - Social - everyone has identity issues	4
SE - Social - ID from nature/genes	10
SE - Social - ID from nurture/upbringing/beyond genetics	71
SE - Social - ID is a changing/evolving concept	4
SE - Social - ID is increasing focus for society	2
SE - Social - ID issues (other)	22
SE - Social - ID issues cannot be known yet	17
SE - Social - ID issues depend on donor status	2
SE - Social - ID issues depend on MtDNA function	2
SE - Social - ID issues for matrilineal societies	3

Code	Count
SE - Social - ID issues less than other procedures	42
SE - Social - ID issues moot/not relevant	3
SE - Social - ID issues more than other procedures	15
SE - Social - ID issues possible	27
SE - Social - ID issues similar/no different to other procedures	131
SE - Social - ID will become fluid/clouded/less clear	5
SE - Social - ID/issues complex/different for everyone	25
SE - Social - impact on family relationships (not third parent)	32
SE - Social - impact on future generations	23
SE - Social - impact on lineage/traceability	25
SE - Social - issues from having MD/disability	7
SE - Social - legal implications/issues	20
SE - Social - lineage/traceability other issues	14
SE - Social - minimal/insignificant ID issues	34
SE - Social - no ID issues/implications foreseen	100
SE - Social - no implications/concerns	4
SE - Social - no lineage/traceability concerns	4
SE - Social - no third party parentage issues	26
SE - Social - ongoing monitoring/follow-up	7
SE - Social - overall societal benefit/not harmful	2
SE - Social - overall societal impact	12
SE - Social - parent psychological impact	27
SE - Social - parent rights/responsibilities	49
SE - Social - parents should not be pressurised	1
SE - Social - positive impact on ID/other	23
SE - Social - public/societal response/fear	9
SE - Social - third party parentage issues	232
SE - Social - who should know the details	5

#### 4. The status of the mitochondria donor

a) In your view how does the donation of mitochondria compare to existing types of donation?  
Please specify what you think this means for the status of a mitochondria donor.

Code	Count
AC - Acceptable - MST	2
AC - Acceptable - MST and PNT/general	10
AC - Acceptable with caveat - MST	1

Code	Count
AC - Not acceptable - MST and PNT/general	47
AC - Not acceptable - PNT	2
AC - Not sure - MST and PNT/general	1
AC - Overall - understand issue/have sympathy	2
CO - Alternatives - other comment	6
CO - Availability - NHS should not cover/fund privately	1
CO - Labelling of techniques - misleading/misunderstood	11
CO - MST and PNT - see no/little difference	2
CO - Patients - information provision/involvement	1
CP - Consultation - challenge information/data	1
CP - Consultation - comment on question	11
CP - Consultation - other comment	3
CP - Consultation - participants not qualified	1
CP - Consultation - question motivations/bias	1
CP - Consultation - specific information	1
CP - Follow-up - further info on specific topic/s	1
CP - Follow-up - public communication/education	1
CP - Website - general	2
CP - Website - video	1
DS - Donor - availability issues/considerations	20
DS - Donor - is important/should be recognised	17
DS - Donor - may have emotional investment/impact	12
DS - Donor - no emotional investment	2
DS - Donor - payment	11
DS - Donor - responsibility for actions/know what they are getting into	22
DS - Donor - risks/exploitation/health considerations	86
DS - Donor function - contributing to life	15
DS - Donor function - not providing reproductive function	5
DS - Donor function - providing medical solution/repair	36
DS - Donor motivation - gift/altruism	32
DS - Donor motivation - other	2
DS - Donor status - does have rights/responsibilities to child	8
DS - Donor status - is clear/unambiguous	3
DS - Donor status - is not parent/relation to child	39
DS - Donor status - is parent/relation to child/partial parent	47

Code	Count
DS - Donor status - is subjective	6
DS - Donor status - is unclear/ambiguous	27
DS - Donor status - legal considerations	31
DS - Donor status - may change/open to review	7
DS - Donor status - no rights/responsibilities to child	37
DS - Donor status - no status	8
DS - Donor status - not primary concern	2
DS - Donor status - other considerations	17
DS - Mitochondria - 'above' blood	10
DS - Mitochondria - 'above' bone marrow	8
DS - Mitochondria - 'above' egg/sperm/embryo	3
DS - Mitochondria - 'above' organ	6
DS - Mitochondria - 'above' tissue	3
DS - Mitochondria - 'below' donation (general)	2
DS - Mitochondria - 'below' egg/sperm/embryo	33
DS - Mitochondria - 'below' face transplant	1
DS - Mitochondria - 'below' organ	4
DS - Mitochondria - 'below' surrogacy	1
DS - Mitochondria - complex/uncomfortable donation	7
DS - Mitochondria - depends on MST/PNT	30
DS - Mitochondria - depends on MtDNA function	5
DS - Mitochondria - depends on sex of child	2
DS - Mitochondria - difference in choice/consent	5
DS - Mitochondria - difference in longevity of impact	16
DS - Mitochondria - difference in method of donation	3
DS - Mitochondria - difference in perception/ethics	2
DS - Mitochondria - difference in timing	8
DS - Mitochondria - difference is third person DNA/genetic information	94
DS - Mitochondria - different to blood	96
DS - Mitochondria - different to bone marrow	27
DS - Mitochondria - different to donation (general)	77
DS - Mitochondria - different to egg/sperm/embryo	121
DS - Mitochondria - different to organ	102
DS - Mitochondria - different to stem cells	1
DS - Mitochondria - different to surrogacy	3



Code	Count
DS - Mitochondria - different to tissue	12
DS - Mitochondria - envelope/carrier/overcoat	3
DS - Mitochondria - less pervasive	2
DS - Mitochondria - minor/uncomplicated donation	3
DS - Mitochondria - mixed comparison	27
DS - Mitochondria - more pervasive	12
DS - Mitochondria - similar to adoption	2
DS - Mitochondria - similar to biopsy	1
DS - Mitochondria - similar to blood	92
DS - Mitochondria - similar to bone marrow	51
DS - Mitochondria - similar to donation (general)	72
DS - Mitochondria - similar to egg/sperm/embryo/IVF	113
DS - Mitochondria - similar to organ	68
DS - Mitochondria - similar to stem cells	4
DS - Mitochondria - similar to surrogacy	5
DS - Mitochondria - similar to tissue	33
DS - Mitochondria - unessential donation	2
DS - Mitochondria - unique type of donation	10
DS - Origin - allow choice	1
DS - Origin - makes no difference	1
DS - Origin - mitochondria bank/anonymous	3
DS - Origin - should be family member/close relative	2
DS - Origin - should be relative/friend	3
DS - Origin - should be same haplogroup	1
DS - Origin - should be unconnected to family	1
DS - Origin - should not be maternal relative	1
DS - Overall - not sure/no view	8
DS - Overall - oppose donation of all/any kind	10
DS - Overall - other comment	7
DS - Overall - support donation of all/any kind	2
DS - Overall - varied views on donation types	6
IN - Age - 18/when reaching adulthood	10
IN - Age - before 18	1
IN - Age - other comment	1
IN - Child identity - should not be known by donor	7

Code	Count
IN - Child rights - no right to contact donor	2
IN - Child rights - other comment	2
IN - Child rights - should take priority	5
IN - Child rights - to information generally	11
IN - Child rights - to know origins/donor/parents	25
IN - Child rights - to understand process/implications	6
IN - Donor identity - available for specific reasons	1
IN - Donor identity - depends on who the donor is	3
IN - Donor identity - not known by parents	1
IN - Donor identity - not relevant/necessary	6
IN - Donor identity - other comment	7
IN - Donor identity - should be available (general)	17
IN - Donor identity - should be optional/not mandatory	27
IN - Donor identity - should not be available (other/general)	26
IN - Donor rights - not to have relationship with child	1
IN - Donor rights - other comment	5
IN - Donor rights - to anonymity/lack of intrusion	22
IN - Donor rights - to know success of treatment	3
IN - Donor rights - to understand procedure	13
IN - Logistics - donor screening	10
IN - Logistics - information storage/records	11
IN - Medical info - available for specific reasons/circumstances	12
IN - Medical info - not relevant/necessary	1
IN - Medical info - should be available (general)	6
IN - Overall - depends on other factor	1
IN - Overall - legal considerations	3
IN - Overall - no information needed	3
IN - Overall - other comment	6
IN - Overall decision - flexible/mutual/depends	3
IN - Overall decision - parents'/family's	4
IN - Personal info - not relevant/necessary	2
IN - Personal info - should be available (general)	1
IN - Personal info - should not be available (other/general)	1
O - Blank response/no comment	17
O - Refer to other question	18

Code	Count
O - Refer to other response	2
RF - Current legislation	4
RF - Current legislation - non UK	4
RF - External document	2
RF - HFEA	3
RF - Historical experience	2
RF - Media coverage	4
RF - Other evidence/examples	2
RF - Participant - friend/relative/child with MD/similar disease	4
RF - Participant - has MD/similar disease	1
RF - Participant - info about	14
RF - Participant - other medical details	1
RF - Politics/government	4
RF - Relevant research	2
RF - Religion	6
RF - Specific individual/organisation/group	5
RF - Views of other people/participants	10
SC - DNA - nuclear DNA/genome not affected	29
SC - DNA - other comment	6
SC - Germ line - should not be altered	1
SC - Mitochondria - function/form	29
SC - Mt DNA - does not determine identity/traits	56
SC - Mt DNA - limited amount/types	5
SC - Mt DNA - may affect identity/traits	10
SC - Mt DNA - origin/not human	2
SC - Mt DNA - other comment	6
SC - Mt DNA - small quantity/impact	64
SC - Other procedures - adoption	2
SC - Other procedures - IVF/egg or sperm donation/surrogacy	5
SC - Overall - addition/alternative suggestions	1
SC - Overall - further research/trials/evidence	3
SC - Overall - invest in other priorities/solutions	11
SC - Overall - motivation of scientists	1
SC - Overall - need more research/don't know enough	7
SC - Overall - object to infertility treatment	4

Code	Count
SC - Overall - question about application	2
SC - Overall - trust/mistrust of scientists	2
SC - Overall - understanding is limited	5
SC - Progress - reducing MD is good/positive	3
SC - Progress - requires caution	1
SC - Regulation - other comment	3
SC - Regulation - specifics	3
SC - Safety - other comment	1
SE - Ethical - comparison with other donations	4
SE - Ethical - consent/choice concern	5
SE - Ethical - embryo rights/usage concern	157
SE - Ethical - embryo rights/usage other	9
SE - Ethical - end does not justify means	1
SE - Ethical - equity of provision	2
SE - Ethical - implications	4
SE - Ethical - interfering with evolution/playing god	22
SE - Ethical - judging value/worth of life	3
SE - Ethical - no implications/concerns	2
SE - Ethical - no right to healthy/genetically related child	3
SE - Ethical - other comment	5
SE - Ethical - right to healthy/genetically related child	1
SE - Ethical - sanctity/dignity of human life	19
SE - Ethical - slippery slope generally/crossing boundary	12
SE - Ethical - slippery slope to designer babies/commoditisation	6
SE - Ethical - slippery slope to eugenics	2
SE - Ethical - slippery slope/similar to cloning	9
SE - General - benefits outweigh issues	3
SE - General - current social/ethical expectations	3
SE - General - implications (Yes)	3
SE - General - implications minimal/insignificant	1
SE - General - other procedures acceptable/better	4
SE - General - preferable to other procedures	4
SE - General - unforeseen problems/impacts/health issues	28
SE - Social - attitudes towards disabled people/MD sufferers	1
SE - Social - attitudes towards those treated	2

Code	Count
SE - Social - availability of counselling/testing/support	1
SE - Social - benefit to future generations	3
SE - Social - benefits to potential parents/families/relationships	5
SE - Social - child emotional/psychological impact	8
SE - Social - child health/wellbeing improved	4
SE - Social - child ID/mixed genetic make-up	24
SE - Social - child rights	1
SE - Social - donor considerations (other)	3
SE - Social - donor/child bond OR lack of bond	12
SE - Social - donor/child relationship difficulties	2
SE - Social - ID from nurture/upbringing/beyond genetics	1
SE - Social - ID issues (other)	2
SE - Social - ID issues cannot be known yet	1
SE - Social - ID/issues complex/different for everyone	2
SE - Social - impact on family relationships (not third parent)	1
SE - Social - impact on future generations	10
SE - Social - impact on lineage/traceability	3
SE - Social - minimal/insignificant ID issues	1
SE - Social - no ID issues/implications foreseen	4
SE - Social - ongoing monitoring/follow-up	3
SE - Social - overpopulation	1
SE - Social - parent psychological impact	1
SE - Social - parent rights/responsibilities	5
SE - Social - risk losing valuable individuals	1
SE - Social - third party parentage issues	13

b) Thinking about your response to 4a, what information about the mitochondria donor do you think a child should have? (Choose one response only)

- The child should get no information
- The child should be able to get medical and personal information about the mitochondria donor, but never know their identity
- The child should be able to get medical and personal information about the mitochondria donor and be able to contact them once the child reaches the age of 18
- Other
- I do not think mitochondria replacement should be permitted in treatment at all

Please explain your choice.

Code	Count
AC - Acceptable - MST	1
AC - Acceptable - MST and PNT/general	2
AC - Not acceptable - MST and PNT/general	103
AC - Not acceptable - PNT	1
AC - Not sure - MST and PNT/general	1
AC - Overall - understand issue/have sympathy	6
AC - Overall - unsure/no strong view	2
AG - Altering DNA - cloning/hybridisation	3
AG - Altering DNA - impact on germ line/lineage	13
AG - Altering DNA - not acceptable	7
AG - Cost - too much/cannot be justified	2
AG - Costs/risks - outweigh benefits	7
AG - Disease - will not be eradicated/not a cure	2
AG - Donation - risk/exploitation	5
AG - Ethics - creation/destruction of egg/embryo	84
AG - Ethics - general/too many ethical issues	39
AG - Ethics - interfering with evolution/playing god	30
AG - Ethics - judging value/worth of life (particularly PNT)	2
AG - Ethics - lack of consent/choice	3
AG - Ethics - no right to healthy/genetically related child	6
AG - Ethics - other comment	1
AG - Ethics - sanctity/dignity of human life	27
AG - Ethics - UK first in crossing ethical boundary	2
AG - Future - risks/impacts/unintended consequences	47
AG - MST - could be more emotionally difficult	1
AG - Population - too big/would increase	1
AG - Preferable alternative - adoption	5
AG - Preferable alternative - decide not to conceive	3
AG - Preferable alternative - IVF	1
AG - Preferable alternative - other treatment/cure of MD	29
AG - Preferable alternative - other/general	1
AG - Regulation - can't guarantee limits	1
AG - Regulation - may not be consistent across the board	2
AG - Science - false hope/may not work	2
AG - Science - just because it is possible does not mean it should be done	4

Code	Count
AG - Science - role/motivation of scientists	4
AG - Science - understanding is limited	2
AG - Slippery slope - cloning	6
AG - Slippery slope - concerns	18
AG - Slippery slope - designer babies/commoditisation	5
AG - Slippery slope - eugenics	7
AG - Social - general/too many social issues	1
AG - Social - impact on child/identity/psychology	45
AG - Social - impact on donor/donor considerations	3
AG - Social - impact on family relationships	2
AG - Social - impact on parents	3
AG - Social - legal implications/scenarios	7
AG - Social - prioritise other issues/solutions	5
AG - Social - third person as parent/donor	23
AG - Social - worth of MD sufferers/disabled people	3
AG - Wider issue - against artificial fertilisation	5
CO - Labelling of techniques - misleading/misunderstood	11
CP - Consultation - comment on question	30
CP - Consultation - cost concern	1
CP - Consultation - other negative comment	2
CP - Consultation - other positive comment	1
CP - Consultation - question motivations/bias	3
CP - Consultation - question process	2
CP - Consultation - specific information	1
CP - Consultation - suspect foregone conclusion	1
CP - Follow-up - public communication/education	1
CP - Follow-up - wider debate	1
CP - Website - general	1
DS - Donor - availability issues/considerations	53
DS - Donor - responsibility for actions/know what they are getting into	10
DS - Donor function - providing medical solution/repair	8
DS - Donor motivation - gift/altruism	14
DS - Donor motivation - other	2
DS - Donor status - does have rights/responsibilities to child	2
DS - Donor status - is not parent/relation to child	29

Code	Count
DS - Donor status - is parent/relation to child	8
DS - Donor status - is part of child's make-up	2
DS - Donor status - is relation but not parent	1
DS - Donor status - is unclear/ambiguous	3
DS - Donor status - no rights/responsibilities to child	5
DS - Origin - makes no difference	1
IN - Age - 18 is too young	1
IN - Age - 18/when reaching adulthood	32
IN - Age - no minimum/from the start	5
IN - Age - no minimum/other factors	2
IN - Age - other comment	9
IN - Child - understand curiosity	13
IN - Child identity - should not be known by donor	3
IN - Child rights - may want to thank donor	17
IN - Child rights - no right to contact donor	7
IN - Child rights - no right/reason to access any information	13
IN - Child rights - not to feel obligated	2
IN - Child rights - other comment	18
IN - Child rights - should take priority	2
IN - Child rights - to information generally	28
IN - Child rights - to know origins/donor/parents	90
IN - Child rights - to understand process/implications	44
IN - Donor identity - depends on who the donor is	5
IN - Donor identity - family likely to know donor	1
IN - Donor identity - not relevant/necessary	44
IN - Donor identity - other comment	2
IN - Donor identity - should be available (general)	12
IN - Donor identity - should be optional/not mandatory	42
IN - Donor identity - should not be available (other/general)	17
IN - Donor identity - would not benefit child	3
IN - Donor identity/info - misrepresents contribution	16
IN - Donor rights - not to have relationship with child	3
IN - Donor rights - other comment	4
IN - Donor rights - to anonymity/lack of intrusion	36
IN - Donor rights - to know/contact family/child	4



Code	Count
IN - Donor status - different to adoption/surrogacy	4
IN - Donor status - different to blood/tissue/organ donor	2
IN - Donor status - different to donation (non specific)	1
IN - Donor status - different to egg/sperm donor	23
IN - Donor status - same as adoption/surrogacy	5
IN - Donor status - same as blood/tissue/organ donor	79
IN - Donor status - same as donation (non specific)	2
IN - Donor status - same as egg/sperm donor	42
IN - Logistics - database/infrastructure resourcing	1
IN - Logistics - donor screening	6
IN - Logistics - information storage/records	9
IN - Medical info - available for specific reasons/circumstances	82
IN - Medical info - not relevant/necessary	3
IN - Medical info - should be available (general)	45
IN - Option - between 1 and 2	2
IN - Option 1 - would be other choice	3
IN - Option 2 - for male children	1
IN - Option 2 - other comment	8
IN - Option 2 - preferred/if have to choose	3
IN - Option 2 - would be other choice	8
IN - Option 3 - for female children	1
IN - Option 3 - opposing comment	1
IN - Option 3 - other comment	8
IN - Option 3 - preferred/if have to choose	12
IN - Option 3 - would be other choice	7
IN - Option 5 - against/but if I have to choose	9
IN - Option 5 - would be other choice	3
IN - Overall - all/any information (option 3)	14
IN - Overall - balancing interests of parties	6
IN - Overall - depends on MST/PNT	17
IN - Overall - depends on other factor	2
IN - Overall - legal considerations	11
IN - Overall - minimum/only in some circumstances	2
IN - Overall - misuse of information	1
IN - Overall - more information than these options provide	4

Code	Count
IN - Overall - no information needed (option 1)	18
IN - Overall - not sure	5
IN - Overall - other comment	11
IN - Overall - rethink if/when research/knowledge progresses	9
IN - Overall - some/limited information (option 1)	1
IN - Overall - some/limited information (option 2)	4
IN - Overall decision - child's	13
IN - Overall decision - donor's	15
IN - Overall decision - flexible/mutual/depends	21
IN - Overall decision - parents'/family's	11
IN - Personal info - available for specific reasons/circumstances	12
IN - Personal info - not relevant/necessary	7
IN - Personal info - not sure	1
IN - Personal info - should be available (general)	25
IN - Personal info - should be optional/not mandatory	1
IN - Personal info - should not be available (other/general)	7
IN - Selected - no answer	6
IN - Selected - none selected	142
IN - Selected - option 1	111
IN - Selected - option 2	153
IN - Selected - option 3	153
IN - Selected - option 4	83
IN - Selected - option 5	514
O - Blank response/no comment	257
O - Other/general comment	2
O - Refer to other question	157
RF - Current legislation	1
RF - Current legislation - non UK	9
RF - External document	1
RF - HFEA	2
RF - Historical experience	7
RF - Other evidence/examples	2
RF - Participant - friend/relative/child with MD/similar disease	1
RF - Participant - info about	11
RF - Participant - other medical details	4

Code	Count
RF - Politics/government	1
RF - Relevant research	2
RF - Religion	17
RF - Specific individual/organisation/group	8
RF - Views of other people/participants	2
SC - DNA - nuclear DNA/genome not affected	15
SC - Mitochondria - function/form	9
SC - Mt DNA - does not determine identity/traits	60
SC - Mt DNA - maternal/female line	4
SC - Mt DNA - may affect identity/traits	2
SC - Mt DNA - other comment	4
SC - Mt DNA - small quantity/impact	39
SC - Mt DNA - suggested source for donation	1
SC - Other procedures - IVF/egg or sperm donation/surrogacy	3
SC - Other procedures - organ/tissue/blood donation	1
SC - Other procedures - stem cell donation	1
SC - Other procedures - vaccination	1
SC - Overall - assessing/managing risk	1
SC - Overall - balancing science/ethics/religion/society	1
SC - Overall - further research/trials/evidence	5
SC - Overall - new procedure/knowledge will grow	2
SC - Overall - other comment	2
SC - Overall - question about application	1
SC - Overall - understanding is limited	3
SC - Regulation - needed	1
SC - Regulation - other comment	1
SC - Regulation - specifics	1
SE - Ethical - consent/choice concern	1
SE - Ethical - consent/choice other	1
SE - General - current social/ethical expectations	3
SE - General - unforeseen problems/impacts/health issues	1
SE - Social - attitudes towards those treated	1
SE - Social - availability of counselling/testing/support	2
SE - Social - child emotional/psychological impact	13
SE - Social - child health/wellbeing improved	1

Code	Count
SE - Social - child health/wellbeing other	1
SE - Social - child ID/mixed genetic make-up	12
SE - Social - ID issues similar/no different to other procedures	1
SE - Social - impact on family relationships (not third parent)	1
SE - Social - impact on future generations	1
SE - Social - impact on lineage/traceability	2
SE - Social - legal implications/issues	1
SE - Social - no ID issues/implications foreseen	2
SE - Social - ongoing monitoring/follow-up	1
SE - Social - parent psychological impact	2
SE - Social - parent rights/responsibilities	10
SE - Social - third party parentage issues	4

## 5. Regulation of mitochondria replacement

If the law changed to allow mitochondria replacement to take place in a specialist clinic regulated by the HFEA, how should decisions be made on who can access this treatment? (Choose one response only)

- Clinics and their patients should decide when mitochondria replacement is appropriate in individual cases
- The regulator should decide which mitochondrial diseases are serious enough to require mitochondria replacement and, just for these diseases, permit clinics and patients to decide when it is appropriate in individual cases
- The regulator should decide which mitochondrial diseases are serious enough to require mitochondria replacement and also decide, just for these diseases, when it is appropriate in individual cases
- I do not think mitochondria replacement should be permitted in treatment at all

Please explain your choice.

Code	Count
AC - Acceptable - MST and PNT/general	5
AC - Not acceptable - MST and PNT/general	114
AC - Not acceptable - PNT	3
AC - Overall - unsure/no strong view	1
AG - Altering DNA - cloning/hybridisation	6
AG - Altering DNA - impact on germ line/lineage	10
AG - Altering DNA - not acceptable	3
AG - Costs/risks - outweigh benefits	7
AG - Disease - will not be eradicated/not a cure	2

Code	Count
AG - Donation - risk/exploitation	4
AG - Ethics - creation/destruction of egg/embryo	50
AG - Ethics - end does not justify means	3
AG - Ethics - general/too many ethical issues	13
AG - Ethics - interfering with evolution/playing god	27
AG - Ethics - judging value/worth of life (particularly PNT)	8
AG - Ethics - lack of consent/choice	1
AG - Ethics - no right to healthy/genetically related child	7
AG - Ethics - sanctity/dignity of human life	25
AG - Ethics - UK first in crossing ethical boundary	8
AG - Future - risks/impacts/unintended consequences	26
AG - Other - other comment	5
AG - Population - too big/would increase	1
AG - Preferable alternative - adoption	4
AG - Preferable alternative - decide not to conceive	4
AG - Preferable alternative - other treatment/cure of MD	20
AG - Preferable alternative - other/general	4
AG - Science - false hope/may not work	6
AG - Science - just because it is possible does not mean it should be done	6
AG - Science - role/motivation of scientists	4
AG - Science - understanding is limited	3
AG - Slippery slope - attitudes to euthanasia	1
AG - Slippery slope - cloning	6
AG - Slippery slope - concerns	27
AG - Slippery slope - designer babies/commoditisation	6
AG - Slippery slope - eugenics	10
AG - Social - general/too many social issues	1
AG - Social - impact on child/identity/psychology	13
AG - Social - impact on family relationships	4
AG - Social - legal implications/scenarios	3
AG - Social - prioritise other issues/solutions	2
AG - Social - third person as parent/donor	11
AG - Social - worth of MD sufferers/disabled people	4
AG - Wider issue - against artificial fertilisation	4
CO - Labelling of techniques - misleading/misunderstood	9

Code	Count
CP - Consultation - comment on question	19
CP - Consultation - outcomes	2
CP - Consultation - question motivations/bias	1
CP - Consultation - question process	6
DM - Clinicians - advise/recommend/input into decision	33
DM - Clinicians - are professional/should be trusted	3
DM - Clinicians - business interest/other motivation	28
DM - Clinicians - have closest knowledge	16
DM - Clinicians - other comment	7
DM - Clinicians - self-regulation/autonomy	6
DM - Clinicians - should decide	12
DM - Clinicians - should decide within boundaries set by regulator	25
DM - Criteria - base on science/facts	9
DM - Criteria - ensure safety	8
DM - Criteria - last resort only	3
DM - Criteria - medical/psychological considerations	4
DM - Criteria - none/any application should be allowed	8
DM - Criteria - none/treat all diseases/individuals	23
DM - Criteria - other	4
DM - Criteria - patient need/want/case by case	45
DM - Criteria - process/difficulty in setting criteria	15
DM - Criteria - seriousness of diseases/impacts	35
DM - Option 1 - could be introduced later	4
DM - Option 1 - opposing comment	4
DM - Option 1 - other comment	3
DM - Option 1 - would be other choice	2
DM - Option 2 - could be introduced later	2
DM - Option 2 - for MST only	1
DM - Option 2 - if shortage of donors	1
DM - Option 2 - opposing comment	3
DM - Option 2 - other comment	5
DM - Option 2 - preferred/if have to choose	11
DM - Option 3 - for MST only	1
DM - Option 3 - in specific/less clear cases	1
DM - Option 3 - opposing comment	9

Code	Count
DM - Option 3 - other comment	2
DM - Option 3 - preferred/if have to choose	18
DM - Option 4 - opposing comment	1
DM - Overall - alternative approach	3
DM - Overall - consider rare/new/uncategorised diseases	14
DM - Overall - different to other procedures	1
DM - Overall - lack of trust in government/regulator	5
DM - Overall - no/minimal risk of abuse/overuse	8
DM - Overall - not sure	1
DM - Overall - other comment	19
DM - Overall - rethink if needed/after set time	8
DM - Overall - risk of abuse/overuse	9
DM - Overall - similar/no different to other procedures	14
DM - Overall - this is workable/sensible option	9
DM - Parliament - should have ultimate control	32
DM - Patient/clinician - able to influence decision	1
DM - Patient/clinician - have closest knowledge	10
DM - Patient/clinician - joint decision	49
DM - Patient/clinician - joint decision within boundaries set by regulator	47
DM - Patient/clinician - self-regulation	3
DM - Patients - have closest knowledge	10
DM - Patients - involvement in decision/choice	20
DM - Patients - may go elsewhere/abroad	2
DM - Patients - other comment	2
DM - Patients - question motivation	7
DM - Patients - should decide	32
DM - Patients - should decide within boundaries set by regulator	8
DM - Regulator - adds bureaucracy/cost/distress	25
DM - Regulator - appeals process	4
DM - Regulator - closer involvement upfront/early on	19
DM - Regulator - doesn't make it OK/ethical	40
DM - Regulator - helps ensure clinic performance/quality	19
DM - Regulator - helps ensure safety/quality	5
DM - Regulator - helps limit cost/distribute limited resource	8
DM - Regulator - helps prevent abuse/overuse/ensure legality	35

Code	Count
DM - Regulator - helps public acceptability	7
DM - Regulator - impartial/independent/trusted	8
DM - Regulator - international implications	5
DM - Regulator - involvement is necessary (general/other)	30
DM - Regulator - makes decisions on individual cases (option 3)	13
DM - Regulator - must be accountable/trustworthy	4
DM - Regulator - not appropriate to involve	20
DM - Regulator - not necessary to involve	8
DM - Regulator - other comment	20
DM - Regulator - oversight/review role	26
DM - Regulator - politically/financially driven	9
DM - Regulator - reference existing PGD approach	12
DM - Regulator - sets boundaries not individual cases (option 2)	66
DM - Regulator - should not be overburdened	5
DM - Regulator - strict/stringent rules needed	20
DM - Regulator - too distant/generalist/lacking in knowledge	27
DM - Regulator - will not be effective	36
DM - Resourcing - concern over NHS resource	2
DM - Resourcing - other comment	5
DM - Resourcing - should be from patients/privately	4
DM - Resourcing - should not take precedence	2
DM - Selected - no answer	12
DM - Selected - none selected	12
DM - Selected - option 1	232
DM - Selected - option 2	185
DM - Selected - option 3	55
DM - Selected - option 4	547
DM - Timescales - should be fast/efficient	4
O - Blank response/no comment	204
O - Refer to other question	178
RF - Current legislation	8
RF - Current legislation - non UK	11
RF - HFEA	37
RF - Historical experience	29
RF - Media coverage	1



Code	Count
RF - Participant - friend/relative/child with MD/similar disease	4
RF - Participant - has MD/similar disease	1
RF - Participant - info about	6
RF - Participant - other medical details	2
RF - Politics/government	19
RF - Relevant research	2
RF - Religion	9
RF - Views of other people/participants	4
SC - Germ line - could reduce in diversity	1
SC - MD - testing mothers	2
SC - MD - variety of forms/impacts	22
SC - Mitochondria - function/form	3
SC - Mt DNA - does not determine identity/traits	1
SC - Other procedures - abortion/termination	9
SC - Other procedures - adoption	1
SC - Other procedures - genetic techniques/gene therapy	6
SC - Other procedures - IVF/egg or sperm donation/surrogacy	3
SC - Other procedures - organ/tissue/blood donation	6
SC - Other procedures - other/general	4
SC - Overall - nature of medicine/science	4
SC - Overall - new procedure/knowledge will grow	7
SC - Overall - other comment	3
SC - Overall - question about application	2
SC - Overall - understanding is limited	3
SC - Progress - has gone too far to stop now	2
SC - Progress - reducing MD is good/positive	3
SC - Safety - other comment	3
SE - Ethical - benefits small number	3
SE - Ethical - embryo rights/usage other	3
SE - Ethical - equity of provision	16
SE - Ethical - ethical imperative to intervene	4
SE - Ethical - having healthy children is a right	2
SE - Ethical - having healthy children not a right/essential	1
SE - Ethical - implications	1
SE - Ethical - no slippery slope/not crossing boundary	2

Code	Count
SE - Ethical - slippery slope generally/crossing boundary	5
SE - Ethical - slippery slope to designer babies/commoditisation	6
SE - Ethical tradeoffs - evolution vs familial distress	1
SE - Ethical tradeoffs - safety vs progress	1
SE - Ethical tradeoffs - society vs individual	1
SE - General - benefits outweigh issues	1
SE - General - current social/ethical expectations	4
SE - General - no implications/concerns (No)	1
SE - General - unforeseen problems/impacts/health issues	4
SE - Social - benefits to potential parents/families/relationships	4
SE - Social - child awareness/understanding	1
SE - Social - child health/wellbeing improved	5
SE - Social - child health/wellbeing other	6
SE - Social - child rights	5
SE - Social - donor considerations	2
SE - Social - impact on future generations	1
SE - Social - issues from having MD/disability	3
SE - Social - legal implications/issues	1
SE - Social - ongoing monitoring/follow-up	2
SE - Social - overpopulation	1
SE - Social - parent rights/responsibilities	1
SE - Social - parents should not be pressurised	1

## 6. Should the law be changed?

In Question 1, we asked for your views on the mitochondria replacement techniques MST and PNT. Please could you now tell us if you think the law should be changed to allow (one or both of) these techniques to be made available to people who are at risk of passing on mitochondrial disease to their child?

Code	Count
AC - Acceptable - MST and PNT/general	5
AC - Not acceptable - MST and PNT/general	114
AC - Not acceptable - PNT	3
AC - Overall - unsure/no strong view	1
AG - Altering DNA - cloning/hybridisation	6
AG - Altering DNA - impact on germ line/lineage	10
AG - Altering DNA - not acceptable	3

Code	Count
AG - Costs/risks - outweigh benefits	7
AG - Disease - will not be eradicated/not a cure	2
AG - Donation - risk/exploitation	4
AG - Ethics - creation/destruction of egg/embryo	50
AG - Ethics - end does not justify means	3
AG - Ethics - general/too many ethical issues	13
AG - Ethics - interfering with evolution/playing god	27
AG - Ethics - judging value/worth of life (particularly PNT)	8
AG - Ethics - lack of consent/choice	1
AG - Ethics - no right to healthy/genetically related child	7
AG - Ethics - sanctity/dignity of human life	25
AG - Ethics - UK first in crossing ethical boundary	8
AG - Future - risks/impacts/unintended consequences	26
AG - Other - other comment	5
AG - Population - too big/would increase	1
AG - Preferable alternative - adoption	4
AG - Preferable alternative - decide not to conceive	4
AG - Preferable alternative - other treatment/cure of MD	20
AG - Preferable alternative - other/general	4
AG - Science - false hope/may not work	6
AG - Science - just because it is possible does not mean it should be done	6
AG - Science - role/motivation of scientists	4
AG - Science - understanding is limited	3
AG - Slippery slope - attitudes to euthanasia	1
AG - Slippery slope - cloning	6
AG - Slippery slope - concerns	27
AG - Slippery slope - designer babies/commoditisation	6
AG - Slippery slope - eugenics	10
AG - Social - general/too many social issues	1
AG - Social - impact on child/identity/psychology	13
AG - Social - impact on family relationships	4
AG - Social - legal implications/scenarios	3
AG - Social - prioritise other issues/solutions	2
AG - Social - third person as parent/donor	11
AG - Social - worth of MD sufferers/disabled people	4

Code	Count
AG - Wider issue - against artificial fertilisation	4
CO - Labelling of techniques - misleading/misunderstood	9
CP - Consultation - comment on question	19
CP - Consultation - outcomes	2
CP - Consultation - question motivations/bias	1
CP - Consultation - question process	6
DM - Clinicians - advise/recommend/input into decision	33
DM - Clinicians - are professional/should be trusted	3
DM - Clinicians - business interest/other motivation	28
DM - Clinicians - have closest knowledge	16
DM - Clinicians - other comment	7
DM - Clinicians - self-regulation/autonomy	6
DM - Clinicians - should decide	12
DM - Clinicians - should decide within boundaries set by regulator	25
DM - Criteria - base on science/facts	9
DM - Criteria - ensure safety	8
DM - Criteria - last resort only	3
DM - Criteria - medical/psychological considerations	4
DM - Criteria - none/any application should be allowed	8
DM - Criteria - none/treat all diseases/individuals	23
DM - Criteria - other	4
DM - Criteria - patient need/want/case by case	45
DM - Criteria - process/difficulty in setting criteria	15
DM - Criteria - seriousness of diseases/impacts	35
DM - Option 1 - could be introduced later	4
DM - Option 1 - opposing comment	4
DM - Option 1 - other comment	3
DM - Option 1 - would be other choice	2
DM - Option 2 - could be introduced later	2
DM - Option 2 - for MST only	1
DM - Option 2 - if shortage of donors	1
DM - Option 2 - opposing comment	3
DM - Option 2 - other comment	5
DM - Option 2 - preferred/if have to choose	11
DM - Option 3 - for MST only	1

Code	Count
DM - Option 3 - in specific/less clear cases	1
DM - Option 3 - opposing comment	9
DM - Option 3 - other comment	2
DM - Option 3 - preferred/if have to choose	18
DM - Option 4 - opposing comment	1
DM - Overall - alternative approach	3
DM - Overall - consider rare/new/uncategorised diseases	14
DM - Overall - different to other procedures	1
DM - Overall - lack of trust in government/regulator	5
DM - Overall - no/minimal risk of abuse/overuse	8
DM - Overall - not sure	1
DM - Overall - other comment	19
DM - Overall - rethink if needed/after set time	8
DM - Overall - risk of abuse/overuse	9
DM - Overall - similar/no different to other procedures	14
DM - Overall - this is workable/sensible option	9
DM - Parliament - should have ultimate control	32
DM - Patient/clinician - able to influence decision	1
DM - Patient/clinician - have closest knowledge	10
DM - Patient/clinician - joint decision	49
DM - Patient/clinician - joint decision within boundaries set by regulator	47
DM - Patient/clinician - self-regulation	3
DM - Patients - have closest knowledge	10
DM - Patients - involvement in decision/choice	20
DM - Patients - may go elsewhere/abroad	2
DM - Patients - other comment	2
DM - Patients - question motivation	7
DM - Patients - should decide	32
DM - Patients - should decide within boundaries set by regulator	8
DM - Regulator - adds bureaucracy/cost/distress	25
DM - Regulator - appeals process	4
DM - Regulator - closer involvement upfront/early on	19
DM - Regulator - doesn't make it OK/ethical	40
DM - Regulator - helps ensure clinic performance/quality	19
DM - Regulator - helps ensure safety/quality	5

Code	Count
DM - Regulator - helps limit cost/distribute limited resource	8
DM - Regulator - helps prevent abuse/overuse/ensure legality	35
DM - Regulator - helps public acceptability	7
DM - Regulator - impartial/independent/trusted	8
DM - Regulator - international implications	5
DM - Regulator - involvement is necessary (general/other)	30
DM - Regulator - makes decisions on individual cases (option 3)	13
DM - Regulator - must be accountable/trustworthy	4
DM - Regulator - not appropriate to involve	20
DM - Regulator - not necessary to involve	8
DM - Regulator - other comment	20
DM - Regulator - oversight/review role	26
DM - Regulator - politically/financially driven	9
DM - Regulator - reference existing PGD approach	12
DM - Regulator - sets boundaries not individual cases (option 2)	66
DM - Regulator - should not be overburdened	5
DM - Regulator - strict/stringent rules needed	20
DM - Regulator - too distant/generalist/lacking in knowledge	27
DM - Regulator - will not be effective	36
DM - Resourcing - concern over NHS resource	2
DM - Resourcing - other comment	5
DM - Resourcing - should be from patients/privately	4
DM - Resourcing - should not take precedence	2
DM - Selected - no answer	12
DM - Selected - none selected	12
DM - Selected - option 1	232
DM - Selected - option 2	185
DM - Selected - option 3	55
DM - Selected - option 4	547
DM - Timescales - should be fast/efficient	4
Holding	1
O - Blank response/no comment	204
O - Refer to other question	178
RF - Current legislation	8
RF - Current legislation - non UK	11

Code	Count
RF - HFEA	37
RF - Historical experience	29
RF - Media coverage	1
RF - Participant - friend/relative/child with MD/similar disease	4
RF - Participant - has MD/similar disease	1
RF - Participant - info about	6
RF - Participant - other medical details	2
RF - Politics/government	19
RF - Relevant research	2
RF - Religion	9
RF - Views of other people/participants	4
SC - Germ line - could reduce in diversity	1
SC - MD - testing mothers	2
SC - MD - variety of forms/impacts	22
SC - Mitochondria - function/form	3
SC - Mt DNA - does not determine identity/traits	1
SC - Other procedures - abortion/termination	9
SC - Other procedures - adoption	1
SC - Other procedures - genetic techniques/gene therapy	6
SC - Other procedures - IVF/egg or sperm donation/surrogacy	3
SC - Other procedures - organ/tissue/blood donation	6
SC - Other procedures - other/general	4
SC - Overall - nature of medicine/science	4
SC - Overall - new procedure/knowledge will grow	7
SC - Overall - other comment	3
SC - Overall - question about application	2
SC - Overall - understanding is limited	3
SC - Progress - has gone too far to stop now	2
SC - Progress - reducing MD is good/positive	3
SC - Safety - other comment	3
SE - Ethical - benefits small number	3
SE - Ethical - embryo rights/usage other	3
SE - Ethical - equity of provision	16
SE - Ethical - ethical imperative to intervene	4
SE - Ethical - having healthy children is a right	2

Code	Count
SE - Ethical - having healthy children not a right/essential	1
SE - Ethical - implications	1
SE - Ethical - no slippery slope/not crossing boundary	2
SE - Ethical - slippery slope generally/crossing boundary	5
SE - Ethical - slippery slope to designer babies/commoditisation	6
SE - Ethical tradeoffs - evolution vs familial distress	1
SE - Ethical tradeoffs - safety vs progress	1
SE - Ethical tradeoffs - society vs individual	1
SE - General - benefits outweigh issues	1
SE - General - current social/ethical expectations	4
SE - General - no implications/concerns (No)	1
SE - General - unforeseen problems/impacts/health issues	4
SE - Social - benefits to potential parents/families/relationships	4
SE - Social - child awareness/understanding	1
SE - Social - child health/wellbeing improved	5
SE - Social - child health/wellbeing other	6
SE - Social - child rights	5
SE - Social - donor considerations	2
SE - Social - impact on future generations	1
SE - Social - issues from having MD/disability	3
SE - Social - legal implications/issues	1
SE - Social - ongoing monitoring/follow-up	2
SE - Social - overpopulation	1
SE - Social - parent rights/responsibilities	1
SE - Social - parents should not be pressurised	1

## 7. Further considerations

Are there any other considerations you think decision makers should take into account when deciding whether or not to permit mitochondria replacement?

Code	Count
AC - Acceptable - MST	2
AC - Acceptable - MST and PNT/general	6
AC - Acceptable with caveat - MST and PNT/general	4
AC - Not acceptable - MST and PNT/general	21
AC - Not acceptable - PNT	2



Code	Count
AC - Overall - understand issue/have sympathy	11
AC - Preference - MST over PNT	1
AG - Altering DNA - cloning/hybridisation	35
AG - Altering DNA - impact on germ line/lineage	36
AG - Altering DNA - not acceptable	28
AG - Cost - too much/cannot be justified	5
AG - Costs/risks - outweigh benefits	2
AG - Disease - will not be eradicated/not a cure	8
AG - Donation - risk/exploitation	9
AG - Ethics - creation/destruction of egg/embryo	10
AG - Ethics - embryo (mainly PNT) creation/destruction	100
AG - Ethics - end does not justify means	34
AG - Ethics - general/too many ethical issues	23
AG - Ethics - interfering with evolution/playing god	66
AG - Ethics - lack of consent/choice	1
AG - Ethics - no right to healthy/genetically related child	38
AG - Ethics - sanctity/dignity of human life	43
AG - Ethics - UK first in crossing ethical boundary	15
AG - Future - risks/impacts/unintended consequences	59
AG - Overall - not our decision to make/no right	6
AG - Population - too big/would increase	4
AG - Preferable alternative - adoption	16
AG - Preferable alternative - counselling/support	2
AG - Preferable alternative - decide not to conceive	2
AG - Preferable alternative - donor eggs	26
AG - Preferable alternative - donor embryo	2
AG - Preferable alternative - IVF	2
AG - Preferable alternative - other treatment/cure of MD	75
AG - Preferable alternative - other/general	16
AG - Preferable alternative - screening eggs/embryos	1
AG - Regulation - can't guarantee limits	5
AG - Regulation - may not be consistent across the board	3
AG - Science - false hope/may not work	70
AG - Science - just because it is possible does not mean it should be done	11
AG - Science - other comment	2

Code	Count
AG - Science - role/motivation of scientists	37
AG - Science - understanding is limited	3
AG - Slippery slope - attitudes to euthanasia	1
AG - Slippery slope - cloning	20
AG - Slippery slope - concerns	38
AG - Slippery slope - designer babies/commoditisation	18
AG - Slippery slope - eugenics	15
AG - Social - general/too many social issues	4
AG - Social - impact on child/identity/psychology	58
AG - Social - impact on donor/donor considerations	7
AG - Social - impact on family relationships	4
AG - Social - impact on parents	5
AG - Social - legal implications/scenarios	1
AG - Social - prioritise other issues/solutions	8
AG - Social - third person as parent/donor	52
AG - Social - will never be able to tackle all diseases	1
AG - Wider issue - against artificial fertilisation	3
CO - Alternatives - other comment	2
CO - Availability - NHS cover	3
CO - Availability - NHS should not cover/fund privately	1
CO - Business interest/involvement	4
CO - Cost/funding - general/who pays	18
CO - Criteria - cost/value	4
CO - Criteria - family situation/ability to provide	2
CO - Criteria - identifying those in need	4
CO - Criteria - medical evidence/advice	3
CO - Criteria - other	6
CO - Criteria - parent/patient choice	10
CO - Criteria - patient need/appropriateness	1
CO - Criteria - patient/clinician joint decision	7
CO - Criteria - regulator should decide	1
CO - Criteria - safety	21
CO - Criteria - seriousness of diseases/impacts	6
CO - Criteria - success rate/efficacy/efficiency	12
CO - Criteria - where proven risk to offspring	3

Code	Count
CO - Donation - availability/origin	4
CO - Donation - risk/exploitation	1
CO - Embryo or egg rights/life - concern	1
CO - Embryo or egg rights/life - general/other	3
CO - Ethics - different to designer embryos/cloning	6
CO - Ethics - interfering with evolution/playing god	3
CO - Ethics - other comment	7
CO - Ethics - should prevail	6
CO - Identity - concerns	1
CO - Labelling of techniques - misleading/misunderstood	7
CO - MST - could be more publically/ethically acceptable	4
CO - MST & PNT - other comparative comment	1
CO - Other priorities - concept of family	1
CO - Other priorities - MD diagnosis	1
CO - Other priorities - other health issues	2
CO - Other priorities - other MD treatment/cure	1
CO - Other priorities - poverty	1
CO - Other priorities - psychological/psychiatric care	1
CO - Overall - complex/unique decision/new territory	9
CO - Overall - needs 'humanising'	1
CO - Overall - needs rational/objective consideration	5
CO - Overall - no further considerations	29
CO - Overall - other comment	3
CO - Overall - same as other IVF/fertility treatment	6
CO - Overall - similar to other existing treatments/techniques	5
CO - Overall - speed of introduction	4
CO - Overall - weigh risks vs benefits/net gain	3
CO - Patients - follow up studies/monitoring	21
CO - Patients - information provision/involvement	16
CO - Patients - may go elsewhere/abroad	2
CO - Patients - support/counselling	9
CO - Population - growth/general	2
CO - Regulation - international considerations	6
CO - Regulation - limitation of use	10
CO - Regulation - needed	6

Code	Count
CO - Regulation - not needed	1
CO - Regulation - other comment	1
CO - Regulation - specifics	22
CO - Regulation - would prevent slippery slope	1
CO - Safety - risks is always present with medical procedures	2
CO - Safety - risks vs benefits	2
CO - Science - further research/trials/evidence	18
CO - Science - other comment	2
CO - Science - should prevail	9
CO - Slippery slope - designer babies/commoditisation	7
CO - Slippery slope - general	10
CO - Social - number of cases	11
CO - Social - parents should not be pressurised	3
CP - Consultation - comment on question	2
CP - Consultation - comment on response form	3
CP - Consultation - cost concern	1
CP - Consultation - lack of information	1
CP - Consultation - other negative comment	2
CP - Consultation - other positive comment	3
CP - Consultation - outcomes	1
CP - Consultation - poor publicity/lack of response	4
CP - Consultation - question motivations/bias	8
CP - Consultation - timing	3
CP - Consultation - welcomed	12
CP - Follow-up - further info on specific topic/s	3
CP - Follow-up - offer of help/further info	3
CP - Follow-up - other	2
CP - Follow-up - public communication/education	16
CP - Follow-up - role of specific sector/group	4
CP - Follow-up - wider debate	5
CP - Respondents - bear in mind experience/knowledge	3
CP - Respondents - comment on response rate	1
CP - Specific groups/views - disregard/do not give undue weight	23
CP - Specific groups/views - other comment	4
CP - Specific groups/views - talk to/consider	35

Code	Count
CP - Website - difficulty	1
CP - Website - lack of information	1
CP - Website - positive comment	1
CP - Website - video	1
CP - Wider issues - fertility treatment overall	2
CP - Wider issues - genetic disease	1
CP - Wider issues - pre-implantation techniques	1
CP - Wider issues - use of animals in research	1
DM - Clinicians - other comment	1
DM - Overall - consider rare/new/uncategorised diseases	1
DM - Overall - other comment	10
DM - Regulator - doesn't make it OK/ethical	1
DM - Regulator - sets boundaries not individual cases (option 2)	1
DS - Donor - payment	3
DS - Donor - responsibility for actions/know what they are getting into	1
DS - Donor function - providing medical solution/repair	2
DS - Donor status - no rights/responsibilities to child	1
DS - Mitochondria - complex/uncomfortable donation	1
DS - Mitochondria - similar to blood	1
DS - Mitochondria - similar to bone marrow	2
DS - Mitochondria - similar to organ	1
DS - Origin - allow choice	1
DS - Origin - should be family member/close relative	1
DS - Parents - payment	1
DS - Parents - responsibility for actions/know what they are getting into	2
FA - Benefits - outweigh cost/other considerations	7
FA - Disease - avoidance important/positive	9
FA - Disease - eradicate	9
FA - Disease - impact on families/sufferers	49
FA - Disease - scale of suffering underestimated	2
FA - Ethics - ethical imperative to intervene	17
FA - Ethics - no concerns	3
FA - Ethics - right to healthy/genetically related child	6
FA - MST - does not destroy embryos	2
FA - Overall - better than other techniques	5

Code	Count
FA - Overall - no reason not to allow	4
FA - Safety - changing law allow techniques to developed safely/responsibly	1
FA - Safety - these techniques are safe/risks acceptable	8
FA - Science - allow to progress as far as it can	2
FA - Science - could lead to new treatments (MD or other diseases)	6
FA - Science - important/positive	9
FA - Science - natural progress	2
FA - Science - other comment	3
FA - Science - UK as a leader in new techniques	5
FA - Slippery slope - not a concern	6
FA - Social - benefits to potential parents/families	24
FA - Social - health/wellbeing of the child	34
FA - Social - reduces burden on services/NHS	17
HOLDING	1
IN - Age - 18/when reaching adulthood	1
IN - Donor identity - should be available (general)	1
IN - Donor rights - other comment	2
IN - Logistics - donor screening	6
IN - Logistics - information storage/records	4
IN - Medical info - available for specific reasons/circumstances	1
IN - Medical info - should be available (general)	1
IN - Overall - conflicts of rights/interests	1
IN - Personal info - should be available (general)	1
LS - Comparison - like IVF/egg/sperm donation	1
LS - Conditions - allow testing/trials only at first	1
LS - Law should change - MD only	3
LS - Law should change - MST&PNT/general	23
LS - Law should change - quickly/asap	7
LS - Law should change w caveats - MST	1
LS - Law should change w caveats - MST&PNT/general	5
LS - Law should NOT change - MST&PNT/general	24
LS - Other - international impetus/influence/implications	7
LS - Other - other comment on law/legal system	5
LS - Other - punishment for undertaking techniques	10
LS - Other - re-examine if needed/after set period	1

Code	Count
LS - Other - specific related laws/legislation	7
LS - Other - specific suggestions for detail	3
O - Blank response/no comment	68
O - Not sure/do not know	4
O - Other/general comment	3
O - Refer to other question	21
O - Refer to other response	2
RF - Current legislation	5
RF - Current legislation - non UK	33
RF - External document	9
RF - External website	4
RF - HFEA	12
RF - Historical experience	69
RF - Media coverage	16
RF - NICE	1
RF - Other evidence/examples	7
RF - Participant - friend/relative/child with MD/similar disease	19
RF - Participant - has MD/similar disease	10
RF - Participant - info about	22
RF - Participant - other medical details	6
RF - Participant - personal details	2
RF - Politics/government	26
RF - Relevant research	12
RF - Religion	45
RF - Specific individual/organisation/group	23
RF - Views of other people/participants	46
SC - DNA - natural mixing	1
SC - DNA - nuclear DNA/genome not affected	2
SC - DNA - other comment	3
SC - Germ line - other comment	1
SC - MD - variety of forms/impacts	7
SC - Mitochondria - function/form	3
SC - Mt DNA - does not determine identity/traits	3
SC - Mt DNA - limited amount/types	1
SC - Mt DNA - origin/not human	1

Code	Count
SC - Mt DNA - other comment	8
SC - Mt DNA - small quantity/impact	2
SC - Mt DNA - suggested source for donation	2
SC - Other procedures - abortion/termination	2
SC - Other procedures - donor cytoplasm	1
SC - Other procedures - IVF/egg or sperm donation/surrogacy	6
SC - Other procedures - organ/tissue/blood donation	4
SC - Other procedures - other/general	1
SC - Overall - balancing science/ethics/religion/society	1
SC - Overall - further research/trials/evidence	1
SC - Overall - invest in other priorities/solutions	2
SC - Overall - motivation of scientists	2
SC - Overall - other comment	7
SC - Overall - question about application	3
SC - Overall - specific consideration for PNT	1
SC - Overall - trust/mistrust of scientists	2
SC - Progress - natural consequence/function of humanity	1
SC - Progress - other comment	2
SC - Progress - requires caution	3
SC - Safety - other comment	1
SE - Ethical - benefits small number	2
SE - Ethical - consent/choice concern	3
SE - Ethical - consent/choice other	1
SE - Ethical - end justifies means	1
SE - Ethical - equity of provision	8
SE - Ethical - interfering/playing god already happens	1
SE - Ethical - judging value/worth of life	1
SE - Ethical - no right to healthy/genetically related child	2
SE - Ethical - slippery slope generally/crossing boundary	1
SE - Ethical - society vs individual	4
SE - General - current social/ethical expectations	2
SE - General - implications	1
SE - General - implications cannot be understood	1
SE - General - unforeseen problems/impacts/health issues	6
SE - Social - attitudes towards disabled people/MD sufferers	10



Code	Count
SE - Social - attitudes towards those not treated	3
SE - Social - attitudes towards those treated	2
SE - Social - availability of counselling/testing/support	1
SE - Social - benefit to future generations	2
SE - Social - child awareness/understanding	3
SE - Social - child emotional/psychological impact	4
SE - Social - child health/wellbeing other	4
SE - Social - child ID/mixed genetic make-up	2
SE - Social - child impacts/damage (other/general)	1
SE - Social - child rights	5
SE - Social - donor considerations	1
SE - Social - ID issues less than other procedures	1
SE - Social - ID/issues complex/different for everyone	1
SE - Social - impact on family relationships (not third parent)	3
SE - Social - impact on future generations	11
SE - Social - issues from having MD/disability	1
SE - Social - legal implications/issues	2
SE - Social - no ID issues/implications foreseen	2
SE - Social - no third party parentage issues	5
SE - Social - overall societal benefit/not harmful	2
SE - Social - overall societal impact	12
SE - Social - parent rights/responsibilities	4
SE - Social - public/societal response/fear	2
SE - Social - risk losing valuable individuals	3
SE - Social - third party parentage issues	3
SE - Social - who should know the details	1

## 8. Non-questionnaire responses

Code	Count
AC - Acceptable - MST and PNT/general	38
AC - Acceptable with caveat - MST and PNT/general	1
AC - Not acceptable - MST	1
AC - Not acceptable - MST and PNT/general	297
AC - Not acceptable - PNT	1
AC - Overall - understand issue/have sympathy	20

Code	Count
AG - Altering DNA - cloning/hybridisation	17
AG - Altering DNA - impact on germ line/lineage	100
AG - Altering DNA - not acceptable	24
AG - Cost - too much/cannot be justified	3
AG - Costs/risks - outweigh benefits	20
AG - Donation - risk/exploitation	5
AG - Ethics - embryo (mainly PNT) creation/destruction	229
AG - Ethics - end does not justify means	13
AG - Ethics - general/too many ethical issues	29
AG - Ethics - interfering with evolution/playing god	91
AG - Ethics - lack of consent/choice	13
AG - Ethics - no right to healthy/genetically related child	3
AG - Ethics - other comment	7
AG - Ethics - sanctity/dignity of human life	181
AG - Ethics - UK first in crossing ethical boundary	109
AG - Future - risks/impacts/unintended consequences	173
AG - MST & PNT - both involve IVF/embryo destruction	4
AG - Population - too big/would increase	2
AG - Preferable alternative - adoption	6
AG - Preferable alternative - counselling/support	1
AG - Preferable alternative - IVF	1
AG - Preferable alternative - other treatment/cure of MD	118
AG - Preferable alternative - other/general	103
AG - Preferable alternative - screening eggs/embryos	2
AG - Regulation - can't guarantee limits	2
AG - Science - false hope/may not work	3
AG - Science - just because it is possible does not mean it should be done	11
AG - Science - other comment	5
AG - Science - role/motivation of scientists	31
AG - Science - understanding is limited	18
AG - Slippery slope - cloning	92
AG - Slippery slope - concerns	17
AG - Slippery slope - designer babies/commoditisation	99
AG - Slippery slope - eugenics	28
AG - Slippery slope - normalising GM	10

Code	Count
AG - Social - hardship is natural/contributes to strength of society	5
AG - Social - impact on child/identity/psychology	198
AG - Social - impact on donor/donor considerations	4
AG - Social - impact on family relationships	33
AG - Social - impact on parents	8
AG - Social - legal implications/scenarios	3
AG - Social - other comment	7
AG - Social - prioritise other issues/solutions	2
AG - Social - third person as parent/donor	249
AG - Social - worth of MD sufferers/disabled people	7
AG - Wider issue - against artificial fertilisation	1
CO - Embryo or egg rights/life - concern	2
CO - Embryo or egg rights/life - not a concern	1
CO - Ethics - different to designer embryos/cloning	3
CO - Ethics - other comment	3
CO - Identity - child should know about conception	1
CO - Identity - concerns	1
CO - Patients - information provision/involvement	2
CO - Regulation - international considerations	1
CO - Safety - risks vs benefits	4
CO - Science - further research/trials/evidence	6
CO - Science - mitochondrial function	4
CO - Science - other comment	4
CO - Science - participant understanding	7
CO - Slippery slope - designer babies/commoditisation	1
CO - Social - number of cases	4
CO - Social - parents should not be pressurised	2
CO - Social - risk losing valuable individuals	1
CP - Consultation - comment on question	2
CP - Consultation - other comment	11
CP - Consultation - other negative comment	6
CP - Consultation - other positive comment	5
CP - Consultation - poor publicity/lack of response	3
CP - Consultation - timing	4
CP - Consultation - welcomed	4

Code	Count
CP - Specific groups/views - disregard/do not give undue weight	2
CP - Specific groups/views - talk to/consider	1
CP - Website - difficulty	6
CP - Website - general	2
DM - Regulator - helps public acceptability	1
DM - Regulator - involvement is necessary (general/other)	3
DS - Donor status - is parent/relation to child	2
DS - Donor status - is unclear/ambiguous	1
DS - Donor status - legal considerations	1
DS - Mitochondria - different to blood	1
DS - Mitochondria - similar to egg/sperm/embryo/IVF	2
DS - Parents - responsibility for actions/know what they are getting into	1
FA - Benefits - outweigh cost/other considerations	2
FA - Disease - avoidance important/positive	6
FA - Disease - eradicate	6
FA - Disease - impact on families/sufferers	18
FA - Disease - scale of suffering underestimated	1
FA - Ethics - ethical imperative to intervene	2
FA - Ethics - right to healthy/genetically related child	2
FA - Identity - no concerns	1
FA - MST and PNT - better/alternative to current options	1
FA - Science - important/positive	4
FA - Science - nuclear DNA not altered	1
FA - Social - benefits to potential parents/families	7
FA - Social - general benefit to society/public health	1
FA - Social - health/wellbeing of the child	8
LS - Comparison - like IVF/egg/sperm donation	1
LS - Comparison - like organ/blood/tissue	1
LS - Further exploration needed - general/both	3
LS - International - impetus/influence/implications	1
LS - Law should change - MST&PNT/general	5
LS - Law should NOT change - MST&PNT/general	222
LS - Other - international impetus/influence/implications	12
LS - Other - lack of trust in government/regulators	2
LS - Other - punishment for undertaking techniques	56

Code	Count
LS - Other - specific related laws/legislation	2
LS - Punishment for undertaking techniques	1
O - Additional attachment	1
O - Other/general comment	43
O - Refer to other response	1
RF - Culture/literature	3
RF - Current legislation	7
RF - Current legislation - non UK	145
RF - External event/discussion	4
RF - HFEA	7
RF - Historical experience	19
RF - Participant - friend/relative/child with MD/similar disease	36
RF - Participant - has MD/similar disease	7
RF - Participant - info about	60
RF - Participant - personal details	11
RF - Politics/government	10
RF - Relevant research	37
RF - Religion	105
RF - Scientific review panel	1
RF - Specific individual/organisation/group	18
RF - Views of other people/participants	9
SC - DNA - nuclear DNA/genome not affected	1
SC - DNA - other comment	2
SC - MD - diagnosis	2
SC - Mt DNA - does not determine identity/traits	1
SC - Mt DNA - may affect identity/traits	1
SC - Mt DNA - other comment	1
SC - Other procedures - adoption	1
SC - Other procedures - IVF/egg or sperm donation/surrogacy	1
SC - Other procedures - organ/tissue/blood donation	2
SC - Overall - other comment	3
SC - Overall - trust/mistrust of scientists	1
SC - Progress - other comment	2
SC - Progress - reducing MD is good/positive	1
SC - Safety - other comment	3

Code	Count
SE - Ethical - consent/choice other	1
SE - Ethical - embryo rights/usage other	1
SE - Ethical - slippery slope generally/crossing boundary	1
SE - Ethical - slippery slope/similar to cloning	2
SE - Ethical - UK first in crossing ethical boundary	2
SE - General - implications	2
SE - General - other procedures acceptable/better	1
SE - Social - child rights	1
SE - Social - cost/resources	1
SE - Social - donor/child relationship difficulties	1
SE - Social - issues from having MD/disability	2
SE - Social - public/societal response/fear	1
SE - Social - third party parentage issues	1

---

# **Medical frontiers: debating mitochondria replacement**

## **Annex IV: Summary of the 2012 open consultation questionnaire**

---

**Report to: Human Fertilisation and Embryology Authority**

**February 2013**

**Prepared by Dialogue by Design**

Dialogue by Design  
252B Gray's Inn Road  
London WC1X 8XG

Telephone: 020 7042 8000  
Email: [facilitators@dialoguebydesign.com](mailto:facilitators@dialoguebydesign.com)  
Website: [www.dialoguebydesign.net](http://www.dialoguebydesign.net)

Company registration no. in England and Wales: 3856988  
VAT registration no. 123 4151 58

# Contents

---

<b>Executive Summary</b>	<b>4</b>
<b>Chapter 1            Introduction</b>	<b>8</b>
<b>Chapter 2            The consultation process</b>	<b>10</b>
2.1   Summary of consultation activities	10
2.2   Responses	10
2.3   About the respondents	11
<b>Chapter 3            Methodology</b>	<b>14</b>
3.1   Receiving responses	14
3.2   Analysing responses	14
3.3   About this report	16
<b>Chapter 4            Question 1: permissibility of new techniques</b>	<b>19</b>
4.1   Headline findings	19
4.2   Summary of comments	20
4.2.1   Arguments for the introduction of the techniques	20
4.2.2   Arguments against the introduction of the techniques	23
4.2.3   Other considerations	25
<b>Chapter 5            Question 2: changing the germ line</b>	<b>29</b>
5.1   Headline findings	29
5.2   Summary of comments	30
5.2.1   Uncertainty and risk	30
5.2.2   Social implications	32
5.2.3   Ethical implications	34
5.2.4   The science of the germline	35
<b>Chapter 6            Question 3: implications for identity</b>	<b>39</b>
6.1   Headline findings	39
6.2   Overview of comments	40
6.2.1   Reflections on identity	40
6.2.2   Ethical implications	42
6.2.3   Social implications	43
6.2.4   Comparing with other procedures	49
<b>Chapter 7            Question 4a: the status of the mitochondria donor</b>	<b>51</b>
7.1   Headline findings	51
7.2   Summary of comments	51
7.2.1   Comparing mitochondrial donation	51
7.2.2   The mitochondrial donor	55



<b>Chapter 8</b>	<b>Question 4b: the status of the mitochondria donor</b>	<b>58</b>
8.1	Headline findings	58
8.2	Summary of comments	60
8.2.1	Option 1 (no information) & option 2 (some information but not identity)	60
8.2.2	Option 3 (information and ability to contact once child is 18)	62
8.2.3	Option 4	64
8.2.4	Option 5	66
8.2.5	Other comments	66
<b>Chapter 9</b>	<b>Question 5: regulation of mitochondria replacement</b>	<b>67</b>
9.1	Headline findings	67
9.2	Overview of comments	69
9.2.1	Responses to option 1 (clinics and patients to decide)	69
9.2.2	Responses to option 2 (regulatory framework; clinics and patients decide)	71
9.2.3	Responses to option 3 (regulator decides)	73
9.2.4	Responses to option 4 (mitochondria replacement should not be permitted)	74
<b>Chapter 10</b>	<b>Question 6: should the law be changed?</b>	<b>76</b>
10.1	Headline findings	76
10.2	Overview of comments	78
10.2.1	Arguments against a change in law	78
10.2.2	Arguments in favour of a change in law	80
10.2.3	Other legal and regulatory considerations	82
10.2.4	Other considerations	84
<b>Chapter 11</b>	<b>Question 7: further considerations</b>	<b>85</b>
11.1	Headline findings	85
11.2	Overview of comments	86
11.2.1	Arguments against the introduction of the techniques	86
11.2.2	Arguments for the introduction of the techniques	88
11.2.3	Other considerations	89
11.2.4	Context and decision making	92
<b>Appendix</b>		<b>95</b>
A.1	Consultation questions	95
A.2	Responding organisations	97
A.3	Analysis: List of themes	100
A.4	Analysis: List of codes applied per question	101

## Executive summary

---

### About the consultation

The Office for Public Management (OPM), in partnership with Forster and Dialogue by Design (DbyD), was commissioned by the Human Fertilisation and Embryology Authority (HFEA) to conduct a multi-method research and engagement project looking at the possible social and ethical issues relating to two techniques for the avoidance of mitochondrial disease: pronuclear transfer (PNT)<sup>1</sup> and maternal spindle transfer (MST)<sup>2</sup>.

As part of this research and engagement, *Medical Frontiers: debating mitochondria replacement*, an **open consultation** ran from 17 September to 7 December 2012.

Respondents were invited to consider a range of information presented on the consultation website, and to respond to seven questions using the online questionnaire.

A total of **1,836 responses** were received, the majority of which were via the consultation website. Respondents include stakeholder organisations, individuals with personal experience of mitochondrial disease, as well as many members of the public.

The consultation process was managed by Dialogue by Design (DbyD), a company specialising in managing large or complex consultation processes. DbyD received, processed and analysed all responses to the consultation in close liaison with the HFEA.

It is important to note that the open consultation provided an opportunity to participate for individuals and organisations keen to have their views heard. As anyone who wanted to could participate, the views expressed **cannot be considered representative of the wider population**.

### Emerging themes

The consultation questionnaire asks respondents to consider a number of questions relating to making MST and pronuclear transfer PNT techniques available to people at risk of passing on mitochondrial disease to their child.

Throughout responses to all consultation questions a number of themes are highlighted repeatedly, mostly as part of a narrative that is either supportive of the introduction of the techniques, or one that articulates opposition.

**Respondents who argue against** the introduction of mitochondria replacement techniques often express concern that such a move would cross an ethical boundary or amount to inappropriate interference with the natural or spiritual aspect of reproduction. Many specify that they believe it is problematic that children born as a result of the techniques will carry DNA from three people, for a range of reasons further discussed below. Another strand to some respondents' opposition is the creation and destruction of embryos as part of PNT, which in their view is unethical.

---

<sup>1</sup> Pronuclear transfer involves transferring the pronuclei from an embryo with unhealthy mitochondria and placing them into a donor embryo which contains healthy mitochondria and has had its pronuclei removed. A pronucleus is a small round structure containing nuclear DNA seen within an embryo following fertilisation. A normal embryo should contain two pronuclei, one from the egg (maternal pronucleus) and one from the sperm (paternal pronucleus).

<sup>2</sup> The maternal spindle is a structure within the egg containing the mother's nuclear DNA. Maternal spindle transfer involves transferring the spindle from the intended mother's egg, with unhealthy mitochondria, and placing it into a donor egg with healthy mitochondria.

**Respondents who argue in favour** of the introduction of mitochondria replacement techniques often emphasise the benefits of the techniques to families affected by mitochondrial disease. Many say they believe it is important - some say there is an ethical imperative - to avoid or eradicate the disease, sometimes referring to the suffering that patients may endure. Respondents who support the techniques also tend to employ arguments about the genetic significance of donated mitochondria (or mitochondrial DNA), which they believe is limited and therefore not a great concern. This is further explored in the sections below.

An additional theme emerging both in responses arguing against the techniques and in responses arguing in favour is the **management of risk**. For many respondents supporting mitochondria replacement in principle it is crucial that sufficient evidence is available about the safety of the techniques before they are allowed in a clinical setting. Other respondents highlight that risks cannot be fully managed and that this is part of the reason why they oppose the introduction of mitochondria replacement techniques.

## Consultation questions

Responses to each of the seven consultation questions are discussed below, focusing on issues specific to those questions.

### Question 1

Asked for their **views on offering MST and PNT** to people at risk of passing on mitochondrial disease to their child, just over 500 respondents say they do not think the techniques should be permitted, while almost 500 say that they support the introduction of both techniques. Most respondents with direct or indirect experience of mitochondrial disease argue in favour of the introduction of the techniques.

Where respondents support one technique in particular, they tend to prefer MST because this technique replaces mitochondria in eggs rather than embryos.

### Question 2

Respondents are asked in question 2 whether they think there are social and ethical implications to **changing the germline**.

Those in favour of the techniques argue that there are **no negative implications** or that these are outweighed by the positives. Respondents who oppose the introduction of the techniques specify a range of potential implications, highlighted below.

With regard to the germline the most prominent concern expressed is that consequences of the techniques will affect many **generations down the line**, and that these consequences are to some extent unknown.

Another potential implication outlined in some respondents' views is that making changes to the germline for this purpose could **lead to other changes** becoming more acceptable: many respondents identify the idea of germline change with cloning or the creation of designer babies.

Others argue that any change to the germline is inappropriate because there is no way for all those affected to give **consent**; a view contradicted by a few who see making choices for subsequent generations as a very ordinary part of being a parent.

### Question 3

When asked in question 3 whether they think the techniques have social or ethical implications relating to **a person's sense of identity**, respondents' comments differ widely.

Respondents who believe such implications will be **minor or non-existent** often argue that identity is more a social than a genetic concept, that mitochondrial DNA has no function in determining an individual's characteristics, and that other procedures currently used (including adoption and gamete donation) are likely to have similar or greater implications.

Respondents who consider that implications are likely often say that knowing they carry DNA from three people may saddle children with questions about who they are, and who their parents are, which they say will have a detrimental impact on their **well-being**. Some respondents argue that adopted or donor-conceived children suffer from identity issues and that children resulting from mitochondria replacement could experience similar problems, or worse. A number of respondents think that children born as a result of using PNT might also feel unhappy about the creation and destruction of embryos as part of their conception.

Many respondents believe that parents will be able to **mitigate** any identity implications by being open about how the child is conceived.

#### Question 4a

The consultation questionnaire asks how respondents **view the status of a mitochondria donor** compared to other, existing types of donor. Views differ diametrically on this topic, with mitochondria donation seen as similar to, and different from, each existing type of donation by roughly equal numbers of respondents.

The most frequently made comparisons are with **gamete donation**, closely followed by **tissue, organ and bone marrow donation**. Generally speaking it is the genetic significance of mitochondria donation that informs respondents' comparisons, with those believing mitochondrial DNA is of greater significance more inclined to compare with gamete donation, and others more inclined to compare with organ, tissue or bone marrow donation.

#### Question 4b

This question asks respondents about their views on possible models for governing the disclosure of **information about the mitochondria donor** to the child.

The consultation questionnaire outlines three possible models, each of which are supported by more than 100 respondents. Most of these believe **children should not know the identity** of their mitochondria donor, with opinion divided on whether medical and personal information should be available. About 150 respondents think **children should be able to contact their mitochondria donor** once they reach the age of 18. Some respondents offer alternatives to the models proposed in the question, including suggestions for more flexible arrangements.

Respondents often indicate that their preference is informed by whether or not they regard the mitochondria donor as **a third parent** of the child, with those who think of the donor as a parent more inclined to favour a model that allows contact.

Several respondents think that donors should **consent** to the information that is disclosed, in particular for the model where the donor's identity would be made available to the child. Others argue that the disclosure of identity is part of the responsibilities of the donor.

Respondents who oppose the introduction of the techniques generally do not discuss the models and reaffirm their **opposition** instead.

#### Question 5

In question 5 respondents are asked to indicate a preference for one of three possible **models of regulation** if the law were to be changed to allow mitochondria replacement to be carried out in specialist clinics.

Almost half of the respondents to this question decline to express such a preference, and instead note their objection to mitochondria replacement.

Of those respondents who indicate a preference for a particular model of decision making, close to half opt for a system in which **clinics and individual patients** would make a case-by-case decision about whether or not to use mitochondria replacement (option 1). This preference is often associated with a view that a central regulatory board may lack sensitivity to individual circumstances and a feeling that individual patients should be empowered to choose the best option for their own families.

A similar number of respondents prefer an option that includes a **role for the regulator** (option 2 and option 3). Many feel that an external regulatory framework would provide a buffer against abusive profiteering and promote fairness by making sure that the same criteria are applied for all applications for treatment.

Most respondents who think there is a role for the regulator express a preference for a **broad regulatory framework** in which the regulator sets overall criteria within which patients and clinicians can decide on a case-by-case basis. A minority of respondents express a preference for a model in which a central regulator would maintain responsibility for making decisions about particular cases.

### Question 6

In question 6 of the consultation questionnaire, respondents are **asked whether they believe the law should be changed** to allow mitochondria replacement techniques to be made available to people who are at risk of passing on mitochondrial disease to their child.

A majority of these respondents argue against changing the law, while a substantial minority argue in favour.

Those **arguing against a law change** sometimes refer to the international context and see it as problematic that the UK would be the first or only country to allow the use of MST and PNT. Several respondents argue that other methods should be considered before forging ahead with these new techniques.

Respondents **arguing in favour of law change**, and particularly those adding caveats to their support, highlight a variety of criteria they think need to be met. Respondents also suggest that further work is undertaken to specify which of the techniques (MST and/or PNT) should be allowed, and in which circumstances.

### Question 7

The final consultation question asks respondents whether there are any **other considerations** they think decision makers should take into account.

In addition to reiterating points they made in response to earlier questions, some respondents highlight that decision makers should particularly consider the **views of certain groups** such as patients and relatives, scientists, and religious groups. With regard to the latter there are responses urging decision makers to not give undue consideration to these.

## Chapter 1 Introduction

---

Mitochondria are present in almost all human cells. They are often referred to as the cell's 'batteries' as they generate the majority of a cell's energy supply. For any cell to work properly, the mitochondria need to be healthy. Unhealthy mitochondria can cause genetic disorders known as mitochondrial disease.

There are many different conditions that are linked to mitochondrial disease. They can range from mild to severe or life threatening, and can have devastating effects on the families that carry them. Currently there is no known cure and treatment options are limited. For many patients with mitochondrial disease preventing the transmission of the disease to their children is a key concern.

Mitochondrial disease can be caused by faults in the genes within a cell's nucleus that are required for mitochondrial function or by faults within the small amount of DNA that exists within the mitochondria themselves. It is the latter form of mitochondrial disease that could be avoided using two new medical techniques, termed pro-nuclear transfer (PNT) and maternal spindle transfer (MST) which UK researchers are working on.

These techniques are at the cutting edge, both of science and ethics and are currently only permitted in research. They involve removing the nuclear DNA from an egg or embryo with unhealthy mitochondria, and transferring it into an enucleated donor egg or embryo with healthy mitochondria.

The Human Fertilisation and Embryology Act (1990) (as amended) ('the Act') governs research and treatment involving human embryos and related clinical practices in the UK. The Act currently prevents the clinical use of these techniques (or any other technique that involves genetic modification of gametes and embryos to treat patients). However, in 2008 the Act was amended, introducing new powers which enable the Secretary of State for Health to permit techniques which prevent the transmission of serious mitochondrial disease. The Secretary of State for Health and the Secretary of State for Business, Innovation and Skills asked the Human Fertilisation and Embryology Authority (HFEA) to seek public views on these emerging techniques. On considering advice from the HFEA the Government will decide whether to propose regulations legalising one or both of the procedures for treatment.

The HFEA, together with the Sciencewise Expert Resource Centre<sup>3</sup>, therefore commissioned OPM (in partnership with Forster and Dialogue by Design) to conduct a multi-method research and engagement project looking at the possible social and ethical issues and arguments relating to the techniques. The project consisted of five strands:

1. Deliberative public workshops
2. Public representative survey
3. Patient focus group
4. Open consultation meetings
5. Open consultation questionnaire

As part of this range of activities to seek views of members of the public, the HFEA conducted a open consultation on mitochondria replacement in the autumn of 2012. This report provides a

---

<sup>3</sup> The Sciencewise Expert Resource Centre (Sciencewise-ERC) is the UK's national centre for public dialogue in policy making involving science and technology issues.

summary of the responses to the consultation, which was run by an independent specialist company.

The findings of the consultation have also informed the Summary of Evidence which is published separately, and also contains findings from other dialogue and research activities. The overview report also contains an introduction to the techniques and the issues the HFEA is considering as part of their duty to provide recommendations to Government.

## Chapter 2      The consultation process

---

### 2.1      Summary of consultation activities

The HFEA's public consultation on *Medical Frontiers: debating mitochondria replacement* ran from 17 September to 7 December 2012. It followed an intensive and wide-ranging programme of dialogue and research carried out in the spring and summer of 2012, and the findings from these stages informed the consultation questionnaire. This report covers the public consultation only; please see the Summary of Evidence for summaries of other engagement activities. The purpose of the public consultation was to gather public views on the social and ethical impact of making the proposed techniques available to patients. The HFEA will consider these views when they prepare their recommendations to Government.

The consultation was open to all. Respondents were invited to consider a range of information presented on the consultation website, and to respond to seven questions using the online questionnaire. Although the consultation website encouraged respondents to consider the information presented, respondents may have preferred to respond without considering this information, or to use other sources to inform their response. Respondents were not asked to indicate which information they consulted, so this has not been used as a variable in the analysis or the report.

The consultation documents recommended the use of the online questionnaire, but responses made via email or post were also accepted while the consultation was open. The consultation was managed by Dialogue by Design (DbyD), a company specialised in managing large or complex consultation processes.

The public consultation was an open process, which means that respondents cannot be considered a representative sample of the UK population, as one would expect to find in a survey or referendum. Rather, the consultation attracted responses from individuals and organisations who chose to respond. Its main purpose is to help the HFEA understand the range of views held by respondents as well as the arguments underpinning these views. Although it can be helpful to consider how many respondents express certain views, this is not the primary aim of the consultation or indeed this report.

The HFEA also held two public meetings in London and Manchester, which gave members of the public a chance to share their views in person. The events included a panel of experts who gave some information about the techniques and took questions from the attendees, as well as a chance for members of the public to discuss the issues. These meetings have been reported on separately and have also been covered in the Summary of Evidence.

### 2.2      Responses

A total of 1,836 responses to the consultation were received. Most of these were submitted via the consultation website. Additionally, 524 letters and emails were received. A further 45 respondents completed a response form.



**Table 1 Overview of response types**

Response type	Count
Online questionnaire	1,260
Paper-based response form	45
Letters and emails	524
Total	1,836

Not all respondents answered all consultation questions. In fact, some respondents answered none of the questions, but sent a generic letter or email in which they set out their views. Table 2 below provides an overview of the number of responses each consultation question received.

**Table 2 Overview of responses per consultation question**

Question	Count of responses
Question 1	1,235
Question 2	1,114
Question 3	1,084
Question 4a	987
Question 4b	1,039
Question 5	1,143
Question 6	1,055
Question 7	883
Other responses, not specific to consultation questions	503

## 2.3 About the respondents

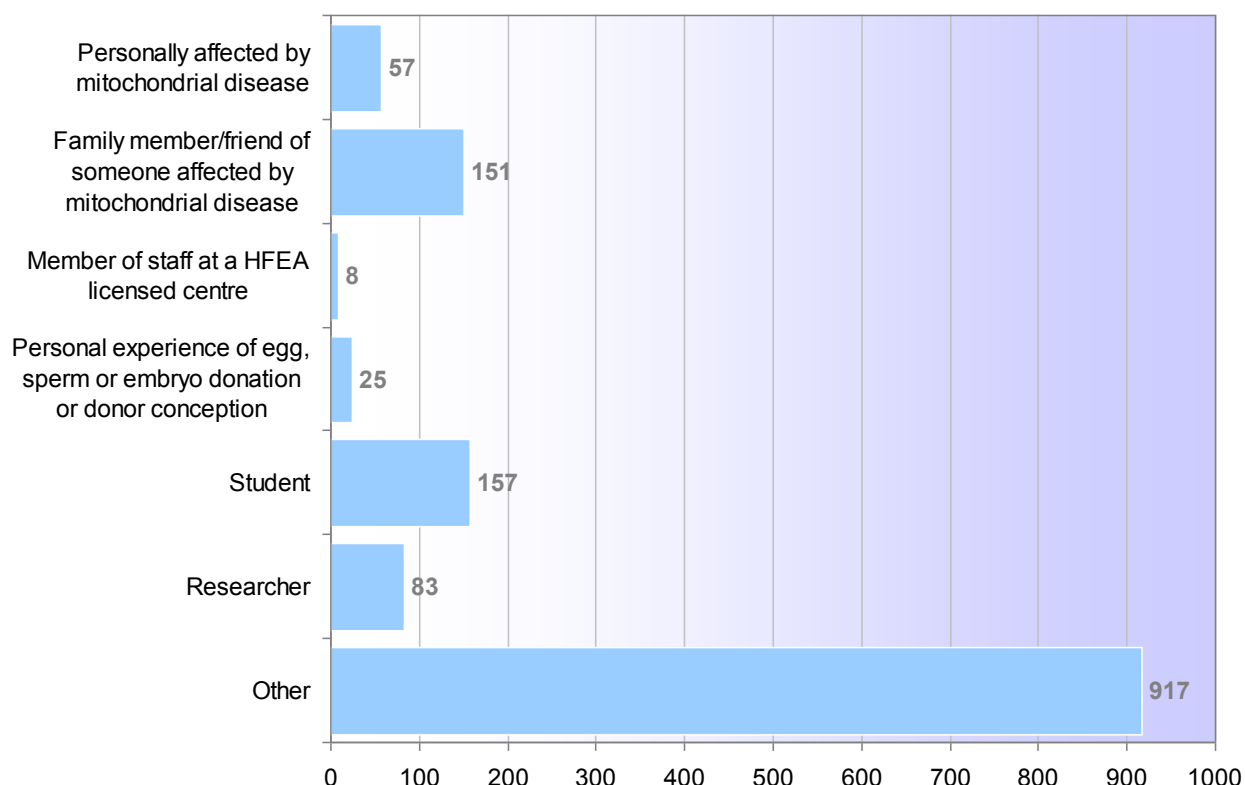
Respondents who used either the consultation website or a response form were asked to answer a small number of questions about themselves, specifying their background and the nature of their interest in the consultation. The responses to these questions are summarised here.

A total of 66 respondents specified that their response was submitted on behalf of an organisation. A list of organisations who participated in the consultation is provided in appendix 2.

The questionnaire also asked respondents to select from a series of listed options which best described them. Respondents could select more than one option if appropriate. An overview of the responses to this question is given in figure 1 below. This respondent information could not be collected for those who responded by email or letter.

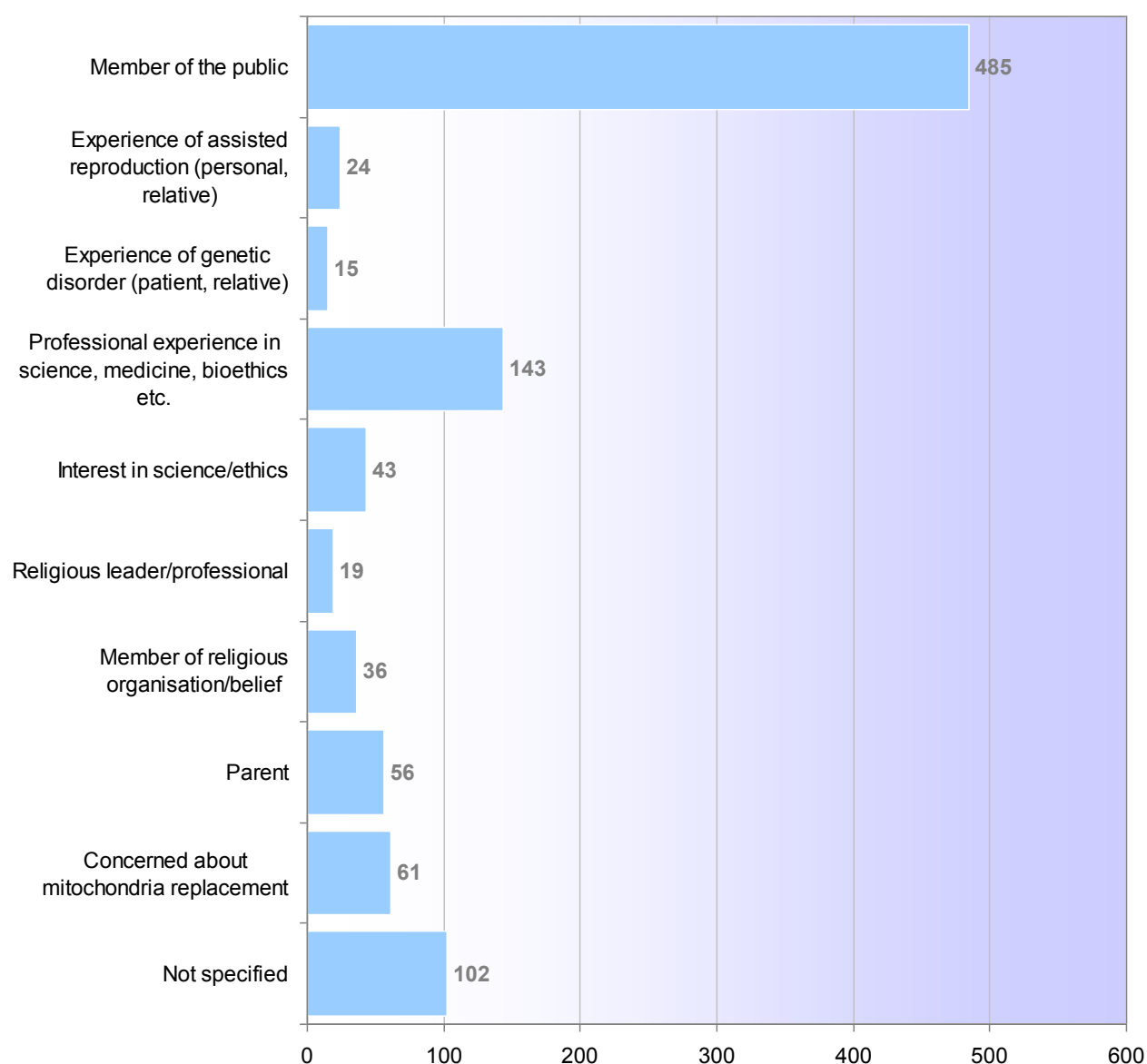
Figure 1 shows that most respondents did not describe themselves as belonging to one of the categories specified in the questionnaire, with 917 respondents choosing 'Other'. Of those who did identify with listed options, 157 respondents indicated they were students and 83 that they were researchers. A total of 151 respondents specified that they were a family member or friend of someone affected by mitochondrial disease; 57 respondents indicated that they themselves were affected. Also, 25 respondents indicated that they had personal experience of egg, sperm, embryo donation or donor conception and 8 respondents identified themselves as staff members at a HFEA licensed centre.

**Figure 1**      **Respondent types (online only)**



As is shown above, the majority of respondents who completed the 'About you' question ticked 'Other' and many of these specified further their interest in the consultation. Roughly half of the respondents who selected 'Other' identified themselves as 'members of the public' or 'citizens'. Smaller numbers of respondents included details about their scientific or professional background, their religious beliefs or involvement, or their experience of related diseases or procedure. A rough breakdown of the respondents within the 'other' category is shown in figure 2. Please note that many respondents included a fair bit of information, therefore sometimes respondents have been counted in multiple categories.

**Figure 2 Respondent type ‘other’: further breakdown based on self-description**



### **Individuals, organisations and organised responses**

It is worth noting that respondents include individuals responding on behalf of themselves (or a small group of people), organisations responding on behalf of their staff or membership, as well as individuals responding in their capacity of supporters of an organisation or group. This is common for open consultation processes: there is no selection of respondents other than the choice of individuals and organisations to respond.

As discussed in section 2.1 above and further clarified in chapter 3, this needs to be kept in mind when considering the summary of responses. In particular, it is possible (and common for this type of high-profile consultation) that a proportion of the responses are a result of initiatives from groups or organisations to raise the prominence of specific points of view. This may have influenced the numbers of responses expressing either strong support for or strong opposition to mitochondria replacement.

## Chapter 3 Methodology

---

### 3.1 Receiving responses

Responses were received in a number of formats: online response forms (via the website), letters and emails. All responses were received by DbyD, at which point they were assigned a unique reference number and entered into the DbyD analysis system.

#### Online response forms

Online responses were imported directly into the DbyD analysis system. Whilst the consultation was open, users were able to update or amend their submission. If respondents updated their submission this was imported into the analysis database with a clear reference that it had been modified, to ensure that any new information was taken into account during the analysis.

#### Paper response forms

Response forms received by post were logged and scanned, then manually written or copied into the analysis database by data entry staff. The data entry process followed the questionnaire structure so that these responses could be analysed in the same way as online responses. Data entry was monitored by the DbyD transcription team to ensure that responses were accurately captured.

#### Emails

Respondents were able to send responses directly to DbyD by email. These responses were logged, imported into our analysis system and analysed alongside the online responses.

#### Letters

Letters sent to DbyD were logged, scanned and written into the database by data entry staff. The data entry process was monitored by the DbyD transcription team to ensure that responses were accurately captured. Once data entry was complete responses were imported to the analysis system and analysed alongside the online responses.

#### Responses sent to the HFEA

A small number of responses were sent directly to the HFEA, either by post or by email. The HFEA informed respondents that their response would be considered as part of the consultation and securely transferred the responses to DbyD, where they were entered into the analysis system as described above.

#### Late submissions

The consultation ended at midnight on Friday 7<sup>th</sup> December. To make allowances for potential delays in the email and postal systems offline responses which arrived no later than Tuesday 11 December 2012 were included in the analysis and this report.

### 3.2 Analysing responses

#### Developing an analysis framework

In order to analyse the responses, and the variety of views expressed, an analytical framework was created. The purpose of the framework was to enable analysts to organise responses by key themes and issues so that key messages as well as specific points of detail could be captured and reported.

A three-tier approach was taken to coding, starting with high level themes, splitting into sub-themes and then specific codes. As an example, a response to question 1 containing a concern about changes to the germ line would be coded into (theme) *Arguments against* - (sub-theme) *Altering DNA* - (code) *impact on germ line/lineage*. Some themes were used more often for particular questions, while others were used equally across the questions as respondents raised similar issues. Table 3 provides a full list of the top level themes used and Table 4 provides an extract from the coding framework showing the use of themes, sub-themes and codes. The full list of themes and codes are available in appendices 3 and 4.

Each code is intended to represent a specific issue or argument raised in responses. The data analysis system allows the analysts to populate a basic coding framework at the start (top-down) whilst providing scope for further development of the framework using suggestions from the analysts engaging with the response data (bottom-up). We use natural language codes (rather than numeric sets) since this allows analysts to suggest refinements and additional issues, and aids quality control and external verification.

**Table 3 Coding framework: themes**

Theme	Acronym
Acceptability	AC
Arguments against	AG
Arguments in favour	FA
Considerations	CO
Consultation process	CP
Decision making	DM
Donation status	DS
Information	IN
Legal Status	LS
Other	O
References	RF
Science	SC
Social and ethical	SE

**Table 4 Coding framework: example codes for SC and SE themes**

Theme	Sample codes
Science	SC - DNA - natural mixing SC - Mitochondria - function/form SC - Mt DNA - does not affect identity/traits SC - Mt DNA - may affect identity/traits SC - other procedures - organ/tissue/blood donation
Social and ethical	SE - Ethical - end does not justify means SE - Ethical - ethical imperative to intervene SE - General - similar to other procedures SE - Social - child awareness/understanding SE - Social - donor/child relationship SE - Social - overall societal impact

### Applying the analysis framework

The analysis team, supervised by the senior analysts who developed the coding framework, worked systematically through each response to the consultation, applying the relevant codes to capture the issues raised. The application of a code from the framework was done simply by highlighting the relevant text and recording the selection. A single response would receive multiple codes to capture the various issues raised by each respondent.

The coding of responses to each question was regularly checked and reviewed by senior analysts to ensure quality and consistency. In addition, HFEA was able to view analysed responses throughout the analysis stage and provide feedback on the coding when required.

## 3.3 About this report

This report provides a summary of the responses to the HFEA consultation on *Medical frontiers: debating mitochondria replacement*. It gives a flavour of the issues raised in response to each of the consultation questions.

As outlined above, this report is produced to help the HFEA understand the range of views held by respondents as well as the arguments underpinning these views. For that reason it is not written with a view to identify majority views, or to emphasise points made by greater numbers of responses only. Rather the report aims to present minority views alongside those held by many, so that each issue is discussed in a manner that does as much justice as possible to the wealth of suggestions presented in responses.

### Summarising a variety of response types

The structure of this report mirrors the structure of the consultation questionnaire (see appendix 1), with a chapter dedicated to each consultation question. Each chapter summarises views expressed in response to the question it covers. This includes comments from stakeholder organisations as well as individuals. The report aims to provide an accurate summary of all respondents' views and efforts were made to ensure that it amply covers responses from organisations as well as individuals.

Chapter 2 includes a breakdown of respondent categories based on what respondents indicated when asked to define their interest in the consultation. Where relevant the report specifically looks at the responses from a particular category of respondents, for instance to consider the views of those with experience of gamete donation on the status of the mitochondria donor.

As specified in chapter 2, not all respondents used the consultation questionnaire: some 500 responses received as emails and letters did not refer to the consultation questions. Non-questionnaire responses were analysed in the same way as questionnaire responses, making up an additional 'question' in the database. In the report, the issues most prominently discussed in these responses are discussed in the most relevant chapter, i.e. comments about changing the law are discussed in chapter 10. As these responses are not directly addressing the consultation question, they are discussed separately from the other responses, and set apart by a different layout.

Both among questionnaire and non-questionnaire responses there are numerous respondents making similarly or identically worded arguments. This indicates that there may have been initiatives to encourage people to respond to the consultation in a certain way. While this does not make such responses less valid or valuable than others, it is important that readers of the report are aware of this. To accommodate this, the report clarifies where particular views are made by many respondents using the same words or suite of arguments.

### **Numbers and quantifying terms**

Where the report refers to how many respondents have raised a specific issue, it is important to keep in mind that this was an open and qualitative consultation process rather than a way to establish dominant views across a representative cross-section of the public. The numbers in the report are useful in clarifying where issues are seen as important by many or by a few respondents. Beyond that, however, they cannot be seen to serve any statistical purposes. This is also true for the numbers reported on in chapters 8 and 9, where the closed questions of the questionnaire are discussed and charts are included to summarise responses.

Similar to the above, the report contains words like 'many', 'some', 'a few' in order to indicate the distribution of opinions among respondents on particular topics. In this way these terms help clarify whether viewpoints discussed are raised by greater or smaller numbers of respondents. The words are only very rarely used in relation to the total number of respondents to the consultation. Rather, the use of these words depends on their context, i.e. 'many' should not be regarded as indicating a precise numeric range.

### **Info-graphics**

The following chapters of the report each contain an info-graphic presenting a diagram of the topics emerging in responses to the consultation question discussed in that chapter. These diagrams aim to clarify how the report breaks down the wide range of issues relating to each consultation question; they do not indicate any further or deeper interpretation of the data.

### **Quotes**

Throughout the following chapters quotes from respondents have been used to illustrate the points raised. Where responses from organisations are quoted, the name of the organisation is mentioned; individual respondents are not identified by name when quoted.

### **Use of the terms social and ethical**

Several consultation questions ask respondents to consider whether the techniques have social or ethical implications. As part of the analysis of these and other questions a distinction was made between implications, or issues, that could be described as ethical and others that would primarily

be social. The distinction used throughout the analysis brands arguments relating to ideologies and value systems as *ethical* and arguments relating to impact on individuals or groups in society as *social*. This distinction has been used consistently across the consultation questions. In this regard it is important to remember that the report merely aims to summarise responses; further interpretation is outside the scope of this report.



## Chapter 4      Question 1: permissibility of new techniques

### 4.1      **Headline findings**

The first question asks:

**Q1: Having read the information on this website about the two mitochondria replacement techniques – maternal spindle transfer and pro-nuclear transfer, what are your views on offering (one or both of) these techniques to people at risk of passing on mitochondrial disease to their child? You may wish to address the two techniques separately.**

1,235 responses were made to this question.

Most respondents took this opportunity to express their view about the acceptability the techniques - with approximately equal numbers supporting and opposing their introduction into clinical practice. Most respondents commented on the acceptability of the techniques taken together or without distinguishing between them: 349 state that they consider both acceptable, while 106 agree but with some caveats, but 502 say they are not acceptable. Among those commenting on the MST technique alone, 20 say the technique is acceptable, compared to 3 who agree with caveats and 2 respondents who say it is not acceptable. Conversely, no respondents commenting on the PNT technique alone say that it is acceptable, but 3 say it is acceptable while acknowledging some caveats, and 24 state that it is not acceptable.

Proponents of the techniques tend to focus on social outcomes, particularly the potential to avoid disease and allow parents the opportunity to have a healthy child. Some feel that if the techniques are possible, there is an ethical obligation to implement them. In contrast those opposing the techniques are more likely to discuss ethical issues, often arguing that use of the techniques would amount to inappropriate interference with the natural or spiritual aspect of reproduction. Others focus on the use of embryos, particularly in relation to PNT, arguing that any artificial or in-vitro manipulation of embryos is unethical. Where respondents support one technique in particular, they tend to prefer MST because it involves eggs rather than embryos. A few respondents say they favour PNT, sometimes stating that this technique has a greater success rate.

Looking at respondent types, there is a visible pattern with regard to their view on the acceptability of the techniques. Among those who describe themselves as 'other', there are 453 respondents stating that the techniques are not acceptable and 156 respondents saying they are. For each of the other respondent categories, such as 'student' and 'family member or friend affected by mitochondrial disease', more respondents say they find the techniques acceptable than unacceptable. Of the respondents describing themselves as personally affected by mitochondrial disease 36 think the techniques are acceptable and three think they are not.

#### **Non-questionnaire responses**

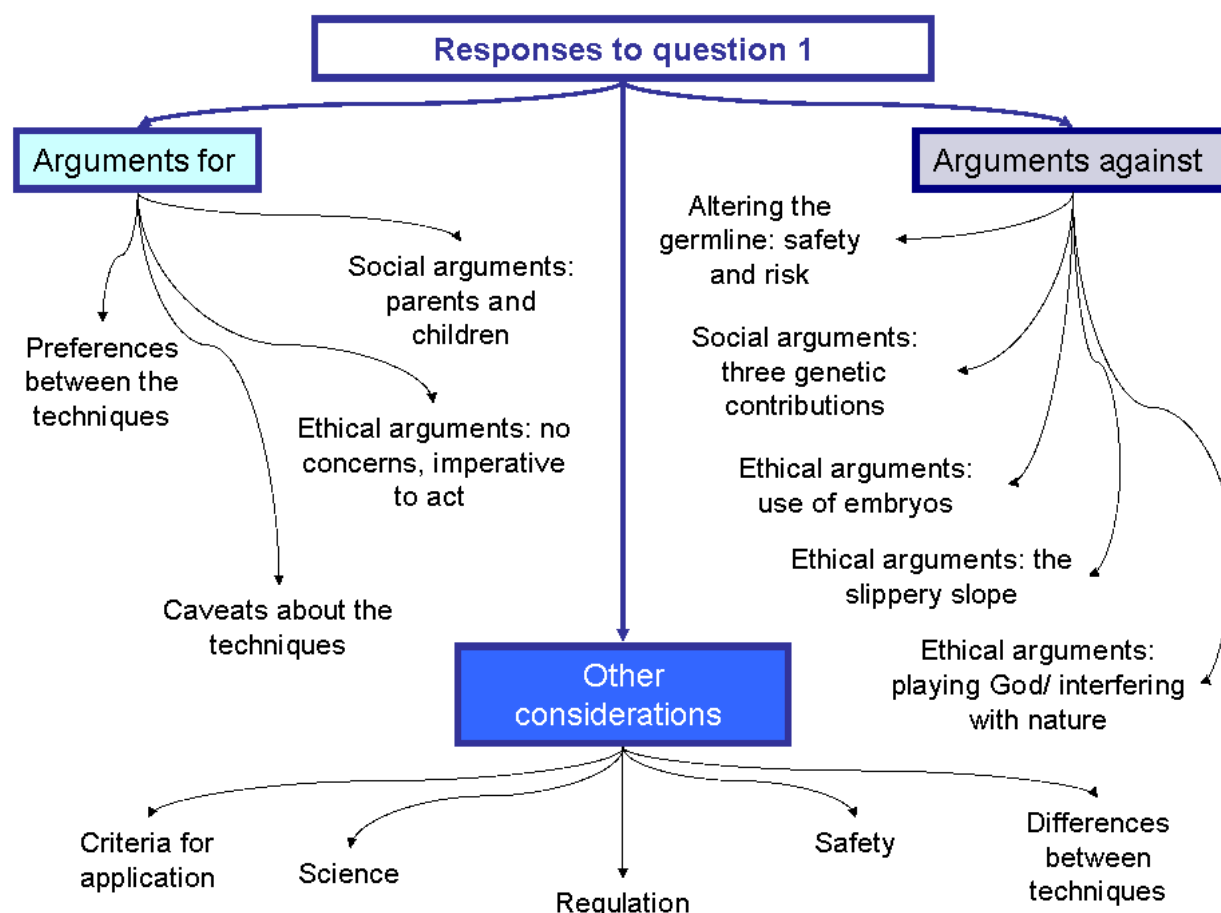
Comments on the permissibility of the techniques are also abundant in the 503 non-questionnaire responses to the consultation. These responses include a large number of letters and emails which make a similar range of arguments, often using very similar wording. Some 300 respondents state that they do not think either of the techniques are acceptable. Often this statement is accompanied by concerns about the use of embryos and/or the idea that children will carry DNA from three people. Respondents also express concern about possible unintended long-term consequences of mitochondria replacement. Some respondents believe the techniques will lead to

the acceptance of cloning and/or designer babies. A substantial number of those who argue against the techniques refer to their religion.

Some 40 respondents who sent a letter or email believe that mitochondria replacement techniques are acceptable. Many of these refer to a particular case of a child that was born with mitochondrial disease, while others sometimes point to the impact of the disease on patients and families more generally.

These arguments and others raised by respondents to question 1 are explored in more detail below under the following sub-headings:

**Figure 3 Responses to question 1**



## 4.2 Summary of comments

### 4.2.1 Arguments for the introduction of the techniques

60 respondents express their support for the introduction of the two techniques without adding any further explanation. Around 400 respondents give an explanation of their support, as summarised here. Stakeholder organisations expressing support include the British Medical Association, the Humanist Society Scotland, and the Association of Clinical Embryologists (ACE) Executive Committee.

#### Social argument: parents and children

The most common reason given by those in support of the techniques is the importance of the health of children, with many respondents seeing the techniques as an opportunity to prevent

future suffering which should not be passed up. As in the quote below, a large proportion of those responding in favour of the introduction of the techniques feel that the outcomes of these techniques are so obviously positive that there is no real reason to oppose them.

“If by introducing both these techniques, we can wipe out mitochondrial diseases and the suffering that goes with it, then it can only be a good thing.”

Individual, Personally affected by mitochondrial disease; Family member/friend of someone affected by mitochondrial disease

Some respondents focus more specifically on the principle of avoiding or eradicating disease, seeing it as a categorically positive step, and supporting both research and introduction of new techniques which can prevent disease. Other respondents talk more generally about scientific progress as beneficial to society. Some respondents specifically address mitochondrial disorders, with some arguing that the potential severity of the symptoms means the benefits of the techniques outweighs any risks or costs they perceive. Personal experience of mitochondrial disease, and other hereditary disorders, is a factor for many respondents who support the techniques.

Another of the most prevalent arguments for introducing the techniques comes from respondents who talk about the benefits to current and potential parents, describing the techniques as giving them a ‘chance’ to have a healthy child, without passing on the disorders. In relation to the experience of potential parents some respondents talk about the emotional experience of a parent who fears passing on a disorder to their child, particularly where the severity cannot always be anticipated. One participant who describes their own family experiences with mitochondrial disease states:

“One cannot underestimate the amount of emotional and psychological damage inflicted on parents knowing they have passed the mitochondrial disease to their children.”

Individual, Family member/friend of someone affected by mitochondrial disease

### **Ethical arguments: no concerns, imperative to act**

There are two main strands of ethical argument from those supporting the introduction of the new techniques in question one. Many respondents simply state that they see no significant ethical concerns in the use of the techniques. Some specify that they have no ethical concerns within the clinical context of mitochondrial disorders, and a few explicitly disagree that this could lead to other uses. Others feel that because the techniques involve mitochondrial rather than nuclear DNA there is no reason to be concerned about the involvement of a third person’s genetic material.

The second major ethical argument for the techniques comes from respondents who feel there is a moral or ethical imperative to intervene wherever suffering can be prevented. Respondents including the British Medical Association and the Humanist Society Scotland talk about a positive duty to help those who are disadvantaged, others feel it is morally unacceptable to restrict the availability of potentially beneficial techniques. These respondents feel that the techniques under consultation will reduce the incidence of mitochondrial disease, and that it is unethical not to take the opportunity to achieve this. For others the imperative is to give parents the opportunity to have a healthy child, or the right to choose to do so:

“The chance to have a healthy baby is something that should be available to all couples regardless of their medical history and this is a step towards that.”

Individual, Student

## Caveats about the techniques

There are 105 respondents including the Church of England (Mission and Public Affairs Council), the Nuffield Council on Bioethics, the Academy of Medical Sciences and the British Fertility Society who qualify their support for the techniques proposed, suggesting that there are further criteria that must be met before they would consider them acceptable. By far the most common group of criteria is to do with the safety and efficacy of the techniques. Some respondents make general statements, for example that the techniques should be made available as soon as they are 'safe', while others call more specifically for further trials or evidence to verify their safety. As noted above, many respondents who do not offer a preference between the two techniques suggest that further research to determine which is the most effective, should determine which technique is used.

"Maternal spindle transfer (MST) and pro-nuclear transfer (PNT) have the potential to prevent mitochondrial disease in future generations, giving affected parents the opportunity to have children without the fear of passing on the condition, or of passing on the risk of having affected children to their own children.

"Both of these techniques are at a research stage and there is not sufficient data available to determine which is better on the grounds of safety, efficacy and feasibility. We do not believe they should be differentiated between at this point. Research into both of these techniques should continue to assess whether they are viable as potential clinical treatments.

We recognise that the two techniques used are different and could raise varying ethical concerns for different people. However the Nuffield Council concluded it was ethical for both to be explored further. Subject to further information about effectiveness and safety, when balancing the benefits of each technique, some people may wish to consider the different methods used by each technique as a factor in this decision...

...We support the Nuffield Council of Bioethics conclusion that "if the PNT and MST techniques are proven to be acceptably safe and effective, on balance it would be ethical for families wishing to use them to do so. This should, however, be subject to the offer of an appropriate level of information and support."

Organisation, AMRC and Genetic Alliance

## Preferences between the techniques

A number of responses to this question either support maternal spindle transfer only (20), or express a preference for maternal spindle transfer over pronuclear transfer (72). The majority of these respondents discuss the fact that the MST technique involves the use of unfertilised gametes, in comparison to the use of embryos in PNT, therefore preferring MST for a range of reasons. Respondents give a range of views on this issue, with some focusing on their own personal beliefs, and others talking more about social perceptions. Some respondents express their belief that life starts at conception, and feel that PNT is unacceptable as it conflicts with that belief. Others describe feeling more 'comfortable' with MST because it involves unfertilised eggs, with some adding the caveat that if PNT is more effective this should be authorised over MST. A few respondents discuss the views of others - suggesting that because some people may feel that the use of embryos is ethically unacceptable, MST is to be preferred.

A related argument expressed by a few respondents is that both techniques should be made available, to ensure that those who feel that the use of embryos is unacceptable are still able to benefit from the research.

"I believe it is important that this option is available, in order to ensure that as many people as possible can benefit from these techniques without regard to their views on whether life starts at conception."

Individual, Other

Of respondents who do not express a preference for one technique or the other, a few specifically state that they say no real difference between the two, but more common is for respondents to say that they prefer whichever technique is proved safer or more effective.

#### **4.2.2 Arguments against the introduction of the techniques**

31 respondents express their opposition to the introduction of the two techniques without adding any further explanation. Stakeholder organisations who argue against mitochondria replacement techniques include the Church of Scotland, ProLife Alliance, and Human Genetics Alert.

##### **Ethical arguments: use of embryos**

The most commonly cited argument against the introduction of the two proposed techniques is that the creation and destruction of human embryos is unethical (231). A handful of these respondents identify themselves as either personally affected by mitochondrial disease or having a family member or friend affected by mitochondrial disease; 200 of the respondents proposing this argument describe themselves as 'other'. While many respondents note that this argument applies specifically to the case of pronuclear transfer, there are many who do not specify which technique they are referring to and a few who suggest that both involve destruction of embryos. There are also a much smaller number of respondents who express similar concerns about the ethical acceptability of the destruction of eggs, as in maternal spindle transfer.

Respondents give detailed accounts of why they feel the use of embryos in PNT is inappropriate, with a range of views. Some respondents state clearly their belief that life starts at conception, and any process that results in the discarding of an embryo is tantamount to the death of a living human. Some of these respondents use terms such as 'the sanctity of life', with a few citing specific passages from the Bible to elaborate their view. Others focus on the fact that a donor embryo is created alongside the intended parents embryo, with the transfer process resulting in only one viable embryo. They see the act of creating an embryo for this purpose, with no expectation that it will have the opportunity to develop, as an act of instrumentalisation - treating human life as a means to an end, rather than an end in itself. Some argue against this on more direct ethical grounds - believing the techniques to be fundamentally immoral, while others express concern about how the parent or child would be affected by knowledge of the 'sacrifice' of one embryo to create another.

"This ethical dilemma would not only have to be tackled by parents but may also have to be tackled by the resulting child who may feel troubled that their life came at the cost of another's."

Individual, Other

##### **Ethical arguments: playing God and/or interfering with nature**

Another key argument made by those opposing the introduction of the techniques is that they represent an 'over-stepping' of an ethical boundary by altering a predetermined outcome (70). Some respondents describe this boundary in religious terms, referring to 'playing God', or suggest that for science to take responsibility for the creation of human life undermines their belief that creation is a process outside of the human domain.

“...there are many in this country who believe our creator God himself has spoken to us about how we should live to please him. It is clear throughout the bible that fiddling with his created order in this way would not only be wrong and yet another expression of our rebellion against him, but would have negative consequences for us as a human race, as he is our good creator and his design MUST be for our good.”

Individual, Other

While many of these responses argue that the techniques are unacceptable on principle, some also discuss potential negative consequences, suggesting that as procreation is a divine act it could not be recreated by science without causing harm.

Other respondents make similar arguments about overstepping boundaries, but refer to nature or evolution, arguing that using these techniques would subvert the process of natural selection which governs all biological life. Some of these respondents are concerned about unforeseen consequences of manipulating the genome, citing our incomplete knowledge. Others suggest that the expression of genetic disorders and associated failure to reproduce acts as a limiting factor on the spread of genetic mutations which would be harmful at a species level. They suggest that by overcoming this ‘natural’ process the techniques proposed will ultimately have detrimental consequences.

“It is not imperative that people have their own biological children, in fact such conditions are nature's way of preventing weaknesses being passed from generation to generation.”

Individual, Other

Both strands of this argument are sometimes couched in terms of the greater good, with respondents anxious to note their compassion for individual sufferers of mitochondrial disorders, while maintaining that ultimately no positive benefit would be served by the introduction of the techniques.

### **Ethical arguments: the slippery slope**

Opposition to the techniques proposed is often accompanied with concern that if they were to be introduced, this would leave the door open for other, less acceptable measures to be taken. Some 70 respondents, including LIFE Charity, refer to ‘designer babies’ as shorthand to describe the use of assisted reproductive techniques to select characteristics of a child before birth. Some respondents talk about the outcome: expressing feelings of moral outrage towards this type of selection, or arguing that it devalues the child to the status of a commodity - a similar line of argument to concerns about the use of embryos as a means to a medical ends.

“I worry that each new step, even if taken for noble concerns such as preventing disease, will only stir up a chorus of voices demanding more and more frivolous treatments be available, such as sex selection. Children are a gift, and not something that should be available to custom-order.”

Individual, Other

While a relatively large number of respondents who oppose the techniques express concerns about the potential for reproductive cloning to become possible as a result of the ‘slippery slope’ little detail is given about this particular possibility. Other respondents raise the concept of eugenics, arguing that the techniques effectively ‘prevent’ the birth of individuals with particular genetic characteristics, in this case mitochondrial defects.

Aside from the potential outcomes, some respondents talk about the process by which these types of techniques might become acceptable, mentioning ‘desensitisation’ to genetic manipulation, or

the setting of a legal precedent which would allow further amendments to the law with less scrutiny. One respondent gives the example of the Abortion Act of 1967 which they believe demonstrate this principle, another discusses the increasing range of conditions for which pre-natal genetic diagnosis (PGD) is now available.

### **Altering the germline: safety and risk**

A total of 160 respondents who disagree with the introduction of the techniques in question 1 express concerns about whether they can be applied safely. Comment on Reproductive Ethics (CoRE) and the Church of Scotland are two of them. Some respondents make general statements about the impossibility of being certain about the consequences, while others specify that they are concerned about the perpetuation of (unknown) side-effects as a result of the germline modification. Views on risk differ between those participants who see the techniques as being likely to result in negative consequences, and those who feel that regardless of the likelihood of the consequences, the severity of side-effects introduced via the germline is so great that any risk is not acceptable. A few respondents give examples of techniques they believe are similar to those proposed and have resulted in negative consequences or side-effects when introduced in human or animal models, for example IVF and cloning.

Alongside the risk of side-effects being passed on, some respondents identify other potential consequences of altering the germline. Some cite the use of mitochondrial DNA to trace matrilineal relationships at the population level, either as a specific feature which would be lost, or as an indicator of the importance of the role mitochondrial DNA plays in maternal relationships.

“Mitochondrial DNA is identification for the human race. It was how the human race was traced back to Africa. Changing such a vital building block of human development in such a complex being may mean in the future, there may be some unforeseen complications or other disease prevailing as a result.”

Individual, Other

### **Social arguments: three genetic contributions**

While the social arguments raised in support of the introduction of the techniques focus on providing opportunities for parents to have healthy children, opponents are primarily concerned with the impact on the child of being conceived in this way. Many respondents who oppose the techniques, including the Anscombe Bioethics Centre, raise the involvement of DNA from a third party as a concern. Some respondents argue that involving the DNA of three people is fundamentally unethical - often citing their belief that Christianity specifies that all children should have one mother and one father. Other respondents believe there is potential for children conceived via these techniques to suffer psychological harm as a result of confusion about their identity. Some cite examples of adopted or donor-gamete born children seeking to contact their biological parents, others feel that the introduction of a third genetic contributor will leave children unable to resolve questions of their own identity. Arguments around whether there are implications for children's identity are covered in more detail in chapter 6.

#### **4.2.3 Other considerations**

While the majority of those responding to question 1 expressed their support for, or opposition to the techniques, many issues are raised which are not clearly for or against.

### **Safety, science, regulation and criteria for application**

The most common considerations cited in relation to the techniques overall are specific criteria which respondents think should be applied to decisions about either which technique/s to take forward and/or which to choose in specific cases, should they become available for clinical use, as

mentioned in section 4.2.1 above. Success rate, efficacy or efficiency of the technique is top of the list of criteria mentioned, closely followed by safety. Other criteria include patient choice or appropriateness, medical evidence and advice, cost or value, as well as others such as opening up the techniques to use for anyone or basing decisions around the use of either technique on scientific input or evidence.

A number of respondents stress that regulation would be needed, should the techniques come to fruition. More specifically, there are comments that regulation could or would help prevent the slippery slope, or that the regulator would have an important role in limiting the use of these techniques. Comments about the role of the regulator are analysed in more detail in Chapter 8, which deals specifically with regulation.

In relation to safety more specifically, some respondents are concerned that there is insufficient evidence to prove the safety of the two mitochondria replacement techniques, whilst others talk about the need to compare risks against benefits. Some express a view one way or the other that either the risks outweigh the benefits or vice versa. In addition, a few respondents point out that risks are always present with medical procedures. Many respondents talk about the need for further research, trials or evidence if or when the techniques are taken forward, including a few comments about the need for follow up studies with patients.

“If shown to be achievable, safe and effective, both techniques have potential to militate against mitochondrial disease. In principle, this is to be welcomed, but some caveats exist.

Current scientific consensus is that mitochondrial DNA (mtDNA) is unlikely to play a role in determining hereditary characteristics; however, understanding of the nature of the interaction between nuclear DNA (nDNA) and mtDNA is far from comprehensive. It has been suggested, for example, that a link exists between mtDNA and cognitive capabilities; caution is, therefore, appropriate.

Some nDNA has effects identical to mtDNA and, if defective, can cause similar illnesses. Mitochondrial replacement therapy will not address this problem. If techniques were developed to counteract these debilitating effects of mutant nDNA it might be assumed that the use of altered nDNA is acceptable, especially if such has already been the case with mtDNA. A separate and full debate on the use of altered nDNA is essential since we know that much nDNA directly affects hereditary characteristics. If mitochondrial replacement is permitted no inference ought to be drawn between it and nDNA manipulation.”

Organisation, Church of England: Mission and Public Affairs Council

“The monitoring of those involved in the first Clinical Trial must be exceptionally careful and long-term - and honest!”

Individual, Other

A number of respondents talk specifically about the function of mitochondria or other scientific aspects of the two techniques.

“... the mitochondria are the power plants of the cell. This is akin to changing a battery in a laptop for instance, the data does not change [sic], the layout does not change, the essence of the human is not altered, merely its power source.”

Individual, Family member/friend of someone affected by mitochondrial disease



“I would liken this to replacing faulty spark plugs in a car, it will look and perform the same but the engine will now run smoothly!”

Individual, Other

Others outline their understanding of the science or suggest an alternative approach. There are also a few comments from respondents who are concerned that science should remain at the heart of the decision making on this topic. Scientific considerations are discussed in more detail in the analysis of question 2 (chapter 5).

### **Ethical considerations**

Ethical considerations are covered in more detail in chapters 5 and 6, with the key points mentioned in response to question 1 outlined here.

Concerns over the use of embryos or eggs, and the difference in embryo usage between the two techniques or how others might feel about this, are mentioned by a number of respondents, with some expressing clear concern about the use of embryos or eggs without necessarily explicitly being opposed to techniques, and others saying they are not concerned about this issue. There are also several comments about ethics more generally, and a few on more specific issues such as the lack of consent or choice from the child’s perspective.

Some respondents mull over the issue of where the line should or could be drawn with respect to this kind of technique, either around screening or genetic modification itself. Others mention more explicitly the need to consider the risk of a slippery slope occurring, either generally or more specifically with designer babies or commodification, or eugenics. There are also some respondents who point out that these techniques are different to those which would be involved in cloning or creating designer embryos.

### **Social considerations**

Social considerations are also covered in more detail in chapters 5 and 6, with the key points mentioned in response to question 1 outlined here.

In terms of social considerations, various potential legal or insurance issues are mentioned, along with the related issue of a third person’s involvement in a child’s conception. A number of respondents suggest considerations around the various actors in a potential mitochondria replacement procedure.

With regard to parents, considerations include primarily the need for information provision and close involvement, but also a desire that, should these techniques come to fruition, pressure is not placed on parents to use them. A small number of respondents discuss related issues around the worth society places on mitochondrial disease sufferers or disabled people. Some feel there is a risk that using these techniques would entail losing valuable individuals, respondents interpret the techniques as replacing an individual with mitochondrial disease with another, different individual..

With regard to donors, considerations include comments about the rights and responsibilities of donors, whether their identity should be known or not, and comparisons to gamete or organ donation, as well as a couple of comments about donor availability. These issues are covered in further detail in chapter 7. Considerations around the child include comments about the potential emotional or psychological impacts on a child resulting from these techniques, as well as a number of comments about implications for the child’s identity. These issues are covered in more detail in chapter 6.

Other social considerations raised by respondents include considerations of the number of people mitochondria replacement would be applicable to, potential impacts on future generations (including the potential for resulting population increase) and a number of comments about costs

or funding; aside from general comments about who should pay, some people specifically say the NHS should not cover the cost of treatment and others that it should. A few respondents comment on the potential business interest or involvement in offering mitochondria replacement treatments. Others mention alternative treatments, including the suggestion that adoption could be made easier.

### Considerations for specific techniques

A number of respondents talk specifically about MST or PNT, or compare the two techniques, with some saying they see little or no difference between the two techniques, for example in terms of ethics. Several respondents say that they think MST could be more publicly or ethically acceptable than PNT, or that PNT is potentially the more controversial of the two because of the use of embryos. Other respondents talk about specific considerations for each of the two techniques, for example whether the use of spare embryos from PNT had been thought about. A few respondents believe that the way the techniques are described is misleading for various reasons.

“There has been a degree of misunderstanding among the public - these interventions are not a “genetic modification”. A genetic modification is when nuclear or mitochondrial DNA sequence is altered - mutated, deleted or inserted. Instead the use of wildtype DNA from a third party is in effect a donation and not a genetic modification.

In other words the human genome is not being modified.”

Individual, Researcher

“I think that it is deceptive to describe this technique as a therapy being offered to prospective parents. The therapy being offered is merely psychological: reassurance that they will not have a defective child. The person affected is the child him or herself.”

Individual, Other

“The term ‘mitochondria replacement’ is misleading as it is the pro-nuclei or spindles that are being replaced in the host cell rather than the mitochondria being replaced.”

Individual, Other

### Other references

Many respondents to question 1 make reference to specific supporting information. A large number of these references are personal to the participant, for example information about their knowledge or expertise, where they have a friend, relative or child with mitochondrial disease or similar, or where they themselves are a sufferer of mitochondrial disease. Several respondents make reference to religion or the Bible as part of their response, while others mention politics or the Government (for example the role – or not – of politics in these kinds of decisions), the HFEA, the views of other people generally, or of a specific group or individual. Current legislation on this topic, either in the UK or abroad, is mentioned by a number of respondents, as well as some references to learning from historical experience (for example the progression of scientific knowledge, Thalidomide, eugenics, and the development of IVF). Other specific supporting evidence is referred to by some respondents in the form of relevant research, documents, literature or discussions.

## Chapter 5      Question 2: changing the germ line

---

### 5.1      **Headline findings**

1,115 respondents answered question 2, which asked respondents:

**Q2: Do you think there are social and ethical implications to changing the germ line in the way the techniques do? If so, what are they?**

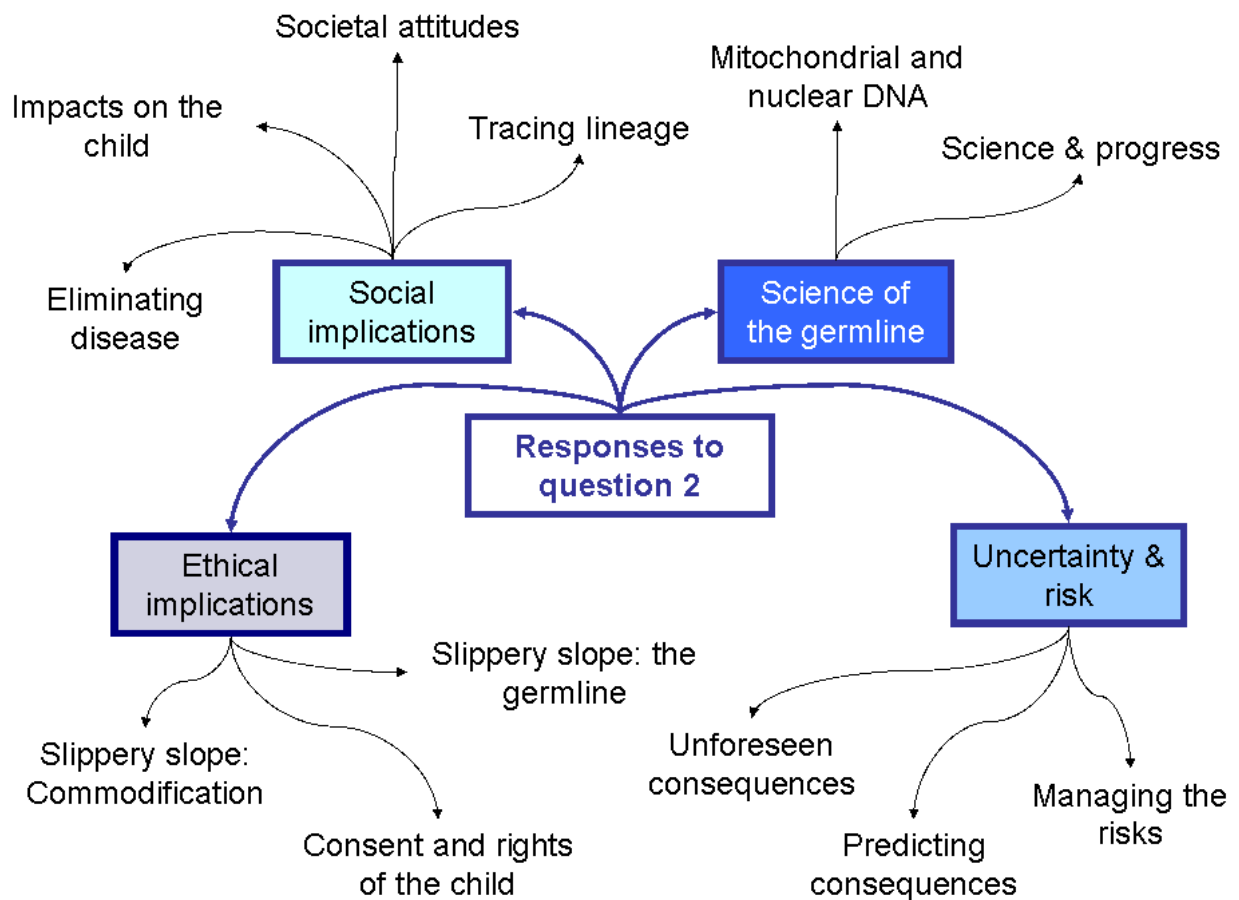
Most responses to this question outline potential implications of changes to the germ line including both negative and positive implications. Some respondents feel the severity of the impacts would outweigh the benefits they believe the techniques will bring; these respondents often cite similar ethical concerns to question 1, or social concerns about the introduction of a third genetic contributor. Others feel that the impacts could be adequately mitigated or are not serious enough to outweigh the benefits - these respondents tend to focus on the social impacts of reducing mitochondrial disease. The implication of changing the germ line is explored by many respondents in question 2, with concerns about the risks of a new scientific procedure, about genetic engineering more generally, and discussion of the role of mitochondrial DNA in the germ line. A number of respondents, including several who identify themselves as mitochondrial disease patients or friends/relatives of patients, state their belief that there are no social or ethical implications of the introduction of the two techniques into clinical practice, or that the only implication is the reduction of instances of mitochondrial disease.

#### **Non-questionnaire responses**

In some of the 503 non-questionnaire responses there is mention of changing the germ line. Overwhelmingly these comments are part of a range of similarly worded points which can be found in around 300 emails and letters. The point included about changing the germ line concentrates on uncertainty about the effects on future generations, which respondents consider a concern.

These arguments and others raised by respondents to question 2 are explored in more detail below under the following sub-headings:

**Figure 4 Responses to question 2**



## 5.2 Summary of comments

### 5.2.1 Uncertainty and risk

The paragraphs below describe the concerns of respondents who believe there are negative consequences of the techniques; in many cases respondents describe the scale and likelihood of the perceived consequences, while a few respondents argue on principle that any risk to future generations is unethical. They feel that the act of taking a decision which imposes these risks is unethical, as the choice is removed from the future individuals - this argument links closely to questions of consent explored under Ethical implications below (section 5.2.1).

#### Unforeseen consequences

The most common issue raised by respondents in relation to the germline is a concern that there may be unforeseen consequences of the proposed techniques, which would then be perpetuated in future generations. Often respondents are concerned with the scale of consequences - they see the potential consequences as too large or dangerous to be acceptable, even if they are very unlikely. Many refer to the idea that many generations would be affected, seeing this as frightening or inappropriate; others describe the potential germline change as being 'uncontrollable' suggesting that:

“... we simply do not know what harm we may be doing, and such harm may extend indefinitely to many generations.”

Organisation, Anscombe Bioethics Centre

Another variation on this theme is the idea that consequences may not be discovered until several generations have passed, by which time it may not be possible to contain the germline change, or even to identify all carriers.

While most respondents who comment on unforeseen consequences cite this as a general principle, a few respondents give examples of particular implications they see arising from use of these techniques, often describing these as unintended consequences. Some of these respondents believe there may be negative health impacts of the techniques, discussing issues such as the combination of mitochondrial and nuclear DNA when the two are inherited from different parents. Others talk in general terms about unpredictable psychological impacts on children born via the techniques and their families (discussed in more detail below).

### **Predicting consequences**

Other respondents discuss the level of risk - they are concerned that we are not able to adequately assess the potential consequences of using these techniques in clinical practice. For some of these respondents our inability to determine the consequences is seen as inherent, and they describe their feeling that the consequences of genetic modification are ‘unknowable’. Others argue that the consequences cannot be known until the techniques are implemented in humans, and even then not necessarily in the first generation, for example:

“The Council noted a number of ethical and social implications, including that using these techniques might create health risks to the resulting child and his or her descendants, particularly as it will not be possible to exhaustively assess the safety of the procedures until several generations have been born using them (paragraph 4.37).”

Organisation, Nuffield Council on Bioethics

A few respondents who believe that negative consequences may emerge in subsequent generations suggest that this would mean monitoring of both children born via the techniques, and their subsequent offspring for several generations.

### **Managing the risks**

Although most respondents who posit unforeseen consequences of the two techniques believe this should prevent them being authorised, some cite potential impacts and then suggest ways in which they can be mitigated. This includes procedural suggestions, such as ensuring that the mitochondrial donor has similar genetic heritage to the intended mother (i.e. has similar mitochondrial genes). Others give suggestions for managing the social consequences for the child, most often recommending that the child should be made aware of the circumstances of their birth, with information given in a considered and sensitive way.

One suggestion made by some respondents is that ongoing monitoring should include subsequent generations, however there are a number of respondents who express concern about the consequences of such monitoring. As described below, some feel it will lead to stigmatisation of the individuals concerned, or that they will feel ‘different’ because of the requirements of monitoring.

There are also a few respondents who discuss the concept of uncertainty and risk, suggesting that fears of the uncertain and unknown are common when novel technologies are posed, and should

not necessarily prohibit their progress. This debate is picked up again in the Science section 5.2.4 below.

### 5.2.2 Social implications

#### Eliminating disease

There are 68 respondents who specify that they believe the benefits of the techniques outweigh any social or ethical implications. The majority of these respondents, including a number of respondents who identify themselves as having personal experience of mitochondrial disease (patient or friend/relative), suggest that the elimination or reduction of instances of mitochondrial disease is a social benefit, offering benefits to children and families, or more generally as an improvement to health at a population level. As in several of the questions, a few respondents emphasise the severity of mitochondrial diseases, and the psychological impact of hereditary disease when weighing up potential benefits and disadvantages of introducing the techniques.

“If I can prevent the inheritance of mitochondrial disease by altering the gene line then this is far preferable than for the risk and fear of disease staying in my family forever.”

Individual, Family member/friend of someone affected by mitochondrial disease

A number of respondents to question 2 discuss benefits they perceive for future generations because of the modification of the germline. They argue that because the mitochondrial defect which causes disease is removed from the germline subsequent generations are also freed from the potential to inherit the disorder, and that this makes the techniques an ideal response to the problem of heritable disease.

#### Societal attitudes

A common issue mentioned in response to question 2 is how the introduction of the techniques to clinical practice might affect attitudes towards different groups, particularly those born as a result of the technique and sufferers of mitochondrial and other disorders. There are 56 comments on social attitudes towards those conceived via the techniques, with a range of views expressed. Some respondents, including the ProLife Alliance, suggest that those ‘treated’ could be ostracised or discriminated against for being ‘created in a lab’, or because of the third genetic contributor. Many of these respondents suggest that the requirements for those born via the techniques to take part in medical monitoring will contribute to them being treated as ‘guinea pigs’. This argument is often associated with ethical concerns about the motivations of parents, clinicians and scientists in implementing the techniques. In contrast, others note that such prejudices do not seem to have arisen in relation to artificial reproductive techniques such as IVF, and feel that it is not a major concern. A third point of view comes from those who feel that discrimination may be an issue in the short term, but will ultimately be overcome:

“Socially, there may be short-term issues with the interaction of treated with non-treated, and with those who opposed use of the techniques. However, that should not prevent us from moving forward with them. ‘Test tube babies’ do not appear to have met with any significant stigma over the long term, and I don't see why these babies would either.”

Individual, Other

A related issue raised by a similar number of respondents is whether making these techniques available will have an impact on attitudes towards those with disabilities (including mitochondrial disease). Some respondents argue that the techniques amount to preventing the births of people with mitochondrial disorders, effectively discriminating against them. A number of these respondents note a link to wider debate about perceptions of disability in society, and of disabled people themselves:

“My only concern about alterations in the germline is that it reifies genetic 'normality', and creates an anti-disability narrative that will encourage people to view themselves or others as 'abnormal'.”

Individual, Researcher

Respondents are concerned that there will be increased levels of intolerance for those with disabilities, especially mitochondrial disorders, with disabled people questioning why the proposed techniques were not used to prevent their disability, and by inference, their birth as disabled individuals. Others see a potential connection between the proposed techniques, decreased tolerance of genetic defects and increased acceptability of other genetic modification techniques and the ‘designer baby’ concept discussed in question 1.

A smaller number of respondents argue that rather than encouraging discrimination against those who are treated, introduction of the techniques will lead to negative attitudes towards those not treated. They argue that once the techniques are available:

“Parents who do not comply with such techniques will indubitably be made to feel irresponsible by scientists, medical personnel, society at large...”

Individual, Other

One or two specifically mention potential problems they see arising within families where some children have been conceived by the techniques, while others have not. Some respondents expand on this theme, suggesting that parents may be pressured into using the techniques either unnecessarily, or against their will, because of a perception that it would be irresponsible not to.

### Impacts on the child

As in most questions throughout the consultation, many respondents comment on the introduction of a third genetic contributor, expressing concern about the psychological impact of a third ‘parent’ to a child conceived via the techniques - these issues of identity are covered in detail under question 3 (Chapter 6). A number of respondents take the opportunity to express their concerns about the psychological or emotional impact on children conceived via these techniques, while a similar number express their belief that the wellbeing of any child would be improved.

A few respondents raise specific concerns about identity issues relating to the germline. In particular there are concerns that kinship and family may continue to be disrupted in subsequent generations.

“Families may not accept future generations as truly related if the germ line is changed, I would certainly be unsure if a child was truly my child if they had donor mitochondria.”

Individual, Other

### Tracing lineage

Mitochondrial DNA can be used to trace the genetic heritage of individuals, and of populations on an historical timescale - some respondents, including the National Gamete Donation Trust, make reference to this in question 2, noting that mitochondria replacement would confuse this genetic ‘family tree’. Most respondents who mention this issue describe it as a minor issue which should not prevent the techniques being used, and a few suggest that steps could be taken to record the identity of the mitochondrial donor in some way to mitigate the impact. One or two respondents raise the issue of criminal investigations using DNA evidence, and question whether mitochondria replacement could affect this.

### 5.2.3 Ethical implications

As in question 1 a number of respondents (158) express concerns about the use of embryos, particularly in the case of pro-nuclear transfer. These arguments are described above in section 4.2.1. Other arguments common to question 1 and explored in more detail there are those relating to 'playing God' and the ethical imperative to intervene.

#### Consent and the rights of the child

A number of respondents in question 2 discuss the concept of whether the modification of an embryo or egg (no distinction is made in this context between the two techniques) could be allowed to take place without the consent of the ensuing individual. There are two strands to this argument, firstly that in the case of the parents who use the technique to conceive, they have made that choice on behalf of the child. As one respondent puts it:

"I feel very uncomfortable with the prospect of making such decisions without the consent of the individual concerned. There's no 'going back' if someone finds the background to their conception difficult."

Individual, Other

Others refer to the importance of informed consent in scientific experimentation, and in medicine more generally - they argue that as it is impossible to gain the informed consent of the 'child' before the procedure is carried out, it is unethical. In contrast, a few respondents note that parents make decisions on behalf of their children as a matter of course, for example the Nuffield Council on Bioethics note that:

"The issue of consent has been raised in the context of germline therapies, given that no child born from such procedures can have consented to them. However, **this issue is common to all reproductive technologies, as well as other prenatal and childhood medical intervention** (paragraph 4.38)."

Organisation, Nuffield Council on Bioethics

The second strand of this argument is that once the change has been made to the germ line, it will be passed on - in effect the children conceived by the technique are not able to choose whether or not they pass on the technique to their children. Again, an opposing view is argued by a small number of participants who question whether this consent is relevant, given the impossibility of ever acquiring consent from future generations about any decisions taken on their behalf.

The argument as stated here focuses on the principle of consent of the individual to the changes; an alternative formulation focusing on the practicalities of making decisions for future generations is described above under uncertainty and risk, (section 5.2.1) where some respondents questioned whether individuals have the right to expose future individuals to particular risks.

#### Slippery slope: commodification

The 'slippery slope' by which the introduction of these techniques could lead to others is a common theme throughout the consultation, with respondents expressing a range of concerns about potential outcomes. There are 150 respondents to question 2 who raise concerns about the introduction of techniques which modify the germline opening the door to parents able to select for characteristics rather than medical need. While some respondents argue by comparison between 'selection' for medical purposes and selection for 'trivial' characteristics, others argue from the principle that any selection on the part of the parents crosses a line.



Once more the new techniques ignore the basic principle of what is meant by uniqueness in the individual. It opens the way to the normalisation of genetic modifications. In time it is inevitable that government will begin to interfere in the decision making process about what forms of offspring will / will not be acceptable. A dangerous threshold will have been crossed and the long term outlook is unknowable.

Organisation, Scottish Council on Human Bioethics

In contrast there are some respondents, including the Muscular Dystrophy Campaign, who state their disagreement with this argument, typically because they feel that sufficient steps will be put in place to prevent such a shift from one purpose to another. One or two suggest that because the proposed modification to the germline is limited to mitochondrial DNA, this argument is less applicable:

“Firstly, these techniques limit germline manipulation to genes of the mitochondria, which are involved solely in programming the functions of these organelles.”

Organisation: The Wellcome Trust

### **Slippery slope: the germline**

Another variation on the slippery slope argument common in question 2 focuses on a perceived relationship between germline modification and eugenics, suggested by 70 respondents. Many respondents who mention eugenics do so without giving detailed arguments, and may be using the term simply to denote all genetic modification or engineering. However others argue specifically that the process of ‘selecting’ against a particular genetic trait is the basis for their concern:

“We are also concerned that changing the germ line will result in the normalisation of genetic modification in humans. While it is admirable to seek to cure disease, we are concerned by the eugenic undertones of any technology that allows doctors and parents to ‘rank’ one embryo above another.”

Organisation, Christian Concern

Another discussion specific to question 2 is whether once germ line changes are introduced for mitochondrial DNA, it will gradually become possible for nuclear DNA changes to be introduced. This debate is brought forward by a small number of respondents, with a few arguing that the difference between the two types of DNA is clear, and one will not lead to the other, while a similar number argue that the difference will not prevent a move towards more techniques being available.

#### **5.2.4 The science of the germline**

There are a number of respondents who take the opportunity in question 2 to discuss aspects of the science around germ line modification which they feel are pertinent to the social and ethical implications of the techniques. Typically these points are made by smaller numbers of participants than the main ethical and social arguments described above, and are less commonly associated with an expressed preference for or against the introduction of the techniques into clinical practice.

### **Mitochondrial and nuclear DNA**

Several respondents talk about the role of mitochondrial and/or nuclear DNA, particularly in relation to the question of identity. The relationship between mitochondrial DNA and identity is covered in detail in chapter 6, dealing with question 3. The most common of these comments, made by the Academy of Medical Sciences and the British Fertility Society among other organisations and individuals, is that the nuclear DNA (and some respondents say the genome) is not affected by the two mitochondria replacement techniques, with some linking this to other comments such as the fact that they therefore have no ethical or social concerns. Other

respondents give conflicting views about mitochondrial DNA, with a number of respondents stating that it does not determine identity or traits and somewhat fewer stating that they think it does or might. The function of mitochondria is the subject of some responses, in particular from respondents who say that the mitochondria are just for energy production and that replacing them would be like changing batteries, although others believe they play a more important role or that we do not fully understand their role.

“I see this essentially as changing the batteries that power the fertilised egg, embryo and ultimately, person but without having the ethical impact of alteration of the expressed DNA.”

Individual, Other

“If mitochondria are so trivially put as powerhouses of the cell why are the consequences so dire when they do not work?”

Individual, Researcher

A number of respondents, including the Wellcome Trust, talk about the small amount of DNA involved in mitochondria replacement, whilst there are a couple of concerns that even this would be too much or have too much impact. There are also a small number of comments about the origin of mitochondrial DNA, specifically that they were originally symbiotic bacteria living in host cells.

“Mitochondria are best viewed as separate organisms living in cooperation with host cells. They are much like the gut bacteria without which we couldn't live a healthy life, there are increasingly numerous examples of organisms that cannot live without one another - plant roots and soil fungi for example.”

Individual, Other

Other comments about mitochondrial DNA are varied and include observations about the importance of mitochondrial DNA for sustaining life, the number of different lines of mitochondrial DNA and a range of other observations about the science surrounding mitochondrial DNA and the implications of mutations or replacement. In addition, there is a focus on the female or maternal line, with respondents saying either that the proposed techniques would only impact the female germ line, or that they would make tracing lineage through the female line more complicated. A few respondents talk about more technical aspects of mitochondria replacement; there are some suggestions about specific sources for the donation such as using the father's mitochondria, those of a close friend or relative, or mitochondria from the same haplogroup as the mother. There are also a small number of comments suggesting that the faulty mitochondrial DNA should be kept for posterity.

Respondents make a range of other comments about nuclear DNA. A few respondents say that DNA mutates naturally anyway over time, a process they see as analogous to the deliberate change introduced by mitochondrial transfer; in the main these comments focus on the argument that these techniques would be speeding up that natural process, although one respondent is concerned that evolution is based on abnormalities and that we should not “deny ourselves the chance to grow and show the best of ourselves”. Others discuss the natural mixing of DNA that occurs through reproduction, often accompanied by the view that this makes the process of mitochondria replacement less significant because it is seen as replicating a natural process.

“Changing the germ line is the very essence of sexual reproduction - the fact that mixing genes can result in a wider variety of characteristics is advantageous to a species. Essentially, it's a very natural thing.”

Individual, Student

There are also a small number of other comments about nuclear DNA, for example around its function, our current knowledge, and the influence of environmental factors on gene expression.

Many respondents talk about the germ line more generally, including the idea of altering it. There are equal numbers of respondents who say it is ok to alter the germ line (for example because this is a positive or purely functional alteration) and that it should not be altered (for example because of unknown consequences or the crossing of an ethical boundary). A few respondents comment that the germ line would not be significantly changed by these techniques. Others discuss specific outcomes they speculate could occur as a result of MST or PNT, for example that the germ line could reduce in diversity, or that the mixing of mitochondrial DNA could cause a genetic advantage or be beneficial, although others say that they think the germ line would simply be repaired rather than enhanced.

Other comments about the germ line include a variety of positive and negative comments about changing the germ line, the statement that we are all related if you go far enough back, that this would be a new step for science because it involves altering the germ line, and comments about the long-term (i.e. multi-generational) changes brought about by alterations to individuals through these techniques.

### **Science and progress**

The nature of science and scientific progress is commonly cited in response to question 2, either specifically in relation to mitochondria replacement techniques or more generally. By far the most popular comment in this respect is that reducing mitochondrial disease is a positive thing, with many of these respondents referencing some of the social benefits already cited in response to question 1. Other comments about scientific progress in relation to mitochondria replacement include: this is natural progress or that scientific progress overall is a function of being human; the possibility of doing something does not mean it should automatically happen or further progression of these techniques requires caution; and progress has gone too far to stop now. There are a few other observations on where these treatments sit in relation to overall scientific progress in this field.

“With the introduction of the treatment there may be a rise in research interests in this area, leading to safer, cheaper treatments, many targeting conditions which have not yet been treated. The treatment may even allow us to clear up any ethical/social concerns regarding germ line engineering of human nuclear DNA in germ line cells.”

Individual, Student

“Changing the germ line is a step change beyond other techniques currently used for infertility treatments.”

Individual, Non-questionnaire response

“This sort of gentic [sic] modification is merely an extension of medicine beyond most people's intuitive comfort zones when it comes to trusting and understanding science.”

Individual, Student

Some respondents comment specifically on the nature of these two techniques, including comments that this could or would be a one-off or single generation treatment, or that it could be restricted to male births. Other respondents express overall objections to fertility treatment, or in several cases talk about preferable priorities for investment such as other treatments or cures for mitochondrial disease.

Concerns that current scientific understanding is limited, for example about the function of mitochondrial DNA, are raised by some respondents, including Comment on Reproductive Ethics (CoRE), alongside other comments on the need for further evidence or research, for example specific suggestions for trials or follow-up studies.

“Should mitochondrial material, and the use of a donor cell wall, have greater purpose than is currently known, we are in danger of harming future generations unless there is a long and rigorous process of testing implemented.”

Individual, Student

There are some comments about the trust or lack of trust in scientists and scientists' motivations, for example concerns that scientists may not always undertake research for the right reasons or more overt expressions of mistrust (some respondents suggest scientists are 'arrogant'), as well as one respondent who says that they do trust scientists. Other respondents discuss the nature of medicine or science, for example stating that its purpose is to treat illness or to benefit humankind, although these statements are used in different ways to either support or oppose the two techniques, for example a number of respondents say that the use of embryos goes against the idea of benefitting humankind. A small number of suggestions for how science should balance with ethical, religious and scientific considerations are also made; some respondents would like to ensure that ethical considerations based on religious views have an important place in the debate, whilst others would like the debate to focus on science and ethics in purely secular terms.

Finally, there is a range of other comments about either the science of these techniques or overall science more generally. For example, some respondents question how effective these techniques would be and others talk about the need to weigh up all considerations for any new technique on a case-by-case basis.

## Chapter 6      Question 3: implications for identity

---

### 6.1      **Headline findings**

1,084 people responded to question 3 of the consultation which asked:

**Q3: Considering the possible impact of mitochondria replacement on a person's sense of identity, do you think there are social and ethical implications? If so, what are they?**

Most respondents make specific comments about how they think mitochondria replacement may have an impact on a person's sense of identity, or why they believe this impact will be limited.

Where respondents state that they believe there will be implications, most describe these. Their comments cover the genetic make-up of children born as a result of mitochondria replacement, the potential issues around children's relationship to their mitochondria donor, and the potential impact on these children's emotional or psychological well-being. A handful of respondents say they believe there will be implications but make no further comment.

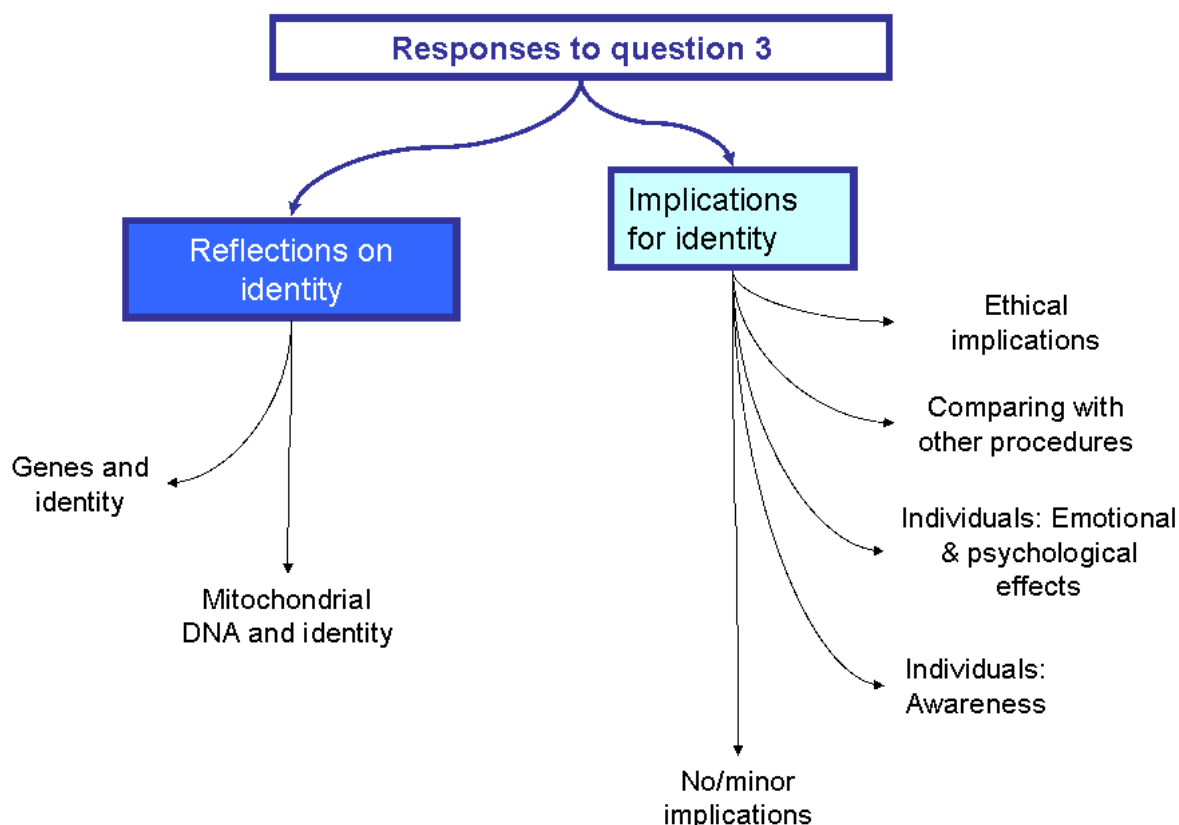
Where respondents indicate that they believe there will be no implications, they tend to argue that mitochondrial DNA does not determine a person's identity. Many suggest too that mitochondria replacement is unlikely to have greater implications than currently used procedures including egg and sperm donation. A total of 38 respondents merely state that they do not think there will be implications.

#### **Non-questionnaire responses**

Comments about possible implications on identity are also made in some of the 503 non-questionnaire responses. Most of these comments are made in letters and emails that follow a similar structure and make a series of similarly worded points. One of these points is a concern about the impact of mitochondria replacement on the well-being of children conceived in that way, who respondents believe may suffer psychological damage as a result of it. Also, the idea that three (or four) people would be involved in the conception process is often cited as a concern, although not always in relation to identity.

These arguments and others raised by respondents to question 3 are explored in more detail below under the following sub-headings:

**Figure 5 Responses to question 3**



## 6.2 Overview of comments

### 6.2.1 Reflections on identity

Question 3 inspires some respondents to reflect on the concept of identity and how personal identity relates to individual genetic make-up. Two broad themes characterise this discussion: whether or not mitochondrial DNA is significant to identity and whether or not a person's genes influence or determine identity at all. These two discussions are described in turn below.

#### The relationship between mitochondrial DNA and identity

When respondents comment on the relationship between mitochondrial DNA and identity, they often argue that this relationship is either negligible or absent. Some 100 respondents including several who identify themselves as mitochondrial disease patients, or friends/relatives of patients, say they believe that an individual's personal characteristics are not affected by their mitochondrial DNA, but rather depend on the genetic information in the nuclear DNA. This view is also expressed in responses of various stakeholder organisations including the Association of Clinical Embryologists (ACE) Executive Committee and the British Medical Association.

"Identity, if it rests anywhere in a person as an embryo, rests in the genetic inheritance in the parts of the DNA that affect personality, traits etc, not their mitochondria."

Individual, Family member/friend of someone affected by mitochondrial disease

The quantity of mitochondrial DNA relative to the quantity of nuclear DNA is discussed by 63 respondents. Most of these emphasise that mitochondria contain a very small part – some mention 1% and others cite smaller percentages – of a person's genetic information. Some respondents also reflect on the nature and function of mitochondria and mitochondrial DNA. Most of these say

that mitochondria are there to help cells produce energy, with several respondents likening mitochondria to batteries in cars or other tools. Respondents using these lines of argument generally think that the quantity and/or purpose of mitochondrial DNA suggest that it is unlikely that mitochondrial DNA has implications for identity.

“MtDNA, which is the only type of genetic material altered by these techniques, encodes just 37 of the 22,000 human genes, or less than 0.002 per cent of the total.”

Organisation, Wellcome Trust

A small number of respondents take a different view on the significance of mitochondrial DNA in the constitution of an individual's identity. Their comments emphasise that we do not know sufficient to be certain that mitochondria are relevant to energy generation alone and that the possibility remains that the genetic information in mitochondrial DNA does affect a person's traits.

“In reality our understanding of the amount, influence and purpose of mitochondria is still limited and conclusions such as this need to be treated with caution.”

Organisation, Christian Medical Fellowship

### **The relationship between genes and identity**

For some respondents a more fundamental question about identity needs to be addressed in relation to this discussion: to what extent is an individual's identity influenced or determined by their genes? Some respondents emphasise that identity is a complex concept which may have genetic as well as environmental and circumstantial components.

“Identity is a complex issue, and is based on a myriad of factors, of which a person's biological origin covers only a handful.”

Individual, Other

Several respondents argue that the extent to which individuals' sense of identity is affected by their genetic make-up, or their understanding thereof, is a personal matter and will vary between people. Some reflect on what they see as the struggle that many young people and adults experience trying to make sense of their identity in today's society, regardless of their family situation or genetic heritage.

“All people search to establish their sense of identity. All people struggle with whatever it is that has made them.”

Individual, Other

About 75 respondents discuss specifically whether it is one's genes (nature) or one's upbringing (nurture) that most influences their sense of identity. The majority of these respondents express the view that identity is predominantly formed during life, and many respondents highlight the role of parents in providing the environment in which a child grows up, saying this is a prime factor affecting their sense of identity. Organisations making this argument include the Humanist Society Scotland and PROGAR. A few respondents cite specific examples to underpin their arguments, such as two genetically identical twins growing up to be different individuals with their own distinct identities.

In contrast, a few respondents emphasise the role of genetic information in shaping a person's identity, stating it is this that makes them unique human beings. Others consider that neither genes nor upbringing are dominant by definition and that this uncertainty should be acknowledged.

“However, this brings us back to the long-debated Nature vs. Nurture argument. It is difficult to say how much of a person’s identity is influenced by their genetics, and how much is influenced by their upbringing.”

Individual, Student

### 6.2.2 Ethical implications

In responding to question 3 most respondents concentrate on social rather than ethical implications. Respondents who do comment on ethical implications often reflect on the proposed techniques in a general fashion. For instance, some argue that the techniques are interfering with nature and some suggest that they cross a boundary and set a precedent for other more controversial techniques. These and other discussions about ethical implications of mitochondria replacement in general are discussed in detail in the chapters on questions 1 and 2.

Several respondents raise an ethical implication specific to identity. These respondents emphasise that children born as a result of mitochondria replacement will not have been able to give their consent. This is generally followed by concerns that these children may experience this as a burden during their lives.

“This procedure also poses the ethical issue of changing a person's identity without his or her consent.”

Individual, Other

A different but related point is made in some of the 53 responses that cite the use of embryos in PNT as a particular ethical concern. Several respondents reflect on the impact of this on the resulting individuals' identity or well-being more generally. They are concerned that some people may feel a sense of guilt or unworthiness when they realise that their conception has been aided by a process that involves the creation and destruction of embryos. A few respondents speculate about the individuals that might have been born if the embryos used had been allowed to develop, and sometimes suggest that these could have become 'better' individuals, leaving the child with a greater than usual sense of having to make up for the potential achievements of those not born. They see this as an additional burden on children born as a result of PNT.

“So quite aside from the issue of parenthood, they will also have to battle with the idea that two distinct human lives were destroyed in the creation of their life.”

Individual, Other

A small number of respondents present views specifically on the ethical trade-off between health and identity, discussing whether one of these should prevail. A few argue that a non-compromised sense of identity should be favoured, whereas most of those reflecting on this trade-off prioritise the individual's health.

“I accept that some individuals will have a different view, but cannot see that such concerns would outweigh the benefits of being born healthy!”

Individual, Personal experience of egg, sperm or embryo donation or donor conception



### 6.2.3 Social implications

#### No implications or minor implications on identity

There are some 130 respondents, including the British Fertility Society, who specify their belief that mitochondria replacement will have little or no social or ethical implications for a person's sense of identity. Respondents who identify themselves either as being affected by mitochondrial disease or as being a friend or relative of someone affected by mitochondrial disease often take this view. Roughly half of those who do not foresee any implications explain their view with references to mitochondrial DNA, stating that this is considered to be insignificant compared to nuclear DNA. Some emphasise that the nuclear DNA of individuals conceived with the assistance of mitochondria replacement would be from both their parents, and that this is what will constitute their genetic make-up. Paragraph 6.2.1 above covers respondents' views on the significance of mitochondrial DNA in more detail.

"I think the implications of having mitochondrial DNA from a donor as well as nuclear DNA from two parents are interesting, but certainly not problematic."

Individual, Family member/friend of someone affected by mitochondrial disease

Several respondents explain that they have come to the view that there are no implications on identity by reflection on their own situation or sense of identity. Some comments concentrate on the respondent's genetic relationship with their parents, others attribute great importance to the family environment they grew up in. One comment is from a donor-conceived person, who states that from their personal perspective there are no implications for identity:

"I don't see any implications for identity, and I say this as a donor-conceived (DC) person who believes that genes help to make us who we are."

Individual, Personal experience of egg, sperm or embryo donation or donor conception

"From a personal perspective, I think if I knew I had different mitochondrial DNA I would see it as an additional part of my identity, rather than confusing my identity. I would still see the people who gave me my nucleic DNA as my biological parents, rather than the mitochondrial donor."

Individual, Other

Similarly a few respondents relate their response to question 3 to personal experiences with mitochondrial disease, generally arguing that they do not consider mitochondria replacement to greatly affect an individual's sense of identity. The Muscular Dystrophy Campaign engaged with families affected by a mitochondrial disease and found that they were not concerned that the proposed techniques would have identity implications:

"When families affected by a mitochondrial disease were asked this question none of them had any concerns that mitochondria replacement could have an impact on their future child's sense of identity."

Organisation, Muscular Dystrophy Campaign

Respondents sometimes emphasise that an individual's environment is important in mitigating the potentially negative implications on their sense of identity. One element of this, according to respondents, is the provision of accurate information to individuals conceived with the help of mitochondria replacement techniques. Some respondents specify that children should be told about the impact of mitochondrial disease as well as the process of mitochondria replacement.

This is usually seen as a task for the parents, and several respondents highlight that they believe children should be made aware of this from an early age.

Another element touched upon by multiple respondents is the quality of close family relationships. Respondents believe parents need to be loving, understanding and open, and that this should prevent children born with donor mitochondria from struggling with their sense of identity.

“As long as there is a loving family who are willing to explain and help the child understand [sic] and the child is disease free and can live a healthy life then there should not be an issue with a person sense of identity.”

Individual, Family member/friend of someone affected by mitochondrial disease

Many respondents who think there will be limited or zero social and ethical implications on identity make comparisons with other, existing procedures. Respondents make rather varied suggestions as to which procedures offer the most appropriate comparison, from blood donation to egg donation to adoption, but their overarching argument is often similar: that the identity implications of mitochondria replacement will be no different from those of the other procedure. For many respondents this equals a view that implications will be minimal, although some respondents feel different about this. Paragraph 6.2.4 below covers the detail of the comparisons respondents draw.

“The question of identity is often overinflated. It is the same argument as adoptive children, step-children, mixed-race children, donated sperm or egg children - it is about the individual and how this acceptance or rejection becomes part of who they are.”

Individual, Family member/friend of someone affected by mitochondrial disease

“Once the novelty of the technique itself has subsided, we do not believe properly informed recipients should have significant identity issues.”

Organisation, AMRC and Genetic Alliance UK

### **Implications for the individual: awareness**

A total of 105 respondents reflect on the need for individuals born after mitochondria replacement to be aware of this, and to understand it as fully as possible. There is not much debate about whether individuals should be told about their genetic make-up; virtually all comments are in favour of sharing this information with children. The topic of child awareness is addressed by several respondents who identify themselves as mitochondrial disease patients or friends/relatives of patients, as well as respondents who indicate that they have personal experience of gamete donation. It also features in responses from various stakeholder organisations including the National Gamete Donation Trust and PROGAR.

Many respondents believe that if parents are open with their children about the unusual way they have been conceived, children will not be troubled about their identity, or at least not more than children conceived in more traditional ways. Where respondents specify this, they generally believe that the information should be presented to children from a young age. Others specify that they believe parents should always be sensitive to their child’s ability to understand the information and pitch the message accordingly. A few respondents highlight the other side of the coin and say that children will be more likely to encounter identity issues if they do not receive clear information early in life.

"I can imagine that if it was not explained clearly to either the parents or the children it could produce issues later in life."

Individual, Other

A small number of respondents discuss the benefits of guidance and support available to parents of children conceived with the help of mitochondria replacement. They believe that this will help ensure that parents feel confident and sufficiently informed to talk to their child.

"The debate around these techniques should be informed by professional bodies so that any children born from these techniques understand that they are just as much their parents' child as if they had their mother's mitochondria."

Individual, Other

A few respondents express concern about parents' willingness or ability to inform their child of the process that led to their conception, with one respondent stating that this is a common problem in families with donor-conceived children. Another respondent raises the concern that individuals with mitochondria from a donor might not inform their future partners about this, which might have consequences for offspring further down the line. In the opinion of another respondent such situations are unlikely to arise, as the need for medical supervision will ensure that the individual is aware.

"Experience has shown that few donor conceived people have been told the truth about their conception by their heterosexual parents and doubtless fewer still will be told the exact nature of the preimplantation changes made to their embryo form at the laboratory stage."

Individual, Personal experience of egg, sperm or embryo donation or donor conception

### **Implications for the individual: emotional and psychological**

Many respondents, 228 in total, comment on the emotional and/or psychological implications mitochondria replacement could have on children resulting from the proposed techniques. Almost all of these respondents, including Comment on Reproductive Ethics (CoRE), think that there will be implications, and generally suggest that these would be detrimental to the individual. Most of these respondents, although not all, have stated their opposition to mitochondria replacement in response to question 1.

The most frequently cited reason for children to suffer emotional or psychological damage is confusion over their mitochondria donor, specified by many respondent as their 'third parent' (with numerous responses also citing a potential 'fourth parent' in relation to pro-nuclear transfer). Respondents highlight issues relating to uncertainty about who the mitochondrial donor is, but more often explore how the existence of the donor might complicate a child's relationship with its parents. There are, among others, some 25 responses using similar or identical words to describe how children conceived with the help of mitochondria replacement could be affected emotionally:

"Children born as a result of either of these processes may be confused or distressed in their understanding of who their parents really are."

Individual, Other

Another concern that many respondents mention is the likelihood that children will feel different because of their unusual genetic make-up. Respondents worry that children will experience difficulty fitting in, either within their family or among peers who have been conceived in more traditional ways. Some specify that children might perceive themselves as a 'freak' or a 'science

experiment' and that this may come with shame or low self-esteem. A few respondents emphasise that children have not been able to consent their conception through mitochondria replacement and suggest this can be an additional emotional burden. Several reflect on how they would personally feel and express their presumed disquiet in a variety of qualifications:

"I would feel disheartened and irreversibly dehumanised to realise that I am not biologically connected to my fellow humans around me in the same way that they all are to each other. My life would be heavily coloured by bitterness towards my parents and the doctors who had in part created me."

Individual, Other

To some respondents, an important component of children's potential emotional and psychological problems lies in the use and discarding of embryos as part of the pro-nuclear transfer technique. They are concerned that children will experience something they describe as 'survivor guilt' or 'survivor syndrome': a sense of guilt about the embryos destroyed in the process of their conception. Some respondents add that this may make the individual feel worthless, or that it will create pressure to live up to expectations of being the 'chosen one' among embryos that were not allowed to develop. A number of respondents qualify a child born through pro-nuclear transfer as a 'clone', stating that this will cause severe identity problems.

"There could also be guilt about any other embryos that have not survived the process and resentment of the fact that the person may not have been acceptable to his/her parents without the replacement."

Individual, Other

The potential impact of mitochondria replacement on an individual's sense of identity within their family, and vis-à-vis parents and siblings, is discussed in many responses. There are many aspects to this discussion, some of which only appear in a small number of responses.

As mentioned above, respondents often foresee emotional or psychological issues in the child's realisation that there is a mitochondria donor who contributed to their genetic identity. Although some respondents believe children will perceive the mitochondria donor as a (third) 'parent', others refrain from this assumption, or reflect on their uncertainty on the matter:

"Will they think of it as three parents? Or just two parents who went to the DNA store and bought some better DNA than their own DNA."

Individual, Other

Respondents believe that the involvement of a mitochondria donor will complicate the relationship between children and their parents. Some feel that family relationships depend on full genetic kinship, and are weakened if mitochondria are acquired from a donor. This, according to respondents, could make children feel inadequate or excluded from the rest of their family.

Another aspect mentioned in various comments is the potential for children to feel that their parents were not ready to accept them in their 'natural' capacity and preferred to artificially improve them through mitochondria replacement. In some comments, respondents conclude that this means parents were more concerned with their children's health or viability than with their 'innate' quality or identity. Another comment suggests that the interference with the child's conception may bring a child to sense that the parents were unhappy with their own identity:

"They could sense that the parents who wanted them did not want to conceive them naturally, as the parents themselves felt to be 'imperfect' and not happy with their own identity."

Individual, Student

There is also a suggestion in a few comments that tensions may evolve between the child and mother, since the mother has mitochondrial disease and the child does not.

Several respondents consider the trade-off between the parents' feelings and happiness and those of the child, sometimes arguing that parents are compromising the well-being of a child by allowing it to be conceived through mitochondria replacement. They believe that the complications around identity are a heavy burden to be imposed on a child.

"Whatever the unknown psychological or physical burdens that resulted, however, it has to be underlined that these would be borne not by the parents, but by the offspring."

Organisation, Comment on Reproductive Ethics [CoRE]

Respondents suggest a variety of other aspects that could disturb or confuse the relationship between the child and their family. Examples are that the child may be curious about 'siblings' it has through its mitochondria donor, and that any family difficulties or behavioural problems could be regarded as a consequence of the child's genetic relationship to its mitochondria donor.

"Despite the fact that it appears there will be no significant inherited characteristics from the procedure there may always be some doubt, particularly of relationships within the family become strained for any reason. The mitochondrial donation could then be blamed, albeit with little foundation."

Individual, Other

In a similar vein, several respondents emphasise that it is likely that the child will have a desire to know its mitochondria donor. Discussions about whether or not this should be possible are covered in chapters 7 and 8; here we focus on the possible impact of the donor's existence on the child's well-being. Respondents to question 3 suggest that children may consider their 'third' parent to be missing from the environment they grow up in. Some offer comparisons with children who were adopted or the product of gamete donation and assert that these children are known to develop a wish to find out about their biological or genetic parents.

"If a child gets DNA from 3 or more parents this will lead to desires to want to know the identity of the donor parent. Reasons could vary from thankfulness, curiosity, identity confusion, or desperate need to be loved."

Individual, Other

A few respondents describe potentially problematic aspects of the presence of a mitochondria donor. One respondent states that donor-conceived individuals are increasingly seeking psychological support, suggesting that this may also be the case for children born with the help of mitochondria replacement. Another believes that if the child's family is not a pleasant one to grow up in, the child may wonder about the family environment their mitochondria donor might offer.

Among many argued cases stating that there will be emotional or psychological consequences for the child, or that there will not, there are a few responses emphasising that the proposed techniques are fundamentally different from what we have knowledge about, and that as a consequence it is not possible to predict how resulting individuals will feel about them. Some respondents highlight the experimental nature of the techniques and the need to consider the long-

term psychological effects for individuals conceived in this way, as they may only encounter identity issues later in life. A few suggest that the potential implications on individuals' sense of identity are likely to decrease if mitochondria replacement would become more common.

"Yes, it is inevitable that the knowledge that they owe their genetic origins to three persons will affect those concerned, in ways that cannot now be predicted, since their situation would be entirely unprecedented."

Individual, Other

The impact of society's response to children conceived with the help of mitochondria replacement is mentioned in several responses to question 3. Some respondents who perceive the mitochondria donor as a 'third parent' worry that children may feel that they do not meet the norm of having two parents and that this could confuse them. Others highlight the risk of negative reactions children may be subject to from people who suffer from mitochondrial disease, or from people with strong views on reproductive ethics or genetic modification.

"Given that many people refuse to eat genetically engineered foods, how does one tell one's friends, family, potential mate that you are genetically engineered?"

Organisation, International Center for Technology Assessment

Another strand of argument broached in a small number of responses is around how public opinions are shaped. Respondents emphasise the risk that children conceived with the help of mitochondria replacement will carry a label that identifies them as a 'three-parent baby' or a 'GM baby' and that this may have a detrimental impact on their well-being. A few respondents specify the role of media in influencing public attitudes, and express concern that this may make children's lives more difficult.

"They fail to reckon with the power of our media which have already represented these techniques as creating 3-parent or 4-parent children. As these concepts are being increasingly embedded in the public consciousness, it will be virtually impossible to uproot them."

Individual, Other

Some respondents make other comments about the implications for wider society. A few discuss the legal status of the mitochondria donor, sometimes stating their belief this is important to consider in the light of kinship and identity. A few others posit a concern about the pressure that intending parents may feel when they would need to decide about the option of mitochondria replacement.

"[...] prospective parents who fear passing on the disease could ultimately be labelled irresponsible if they don't have the treatment, but, at the same time, they could sacrifice bonding with their child if they go ahead."

Individual, Other

Many comments include considerations about the current state of society and interpersonal relationships within it, in some cases to support a view that society will be ready to accept individuals conceived through mitochondria replacement, in other cases deploring that the techniques will further erode traditional structures.

"The multiple parent issue may become a catalyst [sic] to a very dangerous [sic] society change. We are confused enough already, and social studies have backed this up."

Individual, Other

#### 6.2.4 Comparing with other procedures

In considering the potential implications on children's sense of identity, many respondents propose comparisons with other procedures. There are great variations not only between the procedures that respondents liken to mitochondria replacement, but also between the conclusions they draw from this. The following set of quotations captures this very aptly: two respondents each citing both adoption and gamete donation, one as a satisfactory argument that identity implications will be manageable; the other to highlight additional complications specific to mitochondria replacement:

"There are many happy people raised with adoptive parents, surrogate mothers, or sperm-donor fathers; these don't have any bearing on the child's wellbeing."

Individual, Other

"A person who is adopted or born from the result of donor sperm or eggs might find themselves asking where they come from. At least in these situations the question has a definable answer."

Individual, Other

The most commonly cited procedure respondents to question 3 compare mitochondria replacement with is gamete donation. In most of these responses the comparison leads respondents to argue that the potential implications on a person's sense of identity are socially and ethically acceptable, sometimes highlighting that society already accepts the consequences of gamete donation. Many respondents feel that the impact of mitochondria replacement can be viewed as equal to that associated with gamete donation, while several others suggest that the proposed techniques will impact less, as no nuclear DNA is involved.

"We therefore consider that mitochondrial transfer techniques are likely to raise far fewer social and ethical issues surrounding offspring identity than are already raised by existing fertility techniques that are widely accepted, such as gamete donation and surrogacy."

Organisation, Wellcome Trust

A number of respondents are concerned about the implications of gamete donation on children's sense of identity, and emphasise that their concern extends to mitochondria replacement. Some cite publications containing examples of donor-conceived individuals struggling with identity questions.

"We do however have increasing anecdotal evidence about the importance of genetic heritage and parental bonds for those born from donated gametes and their desire to know about their full genetic heritage (3). Some have described anger at feeling like a medical experiment and cited problems with understanding identity for themselves and their own children" (4)"

Organisation, Christian Medical Fellowship

There are numerous comments considering a comparison of the implications of mitochondria replacement on an individual's sense of identity to those of organ, blood, or bone marrow transplantations. Several of these comments are from friends or relatives of people affected by mitochondrial disease. Most of the respondents drawing such comparisons do so to underline their argument that implications will be minor.

"A person can have an entire organ transplanted (heart, lung, liver, kidney, etc...) and not suffer any change to their identity [sic]. Indeed, transplants introduce foreign DNA into the recipient. I do not see this as being any different from using a donor's mitochondrial DNA"

Individual, Other

A small number of respondents specifically disagree with the suggestion that in this context mitochondria replacement can be compared to blood or bone marrow transplantations.

"The SCHB is of the opinion that the donation of an unfertilised or fertilised eggs can certainly not be thought similar to a bone marrow or blood donor. Biological elements partaking in the creation of life are completely different to biological elements that are used in the treatment of an already existing life."

Organisation, Scottish Council on Human Bioethics

Another procedure often referred to in responses to question 3 is adoption. The pattern of these responses is very similar to that referring to gamete donation, with a split of opinion between (more) respondents who believe both procedures have acceptable implications on identity and (fewer) respondents who think both procedures cause identity-related harm.

Some 130 respondents feel that the implications of the proposed techniques on an individual's sense of identity will be equal to other, existing procedures. While 15 respondents assert that the implications of mitochondria replacement will be greater, often identifying the mitochondria donor as the complicating factor; 42 respondents believe that there will be fewer implications, generally referring to the perceived insignificance of mitochondrial DNA. The latter group includes a number of respondents who identify themselves as friends or relatives of a person affected by mitochondrial disease and a few who indicate that they have personal experience of gamete donation.

"As an adoption worker myself I am very aware of the issues of identity and the impact on individuals of not knowing where they came from genetically. I spend much of my working life helping adopted adults find information and trace birth relatives. However, I believe this would be far less of an issue to a person born by the technique proposed and the relief from the anxiety for female children of passing on the disease to their children would be immense."

Individual, Family member/friend of someone affected by mitochondrial disease

The next chapter, chapter 7, discusses respondents' views on other procedures in more detail.



### 7.1      **Headline findings**

987 respondents answered question 4a, which asked:

**In your view how does the donation of mitochondria compare to existing types of donation? Please specify what you think this means for the status of a mitochondria donor.**

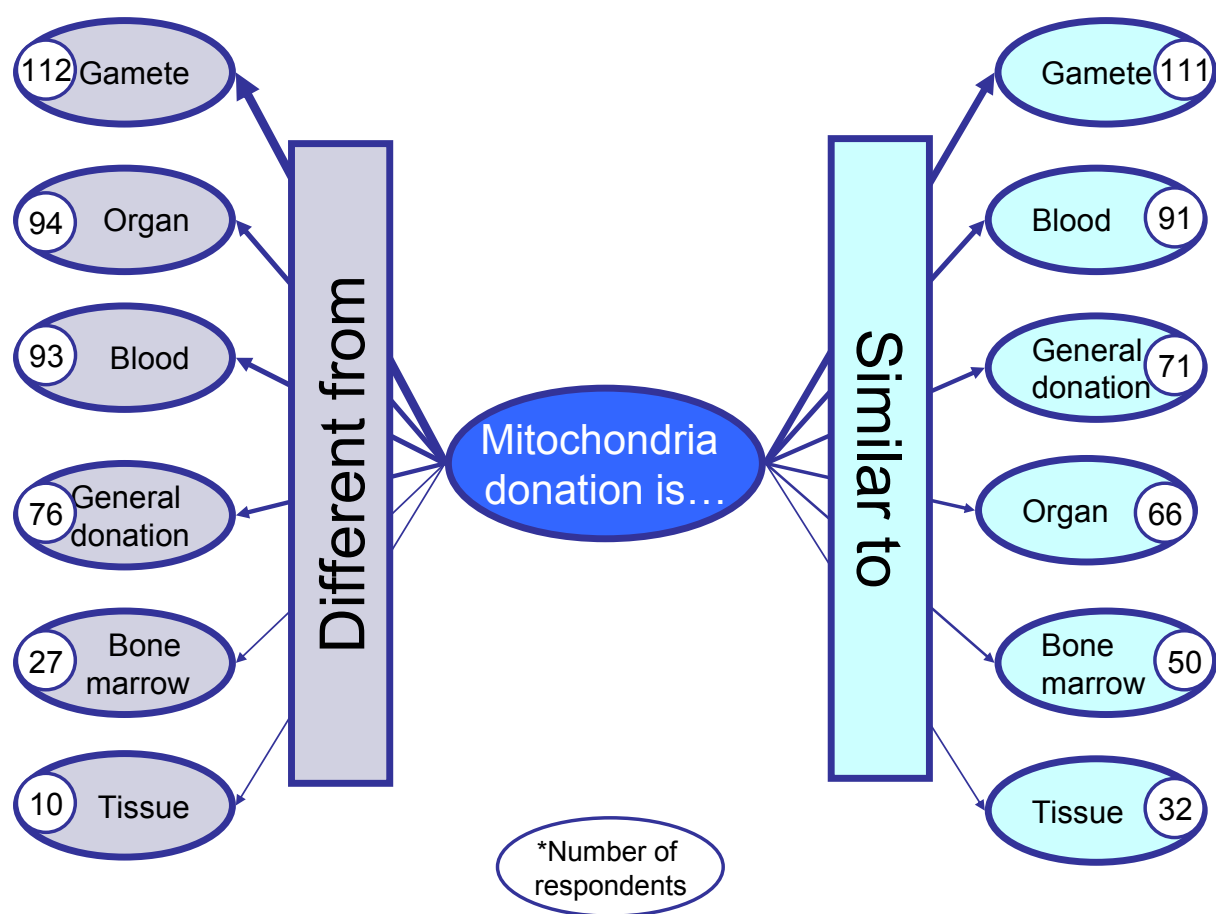
Responses to question 4a included a wide variety of views as to whether mitochondrial donation could be compared to existing types of donation, or represented an entirely different proposition. Typically respondents who believed the significance of mitochondrial donation to be similar to other non-reproductive donations supported its introduction, while those who regarded it as equivalent to donating sperm or eggs were more cautious.

### 7.2      **Summary of comments**

#### **7.2.1      Comparing mitochondrial donation**

The majority of respondents to question 4a suggest existing types of donation, with which to compare donation for mitochondria replacement and the most common are depicted in the diagram below. As the diagram shows, for most comparisons as many respondents thought mitochondrial donation was similar, as thought it was different to another type of donation. As the narrative below describes however, many different explanations were given for these comparisons, and often two respondents would conclude the same thing for entirely different reasons.

**Figure 6**      **Comparative views on mitochondria donation in responses to question 4a**



As shown above, there are a number of respondents who suggest that mitochondria donation is similar, in general, to other kinds of donation without specifying further. These respondents were typically supportive of the techniques being introduced into clinical practice, often citing the perceived benefits of this for health:

“It is very similar. A donor would be increasing the chances [sic] of a more healthy, longer life for an individual. The organ being donated makes no difference.”

Individual, Family member/friend of someone affected by mitochondrial disease

Similar sentiments however are expressed by some respondents who feel that mitochondria donation is totally different from other types of donation in a positive way:

“I think that mitochondrial donation is in a different category from other types and that the emphasis should be on its potentially remarkable role as a contribution to preventive medicine.”

Individual, Other

A more common view among those arguing that mitochondrial donation is fundamentally different is that this difference warrants caution about introducing it to practice; either because it introduces new phenomena such as the genetic contribution of three parties, or because they believe it is unethical. These arguments are explored in more detail in the following sections. Others highlight that the donation differs fundamentally from other (non-reproductive) donations as the impacts persist through the germline rather than affecting one individual only.

Among respondents who indicate that they have personal experience of gamete donation or donor conception there is a divergence in views similar to respondents overall. While six respondents from this category state that they see mitochondria donation as different from gamete donation, five say they think it is similar. Within this category, several respondents suggest that mitochondria donation is similar to organ, blood or tissue donation, while very few emphasise a difference.

### Comparing with gamete donation

The most common comparison made by respondents in question 4a is between mitochondrial donation and the donation of gametes (eggs or sperm), with equal numbers arguing that the two types of donation are similar as argue that they are different. Organisations suggesting similarity include PROGAR and the National Gamete Donation Trust; organisations suggesting difference include the Wellcome Trust and the Nuffield Council on Bioethics as well as the Anscombe Bioethics Centre. Among those who believe that donating mitochondria is similar to donating gametes, some argue that the transfer of genetic material is the deciding factor, which differentiates these procedures from blood or organ donation. A few note that the proportion of genetic material contributed is much smaller than in full gamete donation, but still feel that it is significant.

“It is the same irrespective of the quantum & type of DNA donated. Hence, the status of the donor should be the same as with donated eggs or sperm.”

Individual, Other

For other respondents the key point is whether mitochondria affects identity; where respondents believe that there is no effect on traits or characteristics they suggest the donation can be seen as similar to blood donation, for example, but would be substantively different if such an effect did occur. There are some respondents who state their belief that mitochondrial DNA does not affect identity traits, often likening it to a ‘functional’ structure such as bone marrow. In contrast a few respondents suggest either that the role of mitochondria in identity may be discovered as the science of genetics evolves, or that it does contribute in some sense already, for example:

“The donation of mitochondrial DNA is very personal and individual reflecting a donation of an individual's personal characteristics even if this means how they function biochemically rather than their outward bodily characteristics.”

Individual, Other

An alternate focus for some respondents is the procedure for the donor, which they see as similar to that for egg donation. Some of these respondents suggest this comparison as evidence for the acceptability of the introduction of the techniques (i.e. it's no different than an already widely accepted process). However others express concerns about the existing process which they believe apply equally with the proposed techniques:

“The donation of mitochondria is going to involve egg donation. There are already more eggs wanted than donors ready to provide them. Egg donation is an unpleasant and risky business. It is in no way comparable with easy blood donation.”

Individual, Other

A third line of reasoning for the similarity between mitochondria and gamete donation for some respondents is that the donor in both cases is in some sense a ‘parent’ of the resulting child, either in a biological sense, or for a few respondents, in the sense of having a moral responsibility towards the child (explored more in section 7.2.2 below).

Respondents who state that mitochondria donation is different to donating gametes commonly suggest that the two are different because no nuclear DNA is transferred. Some specifically mention characteristics, arguing that because the donation will not impact on the child in this sense, the mitochondrial donor is not equivalent to an egg or sperm donor. Respondents arguing along these lines tend to support the introduction of the techniques, and feel that the donation of mitochondria is 'less' consequential than classic gamete donation.

In contrast several respondents who oppose the introduction of the techniques also argue that mitochondrial donation differs from egg donation because the procedure results in changes to the donated egg, altering the relationship between donor and child. Some of these respondents describe this change as affecting the extent to which the donor is the 'mother' of the child:

"The spindle is not an egg and without an egg there is no embryo. The egg donor is a kind of partial mother, just as the spindle donor is a kind of partial mother.

In the case of PNT the egg donor is not the mother directly of the final embryo created, but of an embryo who is destroyed to create that final embryo."

Organisation, LIFE Charity

Others argue that potential donors may not understand this apparent difference to typical egg donation, and that this lack of information would make them less informed and able to consent.

### **Comparing with embryo donation**

There are a number of respondents who make a specific comparison between donation for mitochondria replacement and the donation of embryos to research in which they may be destroyed and express ethical concerns about this process (153). The ethical argument made is that the donation of viable eggs which are used to create embryos which are not intended to be born results in the destruction or death of that embryo. Some respondents refer specifically to PNT, arguing that it amounts to the destruction of an embryo in order to create another, while others do not specify one or other of the techniques, and some specifically mention the donation of eggs rather than embryos. In addition to ethical concerns, some of these respondents suggest that the donor in such a situation may experience guilt or remorse after the donation:

"A mitochondrial donor is someone who is substantially risking her health and future fertility if she donates eggs: if she donates embryos, she is delivering her offspring up for destruction. A woman is in the position of one who is giving her embryos up for the purposes of research which is of no benefit to the embryo, and results in its eventual destruction. This is to ask women who donate embryos to treat their offspring as if they were commodities: which might be damaging to her relationship with subsequent or existing children (if one child is a commodity, why not all of them?)"

Individual, Other

Alongside concerns about the 'destructive' use of embryos and eggs in the techniques, often raised alongside concerns about the effect on the donor. Many of these respondents mention the procedures involved in donating eggs, particularly artificial stimulation. Others suggest that exploitation can occur when donors are offered financial reimbursement or access to fertility treatment in exchange - respondents typically note that these concerns exist for all techniques involving egg donation, but suggest they could be exacerbated by the introduction of the techniques into clinical practice. Others raise particular concerns about the availability of donors, either because they believe women will be less likely to donate given the perception of the techniques described above, or because of a general shortage of egg donors.

### **Comparing with organ, tissue and blood donation**

Although many respondents, including the Association of Clinical Embryologists (ACE) Executive Committee and the British Medical Association, specifically mention blood, organ or tissue donation they typically use the same arguments. Those who believe mitochondrial donation is different to these types of donation often refer to the genetic component of mitochondria, as described above. Others note that mitochondria replacement alters the germline, and thus the donation cannot be viewed in the same light as donations such as organs which affect only the individual involved. A small number of respondents argue that difference is based on the donor; they argue that the mitochondria are effectively donated by the egg or embryo (which they view as a separate person), rather than by the mother, and as such no informed consent is given. Others suggest that there are negative consequences of mitochondrial donation for the embryo or egg donated, where tissue donation has no significant effect on the donor:

“I think there is an enormous difference between donations that save lives (such as blood donation) and donations that result in the loss of (embryonic) life, such as egg or mitochondria donation.”

Individual, Other

Those who argue that blood, organ or tissue donation is similar to mitochondrial donation typically argue that there is no nuclear genetic contribution, and thus no impact on characteristics, as described above.

### **Comparisons: variations**

Some respondents specifically address differences they see in the status of donors to each technique. Of these most raise the arguments described above regarding the use of embryos in PNT, but tend still to oppose both techniques. A few respondents discuss their view that donation for MST is equivalent to blood or organ donation, as there is no genetic contribution, or to a sperm donation, in that it is likely to be accepted in a similar way.

There are two respondents who mention the sex of the resulting child - noting that as mitochondria are passed on only via the female line, the germline change is only passed on via female children. One suggests that this effectively makes a mitochondrial donation which results in a female child similar to gamete donation, but a donation resulting in a male child is more like an organ donation, where no change persists beyond the individual.

## **7.2.2 The mitochondrial donor**

### **Status of the donor**

Views on the status of the mitochondrial donor are strongly correlated with views on the status of the donation in relation to other types of donation; this section focuses specifically on the donor as an individual, with many arguments summarised above. The most common points raised by respondents in relation to the donor concern whether they are a ‘parent’ to a child conceived via the proposed techniques - with slightly more respondents supporting than opposing this concept. In responses from respondents who indicate that they have personal experience of gamete donation or donor conception few comments are made about the donor status. Three of these respondents suggest the donor is a parent to the child, one respondent states the donor is not, and two respondents say the donor has no rights or responsibilities towards the child.

"We find no distinction. s.47 of the Human Fertilisation and Embryology Act 2008 states: 'A woman is not to be treated as the parent of a child whom she is not carrying and has not carried'. The Humanist Society Scotland does not believe that the donor of mitochondria [sic] can have the same status as a reproductive egg or embryo donor, nor that mitochondrial [sic] donors should be legally pressured to be identified to the adults born from the donation."

Organisation, Humanist Society Scotland

Those who believe that the mitochondria donor is in some sense a 'parent' to the resulting child tend to focus either on the genetic contribution of the donor, arguing that the fact that their DNA is passed on qualifies them as a 'parent'. Others refer to the essential role of the donor in the conception of the child.

"The person could not exist without this mitochondrial DNA and therefore I feel this makes the mitochondria donor a parent of the child in a very real sense as they have been integral to the process of conception."

Individual, Other

Many of those who state their belief that the donor is a 'parent' qualify this, suggesting that the role is shared with the intended parents (who contribute their nuclear DNA) - a smaller number state specifically that all three genetic contributors have an equal role as parents.

Despite the number of respondents who argue that the donor has a role as a parent, far fewer suggest that they have particular rights or responsibilities towards the child - which may be because many of those who believe the donor is a parent do not believe the techniques should be permitted. Statements about responsibilities of the donor tend to identify that these responsibilities exist without going into detail about what they entail.

"I think that the mitochondria [sic] donor is a third parent. I think that any techniques which use genetic material from three people has this problem."

Individual, Other

In contrast those who argue that the mitochondrial donor should not be considered a parent often suggest that the genetic contribution is not significant enough, or is purely functional, and so does not bestow a parental relationship. Others focus on the social role of parenting, arguing that the donor contributes genetically, but has no role raising the child, and as such is not a parent.

Those who do not believe there should be a parental relationship between donor and child also tend to believe that the donor should not have rights or responsibilities over the child, with several returning to comparisons with other donation scenarios:

"Mitochondrial donation is more akin to giving blood than it is to surrogate parentage. The Mitochondrial donor and child should not have any contact with the child and has no rights over the child's upbringing."

Individual: Student

A number of respondents (24) specifically mention the legal status of the donor, with the majority arguing that there should be no binding legal requirement on the donor with regards to contact or obligation towards the child. This is seen as a potentially challenging issue by some, who suggest that the complexities of the relationship between intended parents, donor and child may result in legal challenge, or cumbersome legislation. The theme of confusion is echoed by others, who

express the view that the status of the donor in general is unclear, with some suggesting that this is symptomatic of overall problems with the techniques.

“We simply cannot predict the meaning that the mitochondrial donor (and the donation itself) will have to those directly affected – and neither is that meaning likely to be (i) static over their lifetimes or (ii) standard either within or across the different ‘groups’ concerned.”

Organisation, PROGAR

Many respondents make comments in question 4a on the extent to which information should be available to a child conceived as a result of the techniques; these arguments are explored in the following chapter. However a number of respondents express more generally their view that the donor should have the right to anonymity, either as a blanket policy or as an option they could choose. Concerns for the right of the donor to anonymity are often associated with the view that the donation is an altruistic act, which should not have harmful implications for the donor. Many of these respondents associate the act of mitochondrial donation with ‘helping’ a child, rather than ‘creating’ one:

“In the same way that organ, egg and sperm donors consent to helping another life, a mitochondrial donor would be doing the same-not wanting a child etc but wanting to help another human being “

Individual, Personally affected by mitochondrial disease

However there are some respondents who take the opposing view, and feel that something about the nature of mitochondrial donation, either its genetic aspect, or the fact that life is ‘created’ as a result, is a significant enough contribution to the resulting child that they must have the right to information about the donor.

### 8.1      **Headline findings**

A total of 1,039 respondents answered question 4b, which asks:

**Q4: b) Thinking about your response to 4a, what information about the mitochondria donor do you think a child should have? (Choose one response only)**

- 1) The child should get no information**
  - 2) The child should be able to get medical and personal information about the mitochondria donor, but never know their identity**
  - 3) The child should be able to get medical and personal information about the mitochondria donor and be able to contact them once the child reaches the age of 18**
  - 4) Other**
  - 5) I do not think mitochondria replacement should be permitted in treatment at all.**
- Please explain your choice.**

As summarised in the figure 7 below, the largest number of respondents chose option 5, implying that the other options are not relevant to them as they would rather not see the techniques permitted. Looking at the different respondent types, the only group where a majority selected option 5 are respondents describing themselves as 'other' (see chapter 2). Among specified respondent types (e.g. patients, relatives, students) the opinion is divided between all five options.

Respondents' choices divided fairly evenly between options 1, 2 and 3, with option 1 receiving the fewest selections and option 2 the most among them. A smaller number of respondents selected option 4, 'other', and suggest different approaches or variations to what is proposed in options 1, 2 and 3.

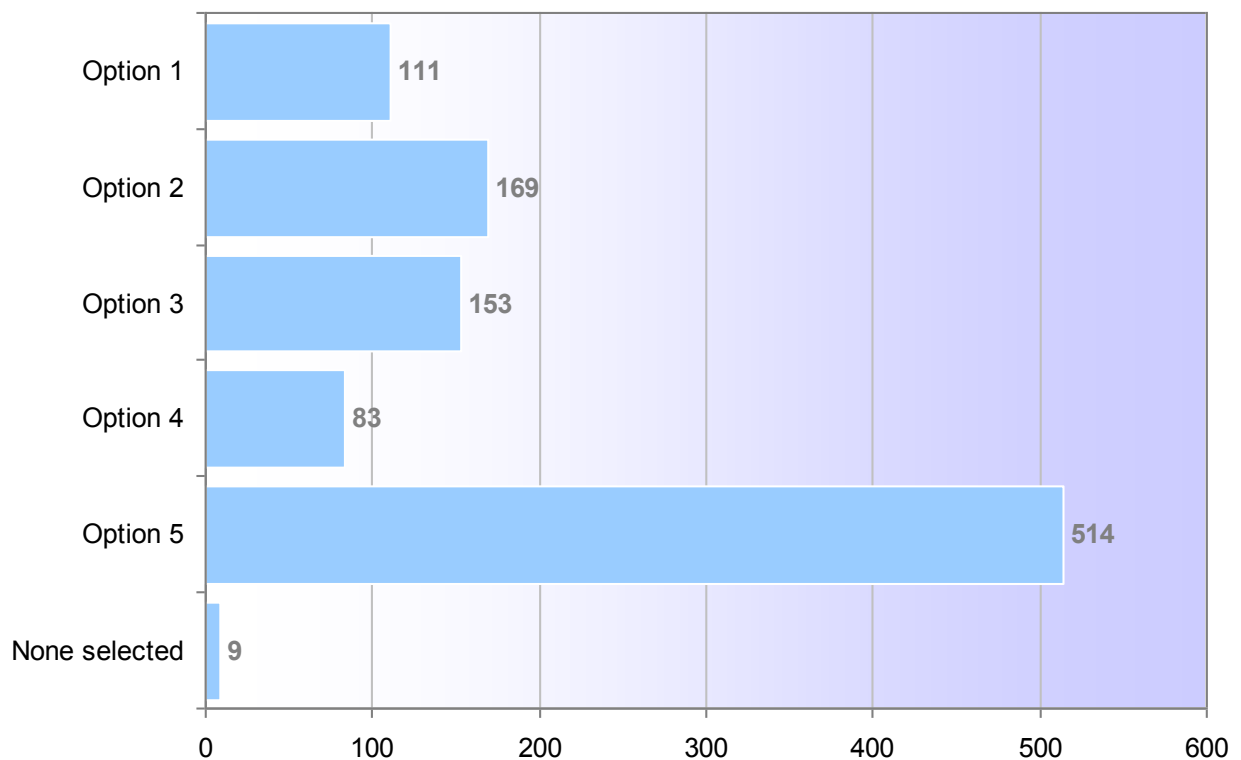
Though most respondents selected one of the 5 options presented, nine respondents made further comments without selecting any of the options presented.

Looking at the options selected by different types of respondents, there is a relatively clear preference for option 2 among those who indicate they are personally affected by mitochondrial disease and/or a friend or relative of someone affected by mitochondrial disease. Among the (few) respondents who indicate that they have personal experience of gamete donation or donor conception, options 2, 3 and 4 are selected more often than option 1. Very few respondents from the categories mentioned here have selected option 5.

Among stakeholder organisations options 1 and 3 are more often selected than option 2. Proponents of option 1 include the British Medical Association and the Nuffield Council on Bioethics; option 3 is supported by the Church of England (Mission and Public Affairs Council) and PROGAR, among others. Human Genetics Alert, the Church of Scotland as well as some other organisations state a preference for option 5.



**Figure 7 Preferred option in responses to question 4b**

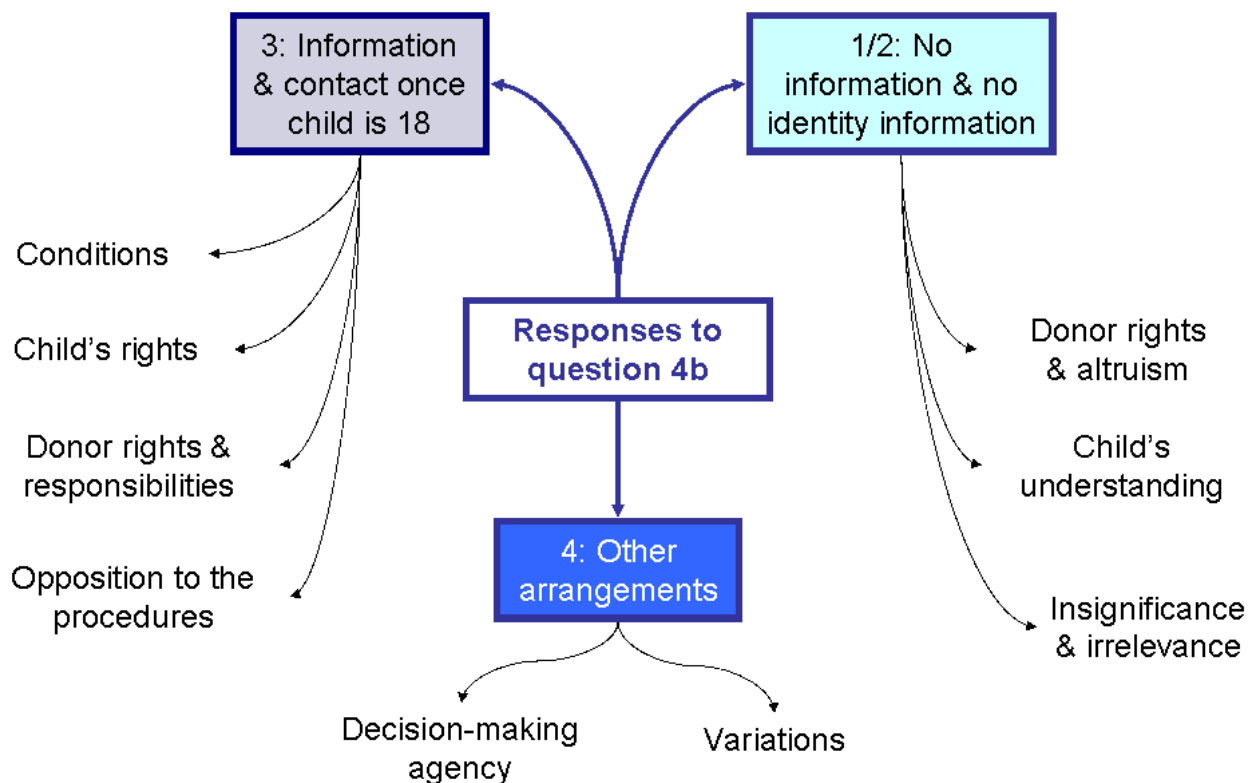


Respondents selecting options 1 and 2 express some similar views in explanation of their perspectives, frequently focusing on the ethical status of the donation and the rights and responsibilities thought to be contingent. A few choosing option 1 state explicitly that option 2 would be their next preference, and vice versa. Similarly, the explanations of respondents selecting options 2 and 3 display some similarities, often anticipating future medical needs and identifying concerns of offspring of the techniques.

Respondents who comment that they oppose the techniques generally selected option 5, although a smaller number selected option 3, in order to express their preference about disclosure of information in the event that the techniques are to be permitted. Their views are explored further in the section on option 3, below.

This chapter examines in turn the explanations of respondents, grouped according to the options they preferred for donor information disclosure. Their explanations are explored in more detail below under the following sub-headings:

**Figure 8 Responses to question 4b**



## 8.2 Summary of comments

### 8.2.1 Option 1 (no information) & option 2 (some information but not identity)

Respondents selecting options 1 or 2 agree that the identity of a donor involved in the techniques should at no point be disclosed to the child, although those who chose option 2 think that medical or personal information should be available to them. Explaining their choices, these respondents raise many similar considerations. Further, three respondents selecting option 1 said option 2 would be their second choice, and three selecting option 2 said option 1 would be their alternative preference.

#### Insignificance and irrelevance

A number of respondents selecting options 1 or 2, including several who are personally affected by mitochondrial disease, or a patient/relative of someone who is, argue that no more information should be disclosed on the grounds that the donation has the same status as a blood or organ donation. They say that as those donations guarantee anonymity, so should the donation involved in these techniques. A smaller number of respondents selecting either option compare the donation to that of eggs or sperm, arguing that its lesser significance for the genetic identity of the child indicates that less donor information should need to be disclosed. A few make similar arguments based on comparison with adoption or surrogacy. A few respondents selecting option 2 suggest the procedure is similar to egg or sperm donation, but suggest disclosing the donor's identity is complicated, or should be conditional on consent.

"The reason children born following donor conception require information about the donor is because the information relates to them, as a person, and the donor's genes have

contributed to their physical appearance and personal characteristics. The same does not apply to donated mitochondrial DNA. The closest analogy is to blood or bone-marrow donation which is carried out anonymously with the recipient receiving no information about the donor.”

Organisation, British Medical Association

Some respondents who refute the need to disclose the donor’s identity based on the comparative status of the donation go on to explain that their views are informed by the function of mitochondrial DNA. They say that as mtDNA does not determine the identity or the traits of the child, the donor’s identity can have no significance. Others say they can’t see circumstances in which it would be necessary or important for the child to access more information about the donor.

“I believe that children conceived by this technique should not need any information on the identity of the mitochondrial donor. As the conceived child will not inherit any personal characteristics or traits from the mitochondrial donor, they will have no legitimate interest in their identity.”

Individual, Member of staff at a licensed HFEA centre, Researcher

Some respondents selecting either option 1 or 2 explain their view that certain circumstances might influence what donor information should be disclosed. A small number of respondents selecting option 1 comment that in case of new medical evidence or other unforeseen developments, the relevant information should be confidentially stored, or the rules about its disclosure might need to be reconsidered. Comment on the circumstances of disclosure is significantly more common among respondents selecting option 2, some of whom mention the possibility of medical developments that might justify more information. Most frequently, they describe these circumstances as likely to be connected to the health of the child, other medical developments in the field, or unforeseen consequences of the techniques.

### **Child’s understanding**

Respondents sometimes link the way children are informed about the techniques to the significance of information about the donor. Some say they believe children should be given no or limited donor information, but do have a right to understand the process that has taken place. Others state concern that making available too much information about the donor could lead the child to an inaccurate understanding of its medical or personal significance to them.

A small number of respondents reflect on the motivation of the child in seeking information about their donor. Some of the respondents favouring option 1 note that a child’s curiosity would be understandable, but that it need not require the disclosure of more information than is fitting for the donor. This view is connected to their feeling that the significance of the mtDNA is limited, and it is vital that children understand this.

“...The child should have the right to know how they were conceived and why, but have it explained that their genetic characteristics such as physical traits, personality traits, intelligence etc come from the parents they are growing up with. I think it would confuse the issue if they were to have the right to know who the donor was given the minimal input from the donor mitochondria to the person's make-up.”

Individual, Family member/friend of someone affected by mitochondrial disease

### **Donor rights and altruism**

Other views common to respondents selecting options 1 or 2 focus on the rights of the donor, or considerations about the experience of donating and about privacy. Some express concerns about

the possibility of intrusion into the donor's life if their identity were to be disclosed. Others note that knowing a child might seek them out later in life would be a disincentive to donate, or note that guaranteeing donor anonymity would likely encourage altruistic donors. Some describe the relationship between the donor and the parents as altruistic or as offering a simple medical 'repair', and so part of a dispassionate and impersonal act of generosity that need not imply future contact or association.

"I feel that using a mitochondria donor would be a gift. A way to erase the spelling mistake within my gene pool. My child would be made up of myself & my partner & very little of the donor. I think having access to medical conditions & personal information would feed any interest but that person isn't the main gene donor & I feel there's enough reassurance there for a child as its still made up of mum& dad genetically with some help from a kind person..."

Individual, Personally affected by mitochondrial disease

### Comments specific to option 2

Though most comments made by respondents favouring either option 1 or option 2 are similar, some comments made by respondents selecting option 2 weren't reflected in comments of those who chose option 1.

Specifically, nine respondents select option 2 and mention specific reasons why personal information should be made available to the child. In most cases respondents say this disclosure should be subject to the relevance or utility of personal information, although one respondent suggests any criminal history of the donor should be available to the child.

"In case of any medical complications in the child, the knowledge of the medical and personal information could be useful to reduce the certain complication. However the donor identity may be unknown as only a small percentage of the donor is a part of the child."

Individual, Student

Four respondents selecting option 2 say that option 3 would be their second choice, usually suggesting that the two differ little, and that the donor's consent for the disclosure of their identity should be the critical factor.

### 8.2.2 Option 3 (information and ability to contact once child is 18)

Respondents selecting option 3 tend to attach greater significance to the results of the technique for the child, and often consider these outcomes at length in their explanations.

A number of these respondents echo explanations given by respondents selecting other options on information disclosure. For instance, some respondents state relatively straightforwardly that they regard option 3 as the appropriate arrangement since they see mitochondria replacement as equivalent to egg or sperm donation.

#### Child's rights

Of respondents choosing option 3, several explain that they feel it is the child's right to know the identity of the donor. Many of these accept the curiosity or the emotional or medical needs of the child, and a number give their explanations in terms of parenthood or origins, connecting the disclosure of the donor's identity with the child's ability to understand their own background. Some respondents who select option 3 cite the child's general right to information about their biological make-up, and others mention that they may wish to thank the donor.

Eight respondents frame the child's rights differently, focusing on the right to understand the process that took place. For most of these respondents this is the responsibility of the child's parents, and they anticipate that if done properly, there would be no need to withhold any information from the child, who may be content not to act on any information they could access.

For nine respondents, the decision on how important knowledge of the donor's identity is must rest with the child. For this reason, they consider option 3 the best arrangement, so that the information should be available when needed.

"Paternalistic and/or culturally discriminatory assumptions about whether or not such offspring will need information to meet their identity (or future medical) needs have no place in the modern world and we should not be risking the future well-being of those offspring for whom it may prove important..."

Organisation, PROGAR

A number of respondents selecting option 3 state in their explanations their support for the provision for disclosure of information when the child reaches adulthood or the age of 18. Some respondents reaffirm this age conditionality, but six suggest that the disclosure might be appropriate or helpful earlier in the child's life, or simply that the age limit ought to be fixed elsewhere.

### **Donor rights and responsibilities**

A smaller number of respondents stress that the child's rights must be balanced against the rights of the donor. Though only four respondents who select this option state that disclosure of the donor's identity should be subject to their explicit consent, a number of other respondents draw attention to the rights of the donor to decline to enter into a relationship with the child, for instance, or to maintain their distance from the child.

"This option seems to provide the maximum freedom to obtain information if the child wishes it on reaching adulthood, without infringing the donor's right to anonymity."

Individual, Other

Eight respondents who select option 3 explain their view that it would be justified to disclose the information and identity of the donor because they regard it as part of the donor's responsibility. Specifically, they suggest the donor should take account of the possibility of future contact before the donation takes place.

Other option 3 respondents, though, feel greater flexibility would be appropriate. Some suggest that the disclosure of donor identities should be flexible to a degree, dependent of the will of some combination of the parties, or else different case-by-case depending on the needs of the child. A few respondents selecting option 3 suggest that disclosing the identity of the donor would be less problematic if the donor were likely to be someone known to the family benefitting.

### **Conditionality**

Many respondents who select option 3 impose conditions on the disclosure of information outlined. A few respondents specify that the rules on donor identity should reflect the technique used: so, a child born using MST should have the right to know the identity of the egg donor, while one born by PNT should know the identities of both the egg and sperm donors involved in the process. Another suggests that since male children will not pass on the donor mitochondria, they need only receive the information implied in option 2, while female children should know the donor's identity too, as in option 3. Others refer to the significance of this transmission through a female child, without asserting the possibility of different rules.

Some respondents selecting option 3 suggest further medical evidence or outcomes as conditions on the disclosure of donor information. Similar to arguments made by respondents selecting option 2, these respondents consider the possibility that information about the donor might be important in future medical research or treatment. A couple suggest that if the techniques were shown to transmit some characteristics to the child, the donor's identity would be important to disclose.

"...as the replacement of mitochondria is a new technique without the benefit of years of results it is possible that unforeseen [sic] problems may arise. I would therefore be in favour of allowing the child to obtain medical and personal information that may help in this case. That said, this should in no way lead to the situation where a mitochondrial donor could be found responsible for the future health and well-being of the child."

Individual, Family member/friend of someone affected by mitochondrial disease, Other

### Opposition to the procedures

Although most respondents opposed to the techniques select option 5 as their preferred model for managing donor information, seven select option 3, and go on to explain their choice. Most explain that they would prefer it if the techniques were not permitted, but in the event that they are, that option 3 would be appropriate because of the biological significance of the procedure for the child.

#### 8.2.3 Option 4

Respondents who selected option 4, signifying some other arrangement for disclosure of information, sometimes propose a specific variation on options 1 to 3. Their focus also tends to be on a more flexible approach, depending on circumstance and often based on mutual agreement between the parties involved. A few respondents, for instance, again suggest the need for different arrangements according to whether MST or PNT is used, or depending on future understanding of the functions of mtDNA or the medical consequences for the child.

"This one-off tick box does not allow those opposed to these techniques to say how to accurately consider the implications of these techniques. If MST is legalised, such children should not be deprived of knowing their egg donor mother.

If PNT is legalised, such children should be fully informed of the procedure and have full knowledge of the woman who donated the second egg and the man whose sperm was used to create the donor embryo with that second egg."

Individual, Other

### Decision-making agency

While some of these respondents repeat the view found above that the decision on disclosure of their identity should rest with the donor, a number of others suggest that the donor should enjoy some discretion in what other information is shared with the child, or even, in one instance, that the decision should be reversible. A few respondents note the possibility that discretion might encourage more donors to come forward.

A few other respondents suggest that the parents should have greatest agency in decisions about what information is shared with the child. One suggests the need for input from medical professionals too, while others say the parents should hold on to the information until the child is better able to understand it.

A number of respondents repeat views described above that attribute a responsibility to the parents for ensuring the child's appropriate understanding of the procedure and whatever information is disclosed to them, and when. In a variation on this perspective, three respondents

believe that protecting or ensuring the welfare and independence of the child is paramount in considering the disclosure of information.

For many respondents, though, the decision on disclosure of information to the child must be shared. Some say it should be negotiated according to the wishes of the child and the donor, while others suggest that the donor and the parents should be the key agents. As seen above, many more respondents than these hint at these possibilities of joint responsibility in describing varied conditions and circumstances of consent and disclosure.

“It should be the choice of each donor as to what information is provided, along with any other conditions of their donation, and the choice of the parents as to whether to accept these conditions. There is no need for blanket conditions; donors can be matched up with compatible parents.”

Individual, Other

## Variations

Some respondents defer in their explanations to established rules governing the disclosure of information in other donation procedures. A few say it should be the same as for organ, blood or bone marrow donation, while one identifies egg or sperm donation as the appropriate model.

A number of respondents selecting option 4 describe an alternative variation on options 1 to 3. A few respondents suggest that only medical information should be disclosed. One respondent argues that as well sharing medical information from birth, personal information about the donor - falling short of identification - could be positive if disclosed once the child reaches 18. A small number of respondents support option 3, but disagree that it should be age-limited. A few others stress that the information shared need only be minimal. A number also distinguish between MST and PNT in exploring these variations.

“That the status of mt donors depends on whether MST or PNT transfer has been undertaken

(a) With MST, the mt donor is in a similar position to a blood donor. If an individual needed blood to save their life and then subsequently went on to conceive a child, it could be said that the child born was as a result of the life-saving blood donation. But the donation is not an integral part of the child's identity. In the case of MST, the healthy egg has been deliberately extracted for this purpose with the donor knowing it would be used in this way without her nuclear DNA, but with the tiny amount of mt DNA being preserved in a future life...

(b) With PNT, it is felt that the donor's identity is stronger (despite it still only being the same tiny amount of mtDNA that is preserved), because of the deliberate creation of the embryo rather than the donation of an egg, perhaps in a similar way to those who have received heart or face transplants where the recipient may question identity. Here there is a donor embryo made up of two people's DNA and whilst the mt is only connected to the maternal line, this healthy mt from the donor embryo is only available because DNA from two people has come together to make the embryo. If we're thinking in a social context, it is possible that the donor conceived person might also want to know the fourth 'donor' involved in this process.”

Organisation, National Gamete Donation Trust

In addition to these views focused on the range of options presented, some respondents comment more broadly on the information proposals. Three respondents criticise the wording of option 5 as apparently precluding a view on the appropriate information arrangements from those opposed to

the techniques. A few others argue in general that transparency around the procedure is important due to its newness and complexity, or that information provision should go beyond any of these options and include information on other parties involved.

“The institutions making the plan, the society approving it, the parents requesting it, the donors participating must all be transparent to the offspring (and their descendants) who will have a social right to criticize their production. Social responsibility amounts to that kind openness.”

Individual, Other

#### **8.2.4 Option 5**

The majority of the very large number of respondents selecting option 5 revisit in their explanations the arguments against the introduction of the techniques they have made in response to earlier questions. 128 refer directly to another question. An additional 96 respondents selecting this option give no further explanation.

Some of those selecting option 5 go on to echo the criticism made by some selecting option 4, that only one option expressing opposition to the techniques limits the ability of those opposed to propose mitigating arrangements. Also, a small number of respondents criticise the label ‘mitochondria replacement’ as a misrepresentation of the MST and PNT techniques.

#### **8.2.5 Other comments**

There are a few other comments about information management made in responses to question 4b. Eight respondents who select various information disclosure options comment on the importance of donor screening. For most, the screening process, ensuring mitochondrial health and checking other potential problems, reduces the importance of keeping or sharing much information or the identity of the donor. In contrast, one respondent suggests there should be age and health restrictions on potential donors.

Some respondents simply note that retaining donor records would be important, mostly in anticipation of future health problems or in case of some other need to follow-up. A few comments are made about the legal implications of the procedures, one calling for more clarity before information rules are set, another suggesting the law could be altered to fit when the personal effects of the techniques on the child are clearer, and one querying how the donor’s role will be legally recorded through the child’s life.



## Chapter 9 Question 5: regulation of mitochondria replacement

### 9.1 Headline findings

Question 5 asks:

**If the law changed to allow mitochondria replacement to take place in a specialist clinic regulated by the HFEA, how should decisions be made on who can access this treatment?**

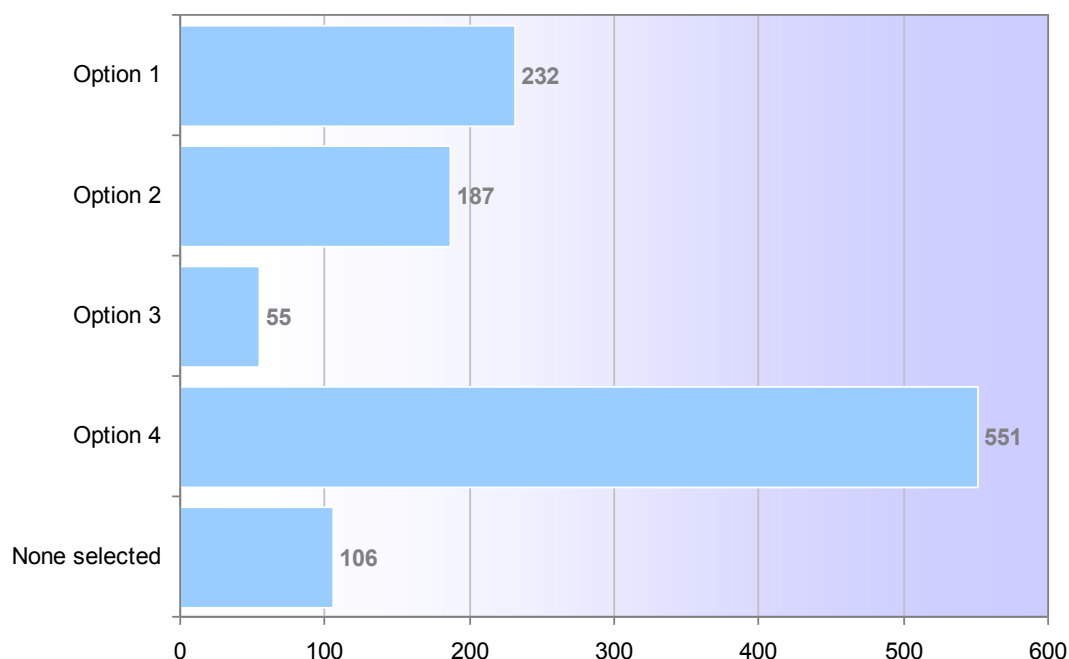
A total of 1,143 respondents answered this question. Respondents were given four options to choose from, and were asked to select one response only:

- 1) Clinics and their patients should decide when mitochondria replacement is appropriate in individual cases.**
- 2) The regulator should decide which mitochondrial diseases are serious enough to require mitochondria replacement and, just for these diseases, permit clinics and patients to decide when it is appropriate in individual cases.**
- 3) The regulator should decide which mitochondrial diseases are serious enough to require mitochondria replacement and also decide, just for these diseases, when it is appropriate in individual cases.**
- 4) I do not think mitochondria replacement should be permitted in treatment at all.**

Respondents were then asked to explain their choice.

A division can be made between options 1-3, which all propose a change in the law to allow mitochondria replacement treatment to take place with differing levels of regulation, and option 4, which states that the law should not be changed at all.

**Figure 9 Options selected in responses to question 5**



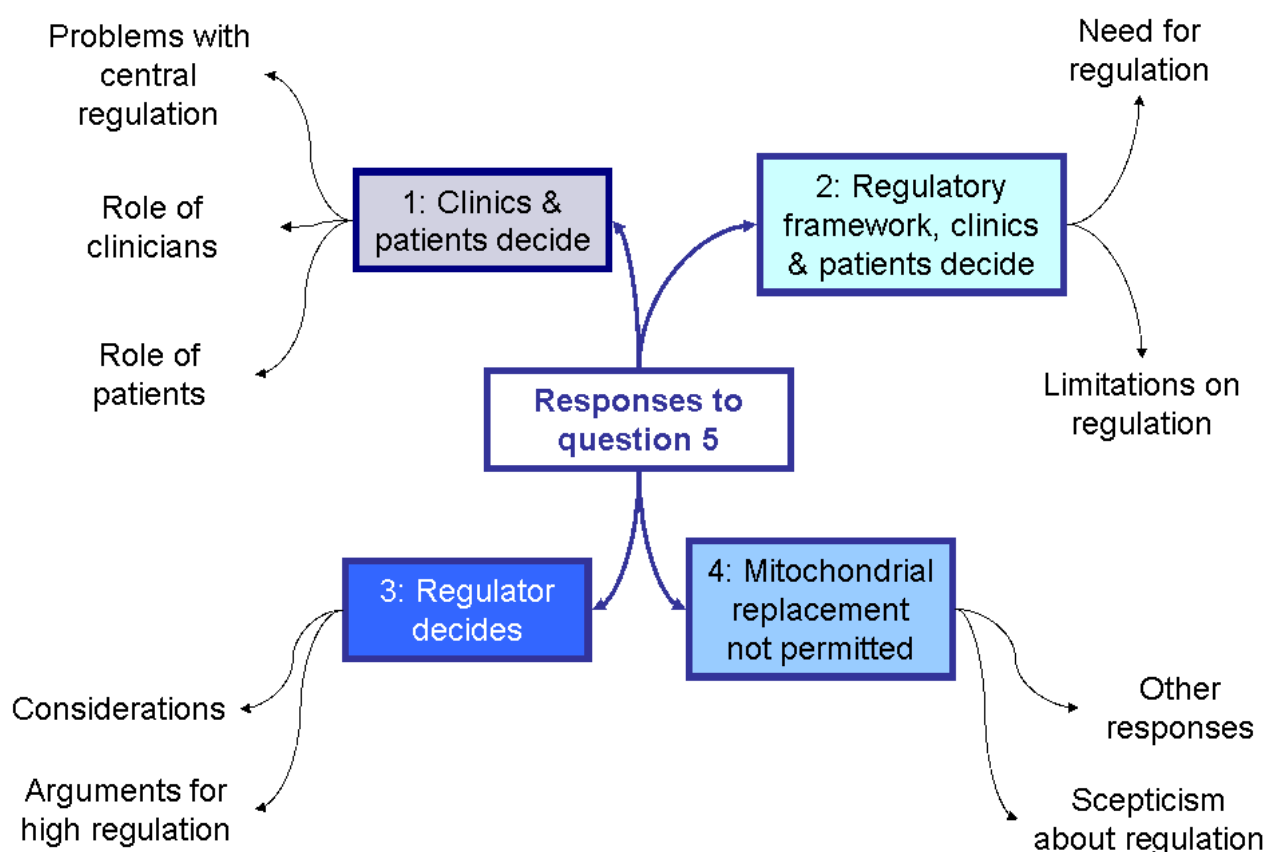
Of the respondents who selected options 1-3, the majority (232) selected option 1 (clinics and patients should decide when mitochondria replacement is appropriate in individual cases). Slightly fewer people (187) selected option 2 (a regulatory framework of diseases deemed serious enough to warrant mitochondria replacement, with clinicians and patients able to make decisions within this framework). Significantly fewer respondents (55) selected option 3, which calls for the highest level of regulation - an external regulatory framework with the regulator also responsible for making individual decisions within this. Just under half of the overall respondents (551) chose option 4, stating that they did not think mitochondria replacement should be permitted at all. The remainder of the respondents did not select an option, most leaving the question blank altogether, and a minority (11) writing general comments. People who left comments but did not select a response commonly said that they did not know, were unsure or had no strong opinion; several offered other suggestions for regulation, for example regulation by Parliament; and others simply reiterated their opposition to mitochondria replacement.

Among respondents who identify themselves as 'personally affected by mitochondrial disease' or 'family member or friend of a person affected by mitochondrial disease' option 1 is by far the most frequently selected option. Among respondents who identify themselves as 'student' or 'researcher' opinions are split between options 1, 2 and 4. Of the very few respondents who indicate that they are a member of staff of an HFEA licensed centre, three select option 1 and three select option 2. Among respondents who identify themselves as 'other' the great majority selected option 4 (see chapter 2 for an overview of respondent types).

There are a few stakeholder organisations in support of each of the options: option 1 is selected by the Association of Clinical Embryologists (ACE) Executive Committee among others; option 2 receives support from the Wellcome Trust, the Muscular Dystrophy Campaign and the Humanist Society Scotland; option 3 is favoured by the National Gamete Donation Trust and others; option 4 is selected by Comment on Reproductive Ethics (CoRE), the Anscombe Bioethics Centre and others.

In the second part of the question, respondents were asked to explain their choice. The reasons for these choices and the arguments surrounding them are explored in detail in this chapter under the following sub-headings:

**Figure 10 Responses to question 5**



## 9.2 Overview of comments

### 9.2.1 Responses to option 1 (clinics and patients to decide)

Option 1 states that ‘Clinics and their patients should decide when mitochondria replacement is appropriate in individual cases’. This option proposes the lowest level of centralised regulation, with decision-making power devolved to the individual clinic level. Of the three options which allow for mitochondria replacement to take place (options 1-3), option 1 proved the most popular with 232 respondents indicating it as their preference. When respondents were asked to explain their choice, typical comments and arguments centred on issues of personalisation and the right to individual choice. Many respondents state their faith in the judgement of clinicians, while others focus on the rights of patients to play a central role in the decision-making process.

#### Problems with centralised regulation

Many respondents raise potential problems with centralised regulation to explain their preference for decision-making at the individual clinic level. The most common concern cited is that a central regulatory board would be rigid, inflexible and generalist, and would not be sensitive to individual circumstances. Many respondents feel that patients and clinicians are better placed to make decisions about the appropriateness of treatment, as they have a deeper understanding of individual circumstances and medical history.

“ACE believes that clinics and their patients should decide when mitochondria replacement is appropriate in individual cases. This allows the expertise of specialist scientists and clinicians to be used to make these decisions rather than relying on a regulator who is unlikely to have the knowledge required to make the decision in an efficient or even appropriate manner.”

Organisation, Association of Clinical Embryologists (ACE) Executive Committee

Another concern respondents mention is that decision-making by a regulatory board would make the process too bureaucratic, expensive, or time-consuming. There are concerns around that centralised regulation would involve onerous levels of red tape and about the effect this would have on patients, particularly the level of distress that may be caused by added bureaucracy and time delays.

“I would feel more comfortable with the decision being taken on a wider scale than just lying in the hands of one regulator.”

Organisation, The Lily Foundation

A number of respondents suggest that the nature of mitochondrial disease means that a ‘list’ of diseases qualifying for mitochondria replacement treatment would not be appropriate. Some point out that mitochondrial disease is extremely varied, and not all variations have been discovered and categorised. Even within established diseases, it is noted, symptoms can vary widely, and can be more or less serious in different cases. Some respondents therefore feel that maintaining a list of qualifying diseases would not be effective or useful, as the following quote illustrates:

“As I understand it, mitochondrial disorders do not all fall into conveniently identifiable syndromes, and the same genetic fault might manifest in different ways. By their very nature, these diseases are inseparable from the distinct individual family stories of patients, and I believe that only they and their doctors can chart the right course.”

Individual, Family member/friend of someone affected by mitochondrial disease

In relation to this point, some respondents raise concerns about the status of new or rare diseases, and suggest that a centralised list of diseases might delay treatment for diseases which had not yet been assessed or categorised by the regulator. One respondent described personal experience of this situation to argue against a regulated list of treatable mitochondrial diseases, which might deny sufferers of unidentified variants the chance of a child free of the disease.

Most of the respondents who chose option 1 feel that central regulation would not be sufficiently effective, efficient or sensitive to individual circumstances, and that clinicians would be better placed to make decisions on a case-by-case basis.

### **The role of clinicians**

Many respondents argue that clinicians have the most familiarity with the individual circumstances and medical history of their patients, and are therefore best placed to make decisions about their treatment. The varied nature of mitochondrial disease, some respondents note, means that it is necessary to take into account the medical history of the individual and their family in establishing the best course of treatment.

Other respondents add that if practitioners are sufficiently well-trained and qualified there should be no need for external regulation.

### **The role of patients**

Many respondents feel that it would be important for the patients themselves to have a central role in the decision-making process. The majority of respondents who selected option 1 feel that a joint decision, made between patients and their doctors, would be the most appropriate. Many argue that individual patients know their own circumstances better than anyone else, and are therefore best placed to make decisions about what is right for themselves and their families.

An argument put forward by several respondents is that it is impossible to set an objective measure on what constitutes a serious disease. The experience of disease, it is argued, is subjective and personal – disease may be experienced as ‘severe’ to different degrees depending on the circumstances of the individual. The following personal vignette illustrates this point:

“Only the patient can identify the severity of their symptoms... I have a disfiguring disease in my family that has led three members to avoid having children. Some might say the condition wouldn't warrant them refusing to have children with a 50/50 chance of contracting the condition, but they have lived it, they have had the operations to attempt to correct it, they've suffered the bullying in school and feeling different as a child. Only the parents can say how severe their condition is to them.”

Individual, Student

It is therefore problematic, some respondents argue, to set an external, objective regulatory standard of what constitutes sufficient severity for treatment, and instead necessary to maintain a more flexible system which allows for individual circumstances.

Similarly, some respondents argue that treatment should be widely available and not restricted to patients with the most serious illnesses only. They argue that everybody has the right to a life free from disease, and that it should not be left to a regulatory board to decide which diseases are serious enough to qualify for treatment. A number of respondents invoke an equality principle, arguing that if the treatment were made available to some patients it should be available to all.

Four respondents who chose option 1 cited personal experience of mitochondrial disease, stating that either they, or a family member, had suffered from the disease. Of these respondents, two argue that all mitochondrial disease was serious for those affected, and they do not believe that treatment should be restricted only to diseases deemed to be most severe. The other two respondents explain their choice on the grounds that the disease of which they have experience is rare and may not be covered by regulatory guidelines.

### **9.2.2 Responses to option 2 (regulatory framework; clinics and patients decide)**

Option 2 states that: ‘The regulator should decide which mitochondrial diseases are serious enough to require mitochondria replacement and, just for these diseases, permit clinics and patients to decide when it is appropriate in individual cases.’ Slightly fewer respondents (187) selected this option than option 1. Most respondents who chose option 2 emphasise that they believe clinicians and patients should have an important role in the decision-making process, but also feel that there is a need for some level of external regulatory framework. Some respondents specify that they think more regulatory oversight will be needed when the techniques are first used.

#### **The need for regulation**

A number of arguments are made for the need for a level of central regulation. Many of these arguments are based on the need to prevent abuse or overuse of mitochondria replacement treatment, and ensure that it is used only when medically appropriate and necessary. The ‘slippery slope’ argument, familiar from previous questions, resurfaces in response to this question. Some respondents argue that allowing mitochondria replacement could potentially open the gates for the rise of eugenics or ‘designer babies’, and that regulation is necessary to ensure that the treatment

is used responsibly and appropriately. Others suggest that regulation is necessary to guard against profiteering on the part of private clinics, who might be inclined to offer the treatment when not strictly necessary. Some respondents feel that the treatment, particularly in the early stages, should be used to treat those most severely affected by mitochondrial disease only, and that regulation is necessary to limit the application of the treatment:

“The technique should be regulated so it is only permitted for certain serious diseases. This would avoid it being labeled [sic] the 'slippery start of the slope' and also protect families from inappropriate/unnecessary treatment if there is no good clinical benefit to outweigh the risks.”

Individual, Other

Another set of arguments is based on the need for centralisation to ensure fairness and equity in the provision of treatment. Some respondents feel that a central regulator is the fairest way of distributing treatment, and making sure all applications for treatment are judged according to the same criteria. Some respondents raise concerns about the possibility of a ‘postcode lottery’, and argue that central regulation is necessary to ensure fairness.

A small number of respondents argue for central arbitration on the ethical questions raised by mitochondria replacement. They suggest that the complexity of the ethical questions involved means that different individuals are likely to have very different views on to what extent and when treatment is appropriate. Central regulation is therefore necessary, it is suggested, to mitigate against the subjectivity of individuals, and to ensure the same ethical standards, for example definitions of the rights and moral status of unborn children, are applied in all cases.

Several respondents draw a parallel between the regulation of mitochondria replacement treatment and Pre-implantation Genetic Diagnosis (PGD). The British Fertility Society calls for regulation of mitochondria replacement treatment to follow the model of regulation of PGD, with a regulator responsible for deciding which diseases are serious enough to warrant the treatment:

“The BFS is of the opinion that the regulator should decide which mitochondrial diseases are serious enough to require mitochondria replacement in line with current approvals for Pre-implantation Genetic Diagnosis, and permit clinics and patients to decide when it is appropriate to treat for these disorders in individual cases.”

Organisation, British Fertility Society

The Association of Medical Research Charities (AMRC) and Genetic Alliance UK echo the views of the BFS on the need for centralised regulation on which diseases should receive treatment, and also offer some suggestions for how these diseases should be identified:

“In reaching a decision on the severity of mitochondrial diseases we believe the regulator should follow the principles used in the regulation of PGD, such as peer review, use of an experienced standing committee, and of stakeholder input.”

Organisation, AMRC and Genetic Alliance UK

## Limitations on regulation

A number of issues and suggestions are raised regarding the role of the regulator, and the limitations which should be placed on centralised regulation. Many respondents emphasise that while they feel that some centralised regulation is necessary, they do not believe that a regulatory board should be responsible for making individual decisions (as proposed in option 3). The reasons for this tend to be similar to those cited in option 1. These respondents argue that it would be too bureaucratic, impersonal and time-consuming for the regulator to be involved in decisions

about individual cases. As in option 1, many respondents state that clinicians are best placed to make decisions in individual cases, and that the individual patient should have an important role in the decision-making process. It is frequently emphasised that clinics and patients should be given the freedom to make decisions about treatment within the parameters set by the regulator:

“It seems unnecessarily bureaucratic and intrusive for a regulator to review individual cases but equally some central, disinterested guidance in what diseases should be treated seems sensible.”

Individual, Family member/friend of someone affected by mitochondrial disease

A number of respondents feel that higher levels of regulation would be necessary in the early stages due to the uncharted nature of the treatment, but suggest that central regulation could be relaxed once the procedures were more established if they proved to be safe and effective.

Several respondents call attention to the need to keep regulation up to date as new diseases are discovered and new scientific developments occur. These respondents argue that the regulatory body should also be subject to monitoring and review to ensure that it keeps step with evolving knowledge of mitochondrial disease.

### 9.2.3 Responses to option 3 (regulator decides)

Option 3 proposes that: ‘The regulator should decide which mitochondrial diseases are serious enough to require mitochondria replacement and also decide, just for these diseases, when it is appropriate in individual cases’. This option proposes the highest level of centralised regulation, suggesting that an external regulator should be responsible not only for providing a regulatory framework, but also for adjudicating in individual cases. This was the least popular option, with significantly fewer (55) respondents choosing it than options 1, 2 or 4. Of the respondents who did choose option 3, many said that they did not think that the law should be changed to allow mitochondria replacement treatment, but that if it were they would choose option 3, as it offered the most intensive regulation of the treatment.

#### Arguments for high regulation

A number of arguments for high levels of regulation are put forward by respondents to this question. Many of these are similar to those addressed in option 2. As in option 2, a number of respondents argue that because of the nature of the treatment it should only be offered in the most serious cases, and that it is necessary for an external body to determine what these cases are. Many respondents report concern about the treatment being overused, and argue that central regulation is necessary to ensure that the treatment is used only when medically necessary and appropriate. As in option 2, many respondents raise concerns about private clinics being driven by a profit motive to offer the treatment in inappropriate cases, and argue that high levels of regulation are necessary to guard against this. The issue of bias or partisanship on the part of clinicians is also raised. Some people suggested that individual doctors might be biased by a personal relationship with a patient, or pressured by patients and their families, into offering treatment which was not appropriate:

“I think this area needs strict regulation to maintain public confidence, and that this extends to individual cases. I am in favour of the use of the technique and would not like to see it potentially mis-used due to pressure from patients or clinics.”

Individual, Other

It is therefore necessary, some respondents argue, for decisions about individual cases to take place at a centralised level, to ensure impartiality and guard against partisanship.

As in option 2, several respondents suggest that high levels of centralised regulation are necessary to safeguard equity and fairness. Concerns about a ‘post code lottery’ resurfaced, with a number of respondents expressing unease about differential access to treatment. Respondents suggested frequently that a centralised decision-making body would be a fairer and more effective mechanism for allocating treatment.

## Considerations

Some respondents add further comments and suggestions about the role of the regulator. Several suggest a flexible model of regulation in which treatment would be highly restricted and monitored at first, but could be relaxed over time, with more decision-making power devolved to clinicians, if the treatment proved to be safe and effective.

A number of respondents mention the need for the regulator to conduct long-term follow-up on the effects of the treatment. Some respondents cite the need for long-term review of the medical consequences of the treatment, suggesting that changes to the germ line could create unpredicted effects on future generations, which would require careful monitoring. Others cite the need for follow-up research to monitor the social and psychological consequences of the treatment for the patients and their families. The Project Group of Assisted Reproduction (PROGAR) offers some suggestions for how this follow-up research should be carried out:

“Regulation and associated research must, in our view, include central attention to psycho-social as well as medical, scientific and developmental psychology aspects. Research must include social science qualitative research, including longitudinal, to capture nuance, ambiguity and meaning to the parties directly concerned.”

Organisation, PROGAR

The role of the regulator, it is suggested, is not only to make decisions about which diseases qualify for treatment, but also to research the broader and more long-term implications of mitochondria replacement.

### 9.2.4 Responses to option 4 (mitochondria replacement should not be permitted)

Option 4 states: ‘I do not think mitochondria replacement should be permitted in treatment at all’. It differs from options 1-3, allowing respondents to register their opposition to mitochondria replacement, particularly if this meant that the other options are not relevant to them. About half of those responding to the question (551) selected option 4. Respondents tend to reiterate arguments made in response to earlier questions, particularly question 1. Many simply direct the reader to refer to their previous responses; others reiterate or elaborate on their opposition to mitochondria replacement treatment. This section will discuss responses directly related to regulation only – wider arguments against mitochondria replacement can be found in other chapters.

#### Scepticism about regulation

Many respondents who selected option 4 are sceptical about either the relevance or the effectiveness of regulation. A substantial proportion of respondents (38) state that no level of regulation could make mitochondria replacement acceptable because it is fundamentally unethical:

“I do not think mitochondria replacement should be permitted in treatment at all because regulating or licensing unethical action does not make it right.”

Individual, Other

These respondents often go on to reiterate ethical arguments against mitochondria treatment, or direct the reader to refer to their previous answers.



Others respondents raise concerns about the effectiveness of regulation, or state their scepticism that strict regulation would be maintained in the long term. Some specifically cite their lack of trust in the HFEA. There is a concern that regulation tends to relax over time, and some respondents feel that even if treatment were strictly regulated at first, regulation would gradually become less stringent and treatment more widely available. Some respondents referred to historical precedents of regulations which have become less stringent over time. Several used the regulation of abortion as a comparative example, as the following quote illustrates:

“Political safeguards are as reliable as chocolate teapots. When abortion was first legalised we were told that strong safeguards would be put in place in order to eliminate abuse. These so-called safeguards were watered down, or totally ignored, as the years went by. What we now have, in effect, is abortion on demand. The same would happen with the procedures under discussion. Any safeguards would, over the years, be watered down and then ultimately ignored.”

Individual, Student

Most respondents who selected option 4 feel that regulation would be inappropriate or ineffective and therefore feel that the law should not be changed to allow mitochondria replacement at all.

### **Other responses**

A small number of respondents who selected option 4 on the grounds that they did not want the law to be changed also indicate what kind of regulation they would choose if the law were to change. Of these respondents the majority say that they would choose option 3, on the grounds that this proposes the strictest level of centralised regulation. Four respondents say that they would choose option 2.

A number of respondents suggest that if the law were to be changed, regulation should take place at a parliamentary level. Many of these respondents cited a lack of trust in other regulatory safeguards, and raised concerns about the slackening of regulation and expanding use of techniques over time. The following quote illustrates this perspective:

“I have no confidence in regulatory bodies, as their recent history has been lamentable. Should such techniques be approved at all, I think their [sic] should be a clear set of laws limiting them, saying both what is allowed and what is not, debated and passed in parliament, with no room for ambiguity, interpretation or other erosion. The regulator's role should be to enforce the law, not interpret or soften it, or campaign for its creative reinterpretation etc.”

Individual, Student

Respondents who advocate for parliamentary regulation tend to feel that regulation enshrined in law and overseen by Parliament would be more stringent and effective, and therefore preferable to other forms of regulation.

## Chapter 10      Question 6: should the law be changed?

---

### 10.1      **Headline findings**

Question 6 asks:

**In Question 1, we asked for your views on the mitochondria replacement techniques MST and PNT. Please could you now tell us if you think the law should be changed to allow (one or both of) these techniques to be made available to people who are at risk of passing on mitochondrial disease to their child?**

1,055 people responded to this question.

The overall views of respondents in response to this question broadly reflect the views about acceptability expressed in response to question 1. Overall, 558 respondents commenting on question 6 oppose a change of law. A further 316 of respondents indicate that they support a change in the law, and 82 say that they would if their caveats are addressed. A few respondents think the law should only change for one of the proposed techniques. Only 7 respondents do not express an explicit opinion either way on whether or not the law should change, instead discussing related issues and considerations.

That the numbers reported above are not completely equal to those of respondents arguing in favour or against the techniques in their responses to question 1 is mainly a consequence of the fact that not all respondents answered all consultation questions. There are fewer than a handful of respondents each way whose comments about changing the law (question 6) are seemingly conflicting with their comments about the acceptability of mitochondria replacement techniques (question 1). Additionally, six respondents who say in response to question 1 that the techniques are acceptable if certain conditions are met subsequently argue against a change in the law when responding to question 6.

Respondents who indicate that they are personally affected by mitochondrial disease are overwhelmingly in favour of a change in the law. The same is true for respondents who indicate that they are a friend or relative of someone affected by mitochondrial disease. All in all around 95 respondents from these categories make comments in favour of a change in the law, with a dozen saying they are in favour subject to caveats.

Of respondents who indicate they have personal experience with gamete donation or donor conception, 13 say they are in favour of changing the law and three state the opposite.

Organisations in favour of changing the law include the Wellcome Trust, the Muscular Dystrophy Campaign and the Humanist Society Scotland. The British Medical Association, the Academy of Medical Sciences, the Association of Medical Research Charities and the Genetic Alliance UK, and the British Fertility Society support a change in the law in principle, but make caveats. Human Genetics Alert, the ProLife Alliance and others are against a change in the law.

## Non-questionnaire responses

A number of the 503 non-questionnaire responses contain comments about changing the law. Many of these comments are made in responses that follow a similar structure and make a range of similarly worded points. More than 200 emails and letters include a statement against a change of the law. In many cases these comments are accompanied by references to legislation in other (EU) countries, with respondents expressing concern that the UK would be the first country to cross a boundary and allow techniques that are illegal elsewhere. There are a few letters and emails with comments endorsing a change of the law.

Those respondents opposing a change in law tend, as with question 1, to focus largely on ethical concerns such as the use of embryos, and interference with the natural or spiritual aspect of reproduction.

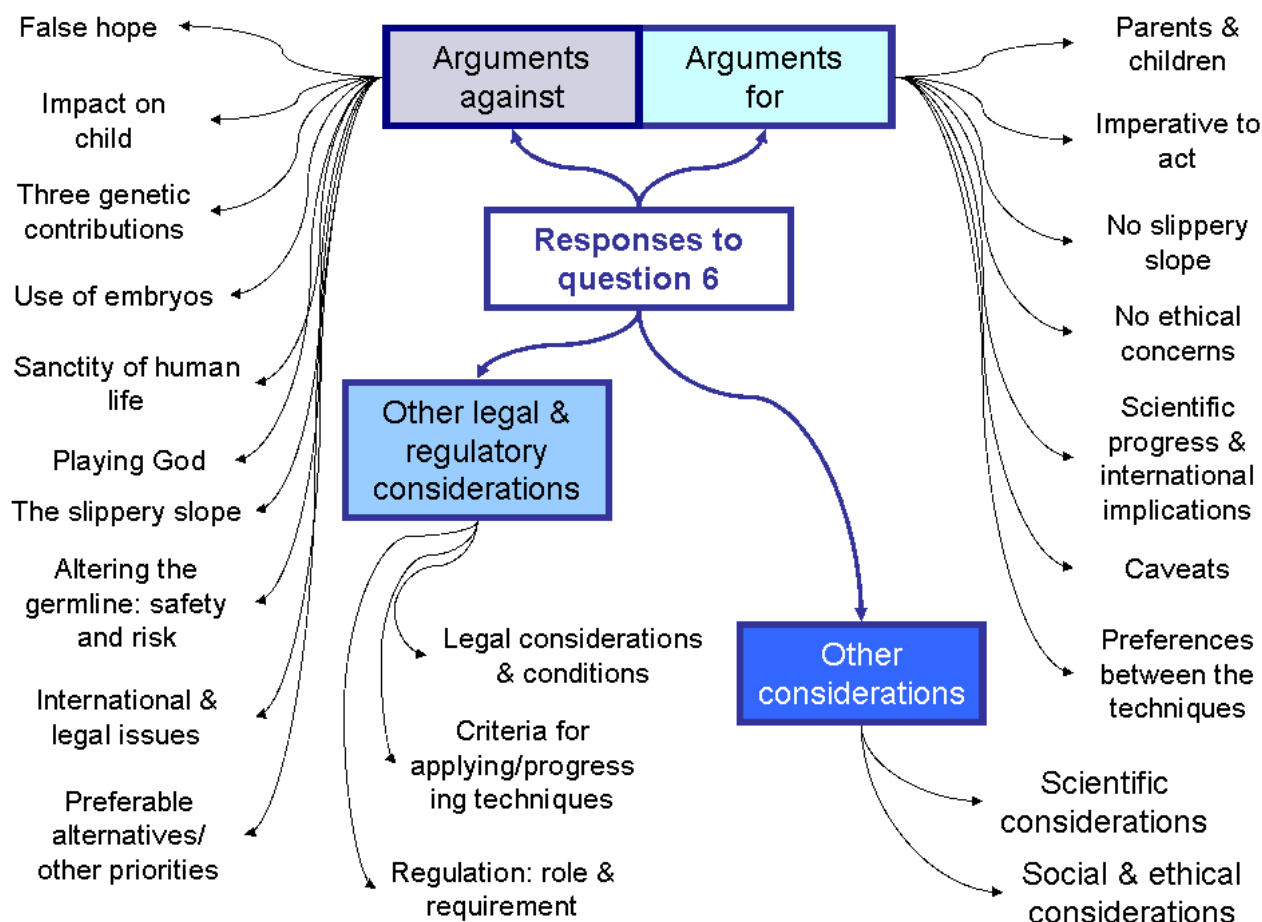
Several respondents mention a preference for other alternative approaches to addressing mitochondrial disease; others express concerns about unknown consequences. There are also concerns expressed about the slippery slope, as well as references to these techniques not currently being legal in other countries.

Those respondents supporting a change in law tend to focus primarily on the benefits the treatments could provide, particularly disease avoidance and the opportunity for parents to have a healthy child, with several discussing the impacts of mitochondrial disease on sufferers and their families. Others talk about the ethical imperative to intervene, again as in previous questions.

Where a preference is expressed for one technique in particular, this again tends to be for MST over PNT, as respondents note that this technique uses eggs rather than embryos. In total, 21 respondents state that the law should be changed to permit MST, and a further 10 agree with a caveat, compared to just one arguing for the law to change to permit PNT. Meanwhile 22 respondents argue that the law should not change to permit PNT, while none make the same case against MST.

These arguments and others raised by respondents to question 6 are explored in more detail under the subheadings reviewed below:

**Figure 11 Responses to question 6**



## 10.2 Overview of comments

### 10.2.1 Arguments against a change in law

A total of 244 respondents say that they oppose a change in law to allow one or both of the two techniques but do not explain their opposition. A number of respondents refer back to supporting arguments made in response to previous questions and some give a fuller explanation in of their opposition to a change in law in response to question 6, as summarised here. Some of these respondents make it clear that they have sympathy for those affected by mitochondrial disease but still oppose a change in law for many of the reasons outlined below.

#### Use of embryos, sanctity of human life, playing God, overall ethical issues

As with question 1, the most commonly cited argument against a change in law is that the creation and destruction of human embryos involved in these techniques (often specifically in PNT) is unethical (75). A number of comments relate to this point. These include points about the sanctity or dignity of human life being jeopardised by these techniques, as well as concerns that these techniques interfere with natural reproductive processes or would involve humans playing God.

“I object to the techniques themselves, since they involve the discarding of embryos. Human life should be respected and yet these techniques are promoting the destruction of life.”

Individual, Other

Other respondents say there are simply too many ethical or moral concerns, with a small number of comments that the end does not justify the means.

“The very fact that there are strong ethical arguments against these procedures and a large lobby against them should make the government very cautious indeed about permitting research to advance in this direction.”

Individual, Other

### **Preferable alternatives and other priorities**

Several respondents, many using similar wording, state that there are other preferable alternatives for the treatment or cure of mitochondrial disease, which should be pursued instead of these techniques (63).

“Other methods (such as repairing faulty mitochondria) are already being developed by scientists and should be examined further instead of considering PNT and MST.”

Individual, Other

Other respondents comment that people do not have an automatic right to a healthy and/or genetically related child; in relation to this, a number of other preferred options for at-risk parents are cited, including adoption, a decision not to conceive, counselling or support, and use of donor eggs.

A few respondents suggest (and these suggestions tend to be general rather than specific) that there are more pressing issues that should receive focus and/or funding over and above the progression of these kinds of techniques.

### **Altering the germ line: safety and risk**

The unknown future risks, impacts or unintended consequences of these techniques are also cited as arguments against their legalisation (57). Many of the comments made are general, for example mentioning ‘potential problems’, ‘complications’, ‘serious risks’, ‘impacts on future generations’ and so on; they also focus on both individual (e.g. health risks) and overall societal risks or impacts.

“As the risks are unknown & the potential for harm in various parameters (social etc) is high, the law should not be changed.”

Individual, Other

Some respondents say explicitly that the costs or risks of these techniques would outweigh the benefits; others talk about the impact of altering mitochondrial DNA on the germ line or genetic lineage or say that altering DNA is simply not acceptable, with some offering the view that these techniques involve cloning or hybridisation as a supporting argument for not changing the law.

### **International and legal issues**

A number of respondents, many using similar wording, note that outside the UK these techniques are not legal or can incur prison sentences. The UK would thus be the first country to cross this particular ethical boundary. Others state that the legalisation of these techniques would contravene international (for example EU or UN) law. A small number of respondents add that the UK should not be allowed to make a decision which could have a global impact.

“No, the law should not be changed. If it were, the UK would become the only country in the world to legalise such procedures and this is one area where there seems to be no benefit in being out on a limb.”

Individual, Other

A few respondents go further in saying that they think the law should be made stricter, for example by restricting the application of existing techniques involving embryos or to further discourage research into or development of any potential new techniques.

### **The slippery slope**

As in their responses to previous questions, respondents raise both general and specific concerns about the introduction of these techniques. Some see them as the start of a slippery slope with negative consequences at its end. Others mention designer babies or commodification of the human, eugenics, cloning, and the normalisation of genetic modification as specific concerns.

“If we permit these procedures which manipulate genetic information, it is possible that future genetic ‘treatments’ for cosmetic reasons will become acceptable.”

Individual, Other

### **Three genetic contributions, impact on child, false hope**

Again, as with previous questions, respondents raise concerns about these techniques involving genetic material from three people. Many of these are related to worries about interfering with natural reproductive processes or playing God by creating ‘three parent families’; others mention concern for the child’s sense of identity, and for their general or psychological wellbeing, as well as the potential for valuable individuals to be lost as a result of these techniques.

“We do not know what the psychological effects will be on a child when they learn they have three or four parents...”

...The sanctity of human life is upheld throughout the Bible. It is very clear that God intends human beings to have two parents – a mother and a father.”

Individual, Other

Some respondents question whether the techniques would actually work, suggesting that they would present ‘false hope’ to parents at risk of passing on mitochondrial disease, while others comment that these techniques are not a cure or will not necessarily eradicate mitochondrial disease.

### **10.2.2 Arguments in favour of a change in law**

A total of 170 respondents say that they would like the law to change to allow one or both of the two techniques without explaining their view. A few of respondents refer back to supporting arguments in response to previous questions and some respondents give a fuller explanation of their support in their response to question 3, as summarised here.

#### **Parents and children**

As with question 1, the most frequent argument in favour of legalising these techniques cites the importance of the health of the child, with the avoidance of mitochondrial disease being passed on, or even its eradication, being seen as a positive step.

Some respondents talk about the impact of mitochondrial disease not only on the sufferers themselves, but also on the parents and families of sufferers, several making reference to personal experience. A number of related comments refer to the benefits of these techniques for potential parents and families overall, for example through offering parents an opportunity to have a child without the worry of mitochondrial disease being passed on. A few respondents state that they think parents have a right to a healthy and/or genetically related child, which these techniques would enable.

"I believe mitochondria replacement to be the human right of the unborn children of women whose damaged mitochondria are likely to manifest in their serious ill health. The progressive and often terminal course of the conditions linked to these mitochondrial abnormalities have a devastating impact on the person and those who love and care for them.

I have watched my oldest friend deteriorate from a fun loving, happy child and teenager to an often angry, frightened and confused 30 year old who experiences drop-seizures daily and is now entirely dependent on her parents. The multi-systemic difficulties associated with mitochondrial conditions are often of late onset and families embark on a harrowing journey where they must try to adapt to each new stage of the disease before the next progression..."

Individual, Family member/friend of someone affected by mitochondrial disease

### **Ethical imperative to act, not a slippery slope, no concerns**

The imperative to intervene if the ability to do so exists is again given as a supporting argument for allowing these techniques.

"Both of these techniques should be made available to all who have need for them. It is unethical to have the technology and not to use it."

Individual, Student, Researcher

Some respondents state that they think the techniques are safe, have an acceptable level of risk, or that the benefits outweigh the risks. A few state explicitly that they have no ethical concerns or, more specifically, no concerns about these techniques representing the start of slippery slope with a negative end. In support of these statements, a small number of respondents point out that these techniques are different to those required for designer embryos or cloning (for example because nuclear DNA is not altered) or that regulation should prevent this from setting the precedent for other techniques they might find unacceptable.

### **Scientific progress and international implications**

A few respondents talk about the development of these techniques being a positive or important scientific advance or natural progress.

"These procedures are hope. They would be a dream come true. They signify years of research & the new ability to overcome genetic disease with amazing technology."

Individual, Other

Related to this are comments about the need to change the law quickly to enable the benefits of these techniques to be felt as soon as possible, and the potential for the UK to be a leader in this new area of science. A small number of respondents talk about the international aspects of these techniques, for example the suggestion that other countries would introduce these techniques if the UK did not and that UK patients or expertise may end up overseas.

### **Caveats for changing the law**

A number of respondents expressing support for a change of law either for both techniques or for MST do so only under the condition that certain caveats are met. These caveats tend to focus on specific criteria for the application of the techniques, the need for regulation, and specific legal considerations or conditions – these are covered in section 10.2.3 below. Other caveats include the need for further research, trials or evidence should these techniques progress, and the expression of a preference for MST over PNT should both techniques be found to be equally

viable. Indeed, the most common caveat for those supporting a change in law for MST only is that PNT be explicitly disallowed.

“Yes both techniques should be available initially, until such data is available to either favour one technique or establish that neither is a worthwhile avenue of treatment. This may necessitate all treatments being part of a national surveillance/tracking project to collect this data as part of a trial period.”

Individual, Researcher

### Preferences between the techniques

As discussed above, where there is a preference for one technique to be legalised over the other, the preference falls with MST over PNT. The arguments in favour of MST over PNT tend to focus on the respondent having fewer ethical concerns about MST because of the use made of embryos in PNT.

“I am in favour of MST because what I have read leads me to believe that the underlying genetic makeup or essence of a person would not be changed i.e. they would be the same person they would always have been except for the sole exception that their cells would work properly. Thus they would have an improved quality of life (as may their families) and no real identify confusion. The procedure would be equivalent to a transplant.

At the moment I am uncomfortable with PNT because two embryos are created meaning two lives could be viewed to have started yet one of them is given no chance to live and is sacrificed for the other. While others would argue an embryo is not really a life until it is several weeks old (the thinking that makes aborting permissible) I have never been comfortable with it.”

Individual, Other

### 10.2.3 Other legal and regulatory considerations

#### Other legal considerations and conditions

The Human Fertilisation and Embryology Act is mentioned a number of times in responses to this question. These response include remarks on individual respondents’ understanding of what the Act does or does not provide for in relation to this particular issue; for example that these kinds of techniques were banned under the original Act, that the Act is ambiguous, or that it does indeed provide for the development of such techniques.

Some respondents have other comments or queries about the law in relation to this topic, or the legal system more generally. These include: whether a change in law is needed; the difficulty of creating a law with no loopholes; the relationship to Scottish law; and the need for the law to protect human rights or human embryos.

Others provide suggestions for specific details, should the law be changed. These include: suggestions that the law should show a preference for a particular technique (e.g. MST in the first instance) or that the law should not specify particular techniques; comments on which diseases or types of diseases should be written into law; a comment on specifying the origin of donor DNA by law; comments on the need for careful drafting and specification of boundaries (for example specify the techniques are to be used for the treatment of mitochondrial disease only) to prevent abuse; the need for a central database of donor information; and suggestions for other changes in law in related areas of fertility and embryology.

A few respondents suggest specific legal conditions, including: only allow PNT in specific circumstances, only allow testing or trials in the first instance, allow one technique only (either,



depending on the evidence). Others say that further exploration is needed, either generally or of PNT specifically, before any change in the law is considered. These conditions or requirements are often given as caveats to support for a change in the law.

Other comments on the legal system include various comparisons with other procedures or donation types, the suggestion that the law could be re-visited after a set period if needed, and a couple of comments stressing that the law does not have a place in these decisions ahead of patient or professional choice.

### **Criteria for applying or progressing techniques**

When it comes to deciding which technique/s should be progressed to clinical use and made available to potential parents, respondents suggest a number of criteria for deciding whether to progress a specific technique, to help choose between the two techniques or to help with a decision about which cases they should be used for. The most commonly mentioned criterion is safety, closely followed by the efficacy or efficiency of the technique. Other criteria include medical evidence or advice, cost or value, patient need or appropriateness, as well as a number of other suggestions.

“PNT raises more problems for me, considering that it involves the destruction of potentially viable embryos. However, on the assumption that this would be performed at a very early stage, it might well be that the benefits are worth the worry if it becomes evident that PNT is safer and/or dramatically cheaper than MST.”

Individual, Student

Several respondents talk about criteria for who decides rather than on what basis the decision is made. For example: it should be down to the parents or the parents and clinician together to decide which technique if any to use; the decision should be down to ‘scientists’; to the regulator, or to parliament. A small number of respondents suggest that there should be no criteria or that the technique should be open to anyone who wants it.

In relation to the point about availability, there is also a small number of comments about the need for equitable provision or ease of access should these techniques become publicly available. A few respondents comment on funding and between them offer opposite arguments: that the NHS should cover these techniques, or that it should not and they should be funded privately by individuals.

### **Regulation: role and requirement**

A small number of respondents note a distinction between regulation and ethical acceptability, stating that the former does not entail the latter. One respondent notes a general lack of trust in the regulators. Aside from these comments, most of those discussing regulation in response to question 6 focus on two areas: the need for regulation and the specific roles of the regulator.

Comments on the need for regulation tend to be at a general level, i.e. regulation is needed should these techniques become legal; several respondents here use words such as ‘suitable’, ‘strict’, ‘close’ and ‘careful’ to stress the level of regulation which they feel would be required. Suggestions of specific roles for the regulator include the following: enabling provision to high-risk patients; monitoring safety; setting boundaries, producing guidelines and preventing abuse such as non-medical usage; assessing and licensing clinics; and maintaining a register of applicable diseases.

“As I stated, all these techniques have come about as a result of our ability to improve and advance ourselves. An old saying about ‘once the genie is out of the bottle...’ comes to mind. In that light I feel all of these options should be legalised and available but again under strict control from the regulator.”

Individual, Other

#### 10.2.4 Other considerations

##### Scientific considerations

Aside from the comments about scientific progress and further research outlined in 9.2.2 above, there are relatively few comments on the scientific aspects of MST and PNT compared to responses to other questions, perhaps because respondents tend to focus on the wider social and ethical arguments for or against progressing these techniques. A few respondents mention mitochondrial function and other procedures such as IVF; others talk about progress in either a cautious (for example, that there is a lack of understanding, proceed with caution) or a positive (for example expand this type of research to other diseases) light, with a small number suggesting that science should prevail or take precedence in decision making.

##### Social and ethical considerations

The number of respondents to question 6 commenting on social and ethical considerations in a more neutral manner tends to be relatively low, with most using ethical and social arguments to support their views about whether or not the law should be changed. Those respondents who do mention social and ethical issues in a more neutral manner tend to reflect on issues already covered in response to other questions. These include reflections on the rights of embryos or eggs, availability of donors, follow-up studies or monitoring, information provision and support to parents and donors, and consideration of the number of people who would benefit from these treatments.

## Chapter 11      Question 7: further considerations

---

### 11.1      **Headline findings**

A total of 883 respondents answered question 7 which asks:

**Q7: Are there any other considerations you think decision makers should take into account when deciding whether or not to permit mitochondria replacement?**

Respondents answering question 7 tend to use their response as an opportunity to do one or more of the following: reiterate arguments for or against taking forward the two techniques; discuss additional considerations they would like decision makers to take into account; or consider the wider context and overall decision-making process.

Arguments for and against the further progression of MST and/or PNT largely echo those expressed previously in response to other questions, with arguments against tending to concentrate on crossing boundaries or the creation and destruction of embryos, and arguments in favour focusing on the benefits to those at risk of passing on mitochondrial disease.

A number of the additional considerations raised by respondents in response to question 7 are also familiar from responses to previous questions, for example those focusing on social or ethical dilemmas and implications. However, there are some specific areas that receive more attention here. These include more detailed comments about the practicalities of taking forward these techniques, for example questions of regulation and criteria for application, as well as other comments about the nature of science and the need for further research and monitoring.

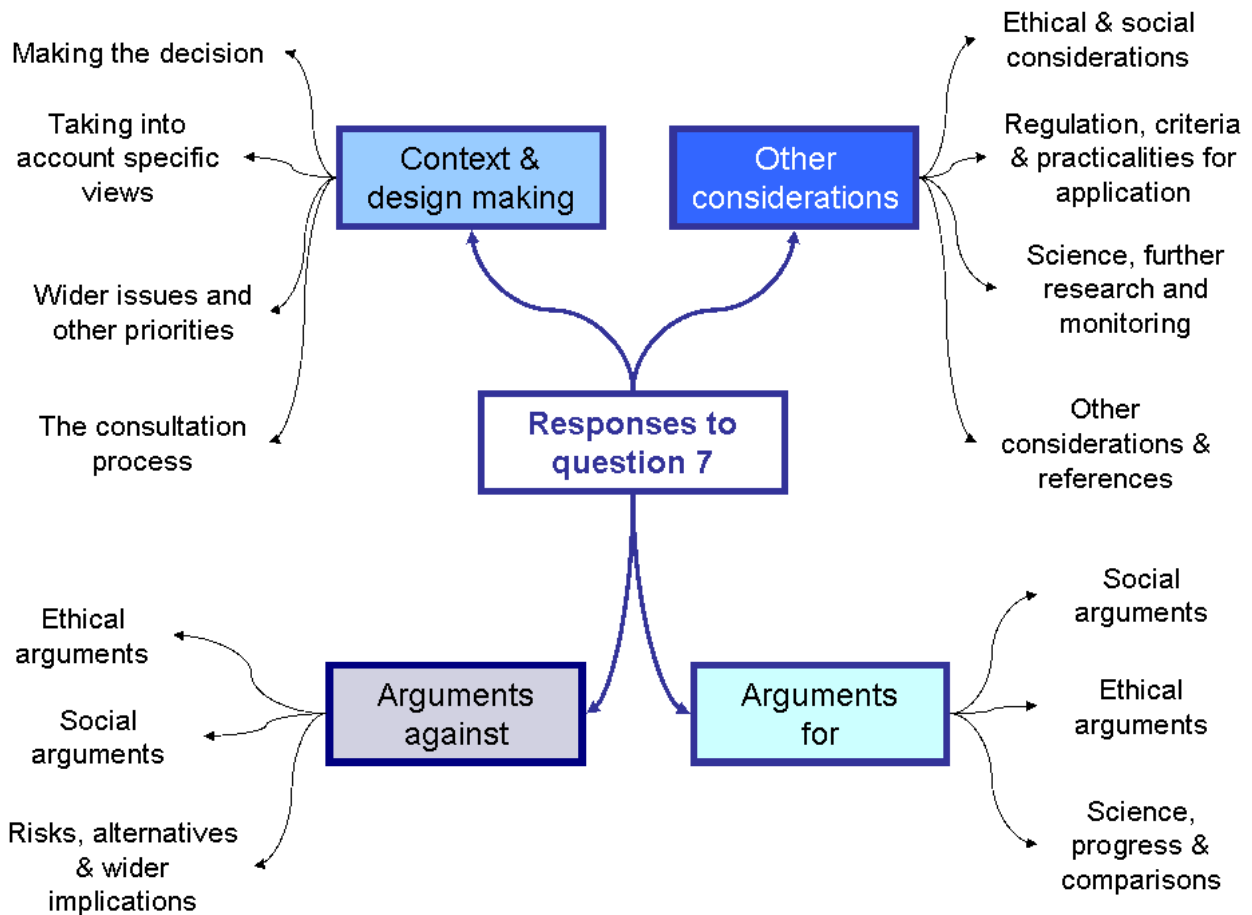
Those respondents who talk about the wider context or the decision making process in response to question 7 cover a range of issues. Some talk about the nature of the decision and the basis on which it should be made, for example with ethics at the centre, or with science at the centre. Others point out that there are wider issues that would benefit from discussion, or other priorities that require focus. A number of respondents ask that decision makers specifically consider the views of certain groups, or do not give undue weight to others. There are also some comments about the consultation itself, both positive and negative.

#### **Non-questionnaire responses**

In some of the 503 non-questionnaire responses there is mention of other treatments of mitochondrial disease, which respondents say are emerging. Overwhelmingly these comments are part of a range of similarly worded points which can be found in around 300 emails and letters. The point respondents make about other treatments is that (research into) these should be prioritised over mitochondria replacement. No specific reference is made as to what these other treatments are, or where they are being developed.

Responses to question 7 are explored in more detail in this chapter under the subheadings summarised below:

**Figure 12 Responses to question 7**



## 11.2 Overview of comments

### 11.2.1 Arguments against the introduction of the techniques

In response to this question some respondents simply state their opposition to the techniques or for a change in law, while others focus on outlining their reasons for opposition in more detail. The majority of these arguments against the two techniques reflect those appearing in response to other questions, and there are also a number of responses to question 7 containing similar text and which gives consistent sets of arguments against the techniques.

#### Ethical arguments

The most common argument given against the two techniques is the involvement of the creation and destruction of embryos, with related concerns about the sanctity of life and interfering with the natural or sacred processes of reproduction. A number of respondents talk about general concerns regarding the slippery slope argument, with others again specifying specific concerns about cloning, designer babies or commodification, and eugenics. A few respondents say that regulation would not necessarily prevent a descent along the slippery slope. Others say that the end simply does not justify the means or that there are too many ethical or moral issues to justify taking these techniques forward.

“Broadly speaking, all the currently proposed techniques involve the instrumentalisation of human life; irreversible changes to the human germ line; destruction and/or manipulation of individual human embryos; radical challenges to our understanding of individual identity.”

Organisation, LIFE Charity

### **Social arguments**

The related issues of a third person as a parent or donor (which itself is related to concerns about playing God) and the impact on the child and its identity are again the most common social arguments against MST and PNT. A few respondents add that there are just too many social issues, or that the impact on the donor (including the risk of exploitation) or on family relationships is of concern.

“The Church of Scotland welcomes the opportunity to comment on these proposed technologies. As indicated above, we are concerned not only about the specifics of these techniques, but also about the general direction in which this will drive society, and also the effective downgrading of the special status of the early human embryo.”

Organisation, Church of Scotland

“It has to be stressed that egg harvesting is not a risk-free procedure. In the process of MST, it is not clear whether the proposals would require the cycle of the donor woman to be timed to coordinate with the cycle of the woman carrying the mitochondrial disease. This would make the whole process fairly precarious in terms of timing. This would once again show how the donor is being used as an object of exploitation.”

Organisation, ProLife Alliance

There is also a common argument which arises in a number of responses to question 7: the concern that historical experience shows embryo research has consistently failed to deliver results and that these techniques would therefore be offering false hope to a vulnerable group of people, and/or that mitochondrial disease would not be eradicated.

### **Risks, alternatives and wider implications**

Another very common response to question 7 is that scientists are already working on other techniques for addressing mitochondrial disease and that these should be pursued instead of MST or PNT. As with previous questions, some respondents state that people have no right to a healthy and/or genetically related child, and a number of preferred alternatives are cited; these include use of donor eggs and adoption.

Unintended or unknown future risks, consequences and impacts are again a concern for a number of respondents. This includes the risks of altering the germ line, with some respondents stating that these techniques involve cloning, and others highlighting the unacceptability of altering DNA at all. There are also concerns that, just because a technique is possible, this does not automatically mean it should be used, and that our current scientific understanding here is limited. The role and motivation of scientists is also of concern to a number of respondents.

As with previous questions, concern is expressed that these techniques are not legal anywhere else (and indeed could result in a prison sentence) and that the UK would be the first to cross this boundary. Some respondents say this is not the UK's decision to make without considering worldwide consequences, or that they are concerned regulation would not be consistent should these techniques become widely available.

Finally, other respondents touch on the cost of these techniques; either specifically that they are too expensive to be justified, or more broadly that there are other issues which should be prioritised. There are also comments expressing concern that the techniques would lead to an increase in population.

### **11.2.2 Arguments for the introduction of the techniques**

In response to this question some respondents simply state their support for the techniques or for a change in law, while others outline their reasons for support in more detail. The majority of these arguments in support of the two techniques again reflect those appearing in response to other questions, and are summarised below.

#### **Social arguments**

The most common argument in favour of the two techniques in response to question 7 is the degree to which mitochondrial disease causes suffering and affects both sufferers and their families, with many citing personal experience. Related to this are a number of other common responses about the benefits to the health of the child and to potential parents or families, as well as the avoidance or eradication of the disease being a good thing. The potential for these techniques to reduce the overall burden on services, including the NHS, is also mentioned by some respondents.

#### **Ethical arguments**

As with previous questions, the imperative to 'help if we can' is the most common ethical argument in favour of MST and PNT. A few respondents state that people have a right to a healthy and/or genetically related child. There are also some more general comments from respondents who have no concerns about the slippery slope specifically, or about ethics more widely, with a couple of comments again favouring MST over PNT because of less involvement of embryos in the former.

#### **Science, progress and comparisons**

Again, some respondents talk about the positive aspect of the two techniques either in terms of general scientific progress or their potential to lay the foundations for other new treatments (either for mitochondrial disease or other conditions). A few respondents suggest that the UK could be the leader in these new techniques, that it is natural progress, or that the underlying science should be allowed to progress as far as it can.

In terms of risks and benefits, some respondents explicitly state they are satisfied that the techniques are safe, that the risks are acceptable or that the benefits would outweigh the costs or other considerations. In addition, a few respondents suggest that these techniques would be preferable to other existing options, or simply that there is no reason not to allow them to progress.

"Objections have been raised against these techniques on the grounds that mitochondrial donation, and germline alterations to DNA, are "unnatural". However, all medical interventions, including transplants, antibiotics, vaccines and even setting of broken bones, are to a greater or lesser extent unnatural. What these procedures, and mitochondrial donation, have in common, is that they offer the potential for humanity to overcome the cruelties of nature, and to offer people affected by disease the chance of a healthier life.

When new medical treatments are given to human beings for the first time, it is never possible to be certain that these will be 100 per cent safe or effective. Even the most exhaustive research can establish only that a technique is sufficiently likely to be safe to justify first-in-man clinical use in a research setting. If medicine is to progress, however, doctors must be permitted to use new techniques when evidence suggests these are

indeed sufficiently safe and effective to use on patients for the first time. In the case of mitochondrial donation, there will be much more evidence for safety and effectiveness available before the first clinical use than was available for many other techniques, such as organ transplants and IVF.”

Organisation, Wellcome Trust

### 11.2.3 Other considerations

Aside from those respondents who do not give any response to question 7, a number explicitly state there are no further considerations beyond what they have already said, while a few say they do not know. Some respondents compare the considerations for mitochondria replacement to those for other existing treatments or techniques, for example IVF. Other considerations and wider issues raised by respondents are summarised here and in section 11.2.4.

#### **Ethical and social considerations**

A number of ethical and social considerations appear in response to question 7, all of which have also appeared in response to previous questions. The most common ethical considerations in response to this question are around consideration of the slippery slope argument (including comments that these techniques are different from those which would be required for cloning or designer babies) and equity of provision. The most common social considerations in response to this question include consideration of overall societal impact, impacts on future generations, the number of people for whom the techniques would be relevant, and the effect these techniques might have on society’s attitudes towards disabled people in general or sufferers of mitochondrial disease in particular.

#### **Regulation, criteria and practicalities for application**

Several respondents discuss regulation in response to this question. Other than saying it is needed (although there is one respondent who says this kind of research should not be subject to government regulation), there are a number of specific suggestions for regulation. These include the role of the regulator in limiting the application of the techniques and ensuring practitioners do not overstep certain boundaries, as well as other roles such as building in a review process (e.g. for newly classified diseases), prescribing the list of diseases, balancing control with flexibility, regulating clinics and physicians, ensuring provision of counselling, and providing guidelines or a code of practice.

“If these techniques are introduced, we wish to see protection and promotion of the autonomy of the various parties that may be affected. This may require additional stipulations beyond current safeguards on matters such as counselling and information for couples and donors. At present, those seeking licensed assisted reproduction treatments in the UK are offered, under the HFEA act, “proper” information and a “suitable opportunity to receive proper counselling about the implications” of the treatment. If introduced, the provision of cell reconstruction treatments should follow this model. Furthermore, given the complex nature of mitochondrial inheritance and the issues of novelty around reconstructing embryos, we suggest that while the initial discussions about the procedure could be within a routine setting, there should be further opportunity offered for prospective parents to speak to a specialist with appropriate training and up to date information in a dedicated unit accustomed to dealing with mitochondrial disorders (paragraphs 5.9-5.10).

We believe that in the first instance that PNT and MST (or any comparable future treatment) should only be offered as part of a research trial in centres specialising in mitochondrial disorders. Consent to follow up would need to be included as a mandatory part of parental consent to participating in the trial (paragraph 5.6).…”

A few respondents talk specifically about international regulation, for example concerns that if the UK does not take these techniques forward then other countries with less rigorous controls in place may do so and that UK patients may go abroad for treatment, or that it might be difficult to follow up patients coming from abroad to receive treatment in the UK.

As with question 6, some respondents suggest a number of criteria for deciding whether to progress a specific technique, to help choose between them or to help decide on which cases they should be used for. Safety and success rate/efficacy/efficiency of the technique are again the most commonly mentioned criteria, with the addition of seriousness of disease or risk to the child, cost or value, medical evidence or advice, family situation or ability to provide, patient need or appropriateness, and others. The parents or the parents and clinician together, and the regulator, are again mentioned as potential decision makers for who is eligible and for which technique. Others mention the need for a national screening programme to determine eligibility for treatment.

“How do we know whether or not we have mitochondrial disease? There needs to be a national screening programme. My family only found out that this disease existed, and that others in the family are at risk, after losing a family member to it. Screening in pregnancy should be mandatory in order to eradicate this disease.”

Individual, Family member/friend of someone affected by mitochondrial disease

In terms of practicalities, the question of who would pay for the treatments is raised by a number of respondents, some of whom say explicitly that the NHS should or should not fund treatment. The need to explore the question of commercial benefits to clinics in offering these techniques is also mentioned by a few respondents. The requirement for patients to receive a good level of information and involvement in the decision, as well as the availability of support and counselling, is a common suggestion. In addition, a small number of respondents discuss donor considerations, such as recruiting and screening donors, storing records of donations and whether or not to pay donors.

### Science, further research and monitoring

A number of respondents discuss the need either for further research, trials or evidence if or as the techniques progress further, or for follow-up studies and monitoring of patients who undergo the procedure/s. There are also some more disparate comments about science in general or in relation to this particular decision.

“Our economy could benefit from a stronger more proactive scientific and technological sector. This could benefit everyone - present and future.”

Individual, Other

“The more information which comes to light about the physical and emotional outcomes from all forms of assisted reproduction, the more it becomes apparent that it is a branch of medicine which seriously conflicts with the Hippocratic oath: “First do no harm”. Scientists are proposing a new and convoluted form of IVF procedure when finally, after 30 years, emerging studies are showing what some of us have worked out for ourselves, despite regular denials from the industry, that babies born through standard IVF are 25% more likely to have birth defects. The use of IVF, with or without the use of donor gametes, should be discouraged.”

Individual, Personal experience of egg, sperm or embryo donation or donor conception



“Decision makers should consider that they will have significant power to influence the course of science in this field.

If allowed, we should make all effort to succeed in the trials (while not obscuring good science) as a simple lack of diligence can cause the door to shut on all therapies of this kind.”

Individual, Student, Researcher

Others mull on the motivations of scientists and the progress made so far, as highlighted by the range of comments below:

“The drive to research these problems that a handful of members of our society face is caring. The possibility that dark forces are at work attempting to subvert society should be rejected as the silly work of over active imaginations.”

Individual, Other

“Those in the medical profession must be humble and seeking the benefit of patients and not personal glory.”

Individual, Other

“I think that the decision makers should take into account that this is not a cure in the traditional sense but should be viewed as preventative medicine at its most advanced.”

Individual, Family member/friend of someone affected by mitochondrial disease, Other

### Other considerations and references

A small number of respondents reflect back on previous responses about donation status and the nature of information received by the child who is produced as a result of this treatment. Others discuss scientific aspects of the techniques, for example: the nature of mitochondria and mitochondrial DNA; other procedures; and the variety of forms of mitochondrial disease.

Similar to responses to previous questions, many respondents make reference to the views of other people generally or other specific individuals and groups, religious views, government and the HFEA. Others comment on the role of the media, either in reference to specific coverage of this issue they have seen or heard, or to the way the issue tends to be framed. The need for a clear, neutral coverage of the facts is suggested by some; and there is also the suggestion from a few respondents that reporting of the techniques so far has been misleading in one way or another:

“The decision makers must consider the significant benefit to the lives of the parents and the child that avoid mitochondrial diseases whilst rising above the sloppy journalism citing 3 parents. The techniques being discussed here DO NOT create 3 parents...”

Individual, Other

Other respondents cite relevant research, documents or websites in support of their responses, as with responses to other questions.

## 11.2.4 Context and decision making

### Making the decision

As well as some questions about who will be making the decision and on what grounds, there are a number of comments on the nature of overall decision to be made in response to question 7, with some respondents recognising that this is a complex decision covering new or difficult territory. Others call for rational and objective consideration of the issue, the need to weigh up the overall risks with benefits or net gain, and the need to humanise the issue away from “cold ethical debate”. On a similar note, the question of whether science or ethics should be central to the decision making process is raised by some respondents:

“The ethical questions should take precedence over the scientific considerations.”

Individual, Other

“I hope that the decision will be taken on consequentialist grounds, following the consensus of the scientific community.”

Individual, Other

The speed of implementation, should a decision to proceed be made, also elicits varied views from those few respondents who comment on it, with some calling for a speedy progression and others for caution:

“It is not urgent in the scheme of things to proceed now, there are many benefits from waiting.”

Individual, Other

“It would be a shame to see one such as this, which has so many benefits andrew [sic] if any drawbacks, not be put into effect as soon as possible.”

Individual, Other

### Taking into account specific views

Primarily in support of their views in support of or opposition to the two mitochondria replacement techniques, a number of respondents suggest that decision makers should talk to or take into account the views of particular groups or people, or that undue weight should not be given to particular views. Illustrating a similar tension as the science/ethics question outlined above, some respondents would like the views of different religious groups or of people with firsthand experience of mitochondrial disease to be specifically listened to; some are also concerned that vocal objections, for example based on ethics or religion, should not overshadow the views or needs of those who would benefit from these treatments.

Examples of specific viewpoints some respondents would like decision makers to take into account:

“The decision makers should talk to people who actually suffer from mitochondrial disease. So little is known about it that even when you talk to some doctors about it, they have never heard of it. The people who make the decision cannot make a proper decision without knowing all the facts, it is a rare disorder most people haven’t got a clue what it does to you and how it makes you feel, they need to know.”

Individual, Personally affected by mitochondrial disease

“People who know more about the treatments should visit people with different religious views and they should take note on their views. The older generations should be questioned too.”

Individual, Student

“I think that if everyone was made to talk to and interact with parents of disabled children they will find out a lot more than just thinking they know from seeing it from a distance.”

Individual, Other

“The views of the wider population should be considered and upheld at all times.”

Individual, Other

“I would want consultation with disabled people and stakeholders to ask what they think of this as well - not just 'normal' people who see disability as a terrible dark thing to be avoided.”

Individual, Personally affected by mitochondrial disease, Family member/friend of someone affected by mitochondrial disease

Examples of specific viewpoints some respondents would like decision makers not to give undue weight to:

“Many people will have philosophical objections to these procedures; based on abstract ideas of what it means to be human, religious concerns about 'playing god', worries about what may possibly lie in the future if we take a step in this direction. While these are all relevant considerations, and issues for society to discuss honestly, these concerns of the majority should not be given undue weight against the real needs of the minority who actually suffer from this disease, those who will suffer the consequences of a decision to deny this treatment. Similar issues surround the introduction of other medical advancements, from medicines to transplants, but the health and quality of life of the vulnerable and the individual is more important than the abstract concerns of others - the same approach should be taken here.”

Individual, Other

“If individual families have objections they will not have the treatment. Those who object should not be allowed to deny access to others who could benefit.”

Individual, Other

Other observations:

“I believe that there is a high correlation between those who do not approve of Mitochondrial Replacement [sic] and those who do not understand either the science behind it or the impact of Mitochondrial Disease upon individuals and their families.

Interestingly, a handful of people commenting on this topic on the BBC website today revealed that they themselves suffered from genetic disorders, including Mitochondrial Disease.

Perhaps surprisingly, all but one stated that they were very much in favour of Mitochondrial Replacement with only one commenting that they found the idea of eradicating genetic disorders to be personally insulting to them.”

Individual, Family member/friend of someone affected by mitochondrial disease

### **Wider issues and other priorities**

Aside from those respondents who focus on other issues or alternatives as part of their opposition to the two techniques, there are also some more neutral comments about wider issues which would be useful topics for further debate or consultation, as well as other societal priorities which respondents feel might be worth looking at either alongside or in preference to mitochondria replacement.

The wider issues mentioned as potential topics for further consultation are fertility treatments, genetic disease more generally, pre-implantation techniques and the use of animals in research. Other priorities suggested as being worth consideration are other health or research priorities more generally, the concept of family, mitochondrial disease diagnosis and/or other treatment avenues, poverty, and psychological or psychiatric care.

### **The consultation process**

Several respondents comment on the consultation process in response to this question. Whilst some say they welcome the consultation and the chance to input or provide other positive comment, others question the neutrality of the consultation or provide other negative comments (for example about poor publicity, bad timing, cost or lack of information). There are also a few specific comments and suggestions about the questions and response form.

“This consultation is extremely premature, since the experiments on safety are years away from being completed. A 10 week consultation period accompanied by as little overall public discussion as other HFEA consultations usually attract is radically inadequate to dealing with the seriousness of the issues posed by human germ line modification.”

Organisation, Human Genetics Alert

Finally, there are a number of comments about follow-up to the consultation. Aside from requests for specific information, these primarily focus on the need for further communication and public education about mitochondria replacement and surrounding issues, including comments on the need for wider debate of the issue (for example utilising more social media) and the ongoing role for the media.

“There needs to be very clear explanations of the technique itself and explanations of the role of mitochondrial DNA made available to the press to help to combat sensationalist reporting. Examples of the significant value of the technique to families carrying mitochondrial diseases [sic] which can be dealt with by the technique also should be well publicised.”

Individual, Other

# Appendix

---

## A.1 Consultation questions

### 1. Permissibility of new techniques

Having read the information on this website about the two mitochondria replacement techniques – maternal spindle transfer and pro-nuclear transfer, what are your views on offering (one or both of) these techniques to people at risk of passing on mitochondrial disease to their child? You may wish to address the two techniques separately.

### 2. Changing the germ line

Do you think there are social and ethical implications to changing the germ line in the way the techniques do? If so, what are they?

### 3. Implications for identity

Considering the possible impact of mitochondria replacement on a person's sense of identity, do you think there are social and ethical implications? If so, what are they?

### 4. The status of the mitochondria donor

a) In your view how does the donation of mitochondria compare to existing types of donation? Please specify what you think this means for the status of a mitochondria donor.

b) Thinking about your response to 4a, what information about the mitochondria donor do you think a child should have? (Choose one response only)

- The child should get no information
- The child should be able to get medical and personal information about the mitochondria donor, but never know their identity
- The child should be able to get medical and personal information about the mitochondria donor and be able to contact them once the child reaches the age of 18
- Other
- I do not think mitochondria replacement should be permitted in treatment at all

Please explain your choice.

### 5. Regulation of mitochondria replacement

If the law changed to allow mitochondria replacement to take place in a specialist clinic regulated by the HFEA, how should decisions be made on who can access this treatment? (Choose one response only)

- Clinics and their patients should decide when mitochondria replacement is appropriate in individual cases
- The regulator should decide which mitochondrial diseases are serious enough to require mitochondria replacement and, just for these diseases, permit clinics and patients to decide when it is appropriate in individual cases

- The regulator should decide which mitochondrial diseases are serious enough to require mitochondria replacement and also decide, just for these diseases, when it is appropriate in individual cases
- I do not think mitochondria replacement should be permitted in treatment at all

Please explain your choice.

## **6. Should the law be changed?**

In Question 1, we asked for your views on the mitochondria replacement techniques MST and PNT. Please could you now tell us if you think the law should be changed to allow (one or both of) these techniques to be made available to people who are at risk of passing on mitochondrial disease to their child?

## **7. Further considerations**

Are there any other considerations you think decision makers should take into account when deciding whether or not to permit mitochondria replacement?

## A.2 Responding organisations

List of responding organisations
Affinity
Alliance for Humane Biotechnology
AMRC and Genetic Alliance UK
Anscombe Bioethics Centre
Association of Clinical Embryologists (ACE) Executive Committee
British Federation of Women Graduates - Northern Region
British Fertility Society
British Heart Foundation
British Medical Association
Cardiff Sixth Form College
CARE
Cathedral School Llandaff
Catholic Parliamentary Office
Centre for Genetics and Society
Christian Concern
Christian Concern & The Christian Legal Centre
Christian Medical Fellowship
Church of England: Mission and Public Affairs Council
Church of Scotland
Clinical Ethics Committee, University Hospitals of Leicester NHS
Comment on Reproductive Ethics (CORE)
Cornwall's Community Standards Association
East Hampshire District Councillor
Escher Fund for Autism
Fareham Community Church
Free Church of Scotland
Friends of the Earth United States and Friends of the Earth England, Wales and Northern Ireland
Galway for life
HEAL UoS (Health Ethics and Law, University of Southampton).
Horsley Evangelical Church
Howell's School Llandaff
Human Genetics Alert

List of responding organisations
Humanist Society Scotland
International Center for Technology Assessment
Islamic Medical Association/UK and on behalf of the Society of Muslim scholars
Justice et Solidarite Mondiales
LIFE Charity
Morality Forum
Muscular Dystrophy Campaign
National Council of Women
National Gamete Donation Trust
Newcastle University
No Less Human
North East Scotland Youth For Christ
Nuffield Council on Bioethics
Our Bodies Ourselves
Porter Dodson Solicitors &Advisors
Pro Life Alliance
Pro-Choice Alliance for Responsible Research
PROGAR
Progress Educational Trust
ProLife Alliance
RedBridge People First
Resident Community of Pilgrims Hall Christian Centre
Retired
Right To Life
Royal College of Obstetricians and Gynaecologists
Royal College of Physicians
Scottish Council on Human Bioethics
Scottish Council on Human Bioethics
Society for the Protection of Unborn Children
Spring Road Evangelical Church
St Bernadette's Catholic Church, Larbert, Stirlingshire
The Academy of Medical Sciences
The Christian Institute



<b>List of responding organisations</b>
The Lily Foundation
Trinity Grace Church, Ramsbottom
University Hospitals of Leicester NHS Trust (Clinical Ethics Committee)
Wellcome Trust
Women and Medical Technologies

### A.3 Analysis: List of themes

Theme	Acronym
Acceptability	AC
Arguments against	AG
Arguments in favour	FA
Considerations	CO
Consultation process	CP
Decision making	DM
Donation status	DS
Information	IN
Legal Status	LS
Other	O
References	RF
Science	SC
Social and ethical	SE

## A.4 Analysis: List of codes applied per question

The tables below list the themes and codes applied to the text of responses to each question of the consultation and the number of times that each code was used.

### 1. Permissibility of new techniques

Having read the information on this website about the two mitochondria replacement techniques – maternal spindle transfer and pro-nuclear transfer, what are your views on offering (one or both of) these techniques to people at risk of passing on mitochondrial disease to their child? You may wish to address the two techniques separately.

Code	Count
AC - Acceptable - MST	20
AC - Acceptable - MST and PNT/general	349
AC - Acceptable with caveat - MST	3
AC - Acceptable with caveat - MST and PNT/general	106
AC - Acceptable with caveat - PNT	3
AC - Not acceptable - MST	2
AC - Not acceptable - MST and PNT/general	502
AC - Not acceptable - PNT	24
AC - Not sure - MST and PNT/general	3
AC - Not sure - PNT	2
AC - Overall - not for me to decide	4
AC - Overall - unable/not qualified to answer	5
AC - Overall - understand issue/have sympathy	32
AC - Overall - unsure/no strong view	4
AC - Preference - MST over PNT	72
AC - Preference - no preference	12
AC - Preference - PNT over MST	11
AG - Altering DNA - cloning/hybridisation	46
AG - Altering DNA - impact on germ line/lineage	109
AG - Altering DNA - not acceptable	41
AG - Costs/risks - outweigh benefits	42
AG - Disease - will not be eradicated/not a cure	9
AG - Donation - risk/exploitation	31
AG - Ethics - egg (mainly MST) creation/destruction	22
AG - Ethics - embryo (mainly PNT) creation/destruction	232
AG - Ethics - end does not justify means	23
AG - Ethics - general/too many ethical issues	56

Code	Count
AG - Ethics - interfering with evolution/playing god	70
AG - Ethics - judging value/worth of life (particularly PNT)	13
AG - Ethics - lack of consent/choice	16
AG - Ethics - no right to healthy/genetically related child	20
AG - Ethics - other comment	18
AG - Ethics - sanctity/dignity of human life	101
AG - Ethics - UK first in crossing ethical boundary	21
AG - Future - risks/impacts/unintended consequences	160
AG - MST - could be more emotionally difficult	2
AG - MST & PNT - both involve IVF/embryo destruction	68
AG - PNT - ethically worse	30
AG - PNT - riskier/no guarantee of survival	4
AG - Population - artificially selected/GM	7
AG - Population - too big/would increase	4
AG - Preferable alternative - adoption	26
AG - Preferable alternative - counselling/support	1
AG - Preferable alternative - decide not to conceive	10
AG - Preferable alternative - donor eggs	12
AG - Preferable alternative - education	1
AG - Preferable alternative - other treatment/cure of MD	79
AG - Preferable alternative - other/general	19
AG - Preferable alternative - screening eggs/embryos	5
AG - Regulation - may not be consistent across the board	1
AG - Science - false hope/may not work	24
AG - Science - just because it is possible does not mean it should be done	13
AG - Science - role/motivation of scientists	10
AG - Science - understanding is limited	33
AG - Slippery slope - attitudes to euthanasia	2
AG - Slippery slope - cloning	35
AG - Slippery slope - concerns	34
AG - Slippery slope - designer babies/commoditisation	71
AG - Slippery slope - eugenics	49
AG - Social - general/too many social issues	6
AG - Social - hardship is natural/contributes to strength of society	3
AG - Social - impact on child/identity/psychology	85

Code	Count
AG - Social - impact on donor/donor considerations	14
AG - Social - impact on family relationships	13
AG - Social - impact on parents	8
AG - Social - legal implications/scenarios	7
AG - Social - other comment	7
AG - Social - prioritise other issues/solutions	10
AG - Social - third person as parent/donor	129
AG - Social - worth of MD sufferers/disabled people	17
AG - Wider issue - against artificial fertilisation	10
CO - Alternatives - encourage/make adoption easier	3
CO - Alternatives - other comment	9
CO - Availability - NHS cover	4
CO - Availability - NHS should not cover/fund privately	5
CO - Business interest/involvement	4
CO - Cost/funding - general/who pays	11
CO - Criteria - cost/value	12
CO - Criteria - medical evidence/advice	16
CO - Criteria - other	6
CO - Criteria - parent/patient choice	30
CO - Criteria - patient need/appropriateness	17
CO - Criteria - safety	57
CO - Criteria - success rate/efficacy/efficiency	66
CO - Donation - availability/origin	2
CO - Donation - like organ/blood	1
CO - Donation - like sperm/egg/IVF	4
CO - Donor status - record identity	3
CO - Donor status - rights/responsibilities	8
CO - Embryo or egg rights/life - concern	23
CO - Embryo or egg rights/life - general/other	26
CO - Embryo or egg rights/life - not a concern	10
CO - Ethics - different to designer embryos/cloning	11
CO - Ethics - interfering with evolution/playing god	3
CO - Ethics - lack of consent/choice	4
CO - Ethics - other comment	20
CO - Ethics - where to draw the line with screening/modification	8

Code	Count
CO - Identity - child access to information	5
CO - Identity - child should know about conception	2
CO - Identity - concerns	6
CO - Identity - no concerns	2
CO - Labelling of techniques - misleading/misunderstood	6
CO - MST - could be more publically/ethically acceptable	27
CO - MST - other consideration	4
CO - MST & PNT - other comparative comment	11
CO - MST & PNT - see no/little difference	20
CO - Patients - follow up studies/monitoring	5
CO - Patients - information provision/involvement	25
CO - Patients - may go elsewhere/abroad	1
CO - Patients - rights/responsibilities	1
CO - Patients - support/counselling	1
CO - PNT - other consideration	5
CO - PNT - potentially controversial	10
CO - PNT - use of spare embryos	5
CO - Population - could increase	1
CO - Regulation - limitation of use	3
CO - Regulation - needed	18
CO - Regulation - other comment	5
CO - Regulation - would prevent slippery slope	7
CO - Safety - evidence insufficient	14
CO - Safety - risks is always present with medical procedures	6
CO - Safety - risks vs benefits	14
CO - Science - alternative/additional suggestion	5
CO - Science - further research/trials/evidence	56
CO - Science - mitochondrial function	12
CO - Science - other comment	19
CO - Science - participant understanding	12
CO - Science - should prevail	10
CO - Slippery slope - designer babies/commoditisation	14
CO - Slippery slope - eugenics	1
CO - Slippery slope - general	9
CO - Social - child emotional/psychological impact	7

Code	Count
CO - Social - impact on future generations	4
CO - Social - insurance considerations	2
CO - Social - legal considerations	14
CO - Social - number of cases	14
CO - Social - parents should not be pressurised	6
CO - Social - risk losing valuable individuals	2
CO - Social - third person as parent/donor	10
CO - Social - worth of MD sufferers/disabled people	2
CP - Consultation - challenge information/data	4
CP - Consultation - comment on question	5
CP - Consultation - lack of information	4
CP - Consultation - outcomes	1
CP - Consultation - participants not qualified	2
CP - Consultation - question motivations/bias	4
CP - Consultation - specific information	3
CP - Follow-up - further consultation	6
CP - Follow-up - further info on specific topic/s	1
CP - Follow-up - further info would help form opinion	6
CP - Follow-up - please keep informed	1
CP - Follow-up - public communication/education	2
CP - Website - difficulty	1
CP - Website - general	8
CP - Website - lack of information	2
CP - Website - positive comment	1
CP - Website - video	3
FA - Benefits - outweigh cost/other considerations	25
FA - Cost - no concerns	1
FA - Disease - avoidance important/positive	69
FA - Disease - eradicate	35
FA - Disease - impact on families/sufferers	15
FA - Disease - risks of passing on	11
FA - Disease - scale of suffering underestimated	3
FA - Donation - like organ/blood	8
FA - Donation - like sperm/egg/IVF	2
FA - Ethics - ethical imperative to intervene	30

Code	Count
FA - Ethics - no concerns	40
FA - Ethics - right to healthy/genetically related child	25
FA - Identity - compare to sperm/egg donation	3
FA - Identity - no concerns	10
FA - MST - destroying eggs no concern	10
FA - MST - does not destroy embryos	35
FA - MST - fewer ethical concerns	10
FA - MST - less wastage of genetic material/does not involve father	2
FA - MST - like organ donation	2
FA - MST - might be easier/more efficient	7
FA - MST - other comment in favour	5
FA - MST and PNT - better/alternative to current options	11
FA - MST and PNT - not different from existing practices	7
FA - PNT - fewer ethical concerns	2
FA - PNT - involves the father/normal inheritance better	4
FA - PNT - less risky	2
FA - PNT - more robust/better success rate/economic sense	6
FA - PNT/general - similar to IVF/donation ethically	8
FA - Safety - techniques are safe/risks acceptable	3
FA - Science - could lead to new treatments (MD or other diseases)	4
FA - Science - important/positive	30
FA - Science - natural progress	8
FA - Science - no concerns	3
FA - Science - no genetic traits are passed on	10
FA - Science - nuclear DNA not altered	7
FA - Science - origin of mitochondria/not human	3
FA - Science - other comment	5
FA - Science - UK as a leader in new techniques	3
FA - Slippery slope - not a concern	21
FA - Social - benefits to potential parents/families	80
FA - Social - general benefit to society/public health	13
FA - Social - genetic parentage/no third parent issues	11
FA - Social - health/wellbeing of the child	97
FA - Social - poor provision of care for sufferers	1
FA - Social - reduces burden on services/NHS	4



Code	Count
O - Blank response/no comment	2
O - Refer to other question	6
RF - Culture/literature	2
RF - Current legislation	20
RF - Current legislation - non UK	36
RF - External document	6
RF - External event/discussion	2
RF - HFEA	14
RF - Historical experience	14
RF - Media coverage	3
RF - Participant - friend/relative/child with MD/similar disease	40
RF - Participant - has MD/similar disease	20
RF - Participant - info about	51
RF - Participant - other medical details	12
RF - Participant - personal details	4
RF - Politics/government	19
RF - Relevant research	14
RF - Religion	43
RF - Scientific review panel	3
RF - Specific individual/organisation/group	8
RF - Views of other people/participants	30

## 2. Changing the germ line

Do you think there are social and ethical implications to changing the germ line in the way the techniques do? If so, what are they?

Code	Count
AC - Acceptable - MST and PNT/general	1
AC - Not acceptable - MST and PNT/general	4
AC - Overall - unsure/no strong view	1
CP - Consultation - challenge information/data	2
CP - Consultation - comment on question	3
CP - Consultation - lack of information	1
CP - Consultation - other comment	1
CP - Consultation - other positive comment	1
CP - Consultation - participants not qualified	2
CP - Consultation - question motivations/bias	2

Code	Count
CP - Consultation - specific information	1
CP - Consultation - welcomed	2
CP - Follow-up - further consultation	7
CP - Follow-up - further info on specific topic/s	2
CP - Follow-up - other comments	1
CP - Follow-up - public communication/education	9
CP - Website - video	2
O - Blank response/no comment	3
O - Other/general comment	2
O - Refer to other question	34
RF - Current legislation	5
RF - Current legislation - non UK	55
RF - External document	2
RF - External website	4
RF - HFEA	7
RF - HFEA - website	3
RF - Historical experience	19
RF - Media coverage	3
RF - Other evidence/examples	3
RF - Participant - friend/relative/child with MD/similar disease	9
RF - Participant - has MD/similar disease	6
RF - Participant - info about	11
RF - Participant - other medical details	4
RF - Participant - personal details	1
RF - Politics/government	6
RF - Relevant research	6
RF - Religion	40
RF - Specific individual/organisation/group	10
RF - Views of other people/participants	50
SC - DNA - mutates anyway over time	7
SC - DNA - natural mixing	7
SC - DNA - nuclear DNA/genome not affected	39
SC - DNA - other comment	5
SC - Germ line - could reduce in diversity	4
SC - Germ line - diversity/mixing is beneficial/genetic advantage	4

Code	Count
SC - Germ line - not significantly changed	7
SC - Germ line - ok to alter	22
SC - Germ line - other comment	39
SC - Germ line - should not be altered	22
SC - Germ line - will be repaired/not enhanced	5
SC - Mitochondria - function/form	18
SC - Mt DNA - does not determine identity/traits	38
SC - Mt DNA - keep faulty DNA for posterity	2
SC - Mt DNA - maternal/female line	19
SC - Mt DNA - may affect identity/traits	10
SC - Mt DNA - origin/not human	3
SC - Mt DNA - other comment	24
SC - Mt DNA - quantity/impact too much	2
SC - Mt DNA - small quantity/impact	30
SC - Mt DNA - suggested source for donation	7
SC - Other procedures - abortion/termination	5
SC - Other procedures - adoption	16
SC - Other procedures - genetic techniques/gene therapy	6
SC - Other procedures - IVF/egg or sperm donation/surrogacy	46
SC - Other procedures - not conceiving	4
SC - Other procedures - organ/tissue/blood donation	21
SC - Other procedures - other/general	5
SC - Other procedures - stem cell donation	4
SC - Other procedures - vaccination	4
SC - Overall - addition/alternative suggestions	3
SC - Overall - balancing science/ethics/religion/society	5
SC - Overall - further research/trials/evidence	14
SC - Overall - invest in other priorities/solutions	18
SC - Overall - motivation of scientists	5
SC - Overall - nature of medicine/science	17
SC - Overall - object to infertility treatment	4
SC - Overall - one-off/single generation treatment	3
SC - Overall - other comment	21
SC - Overall - restricting to male births	4
SC - Overall - trust/mistrust of scientists	18

Code	Count
SC - Overall - understanding is limited	19
SC - Progress - has gone too far to stop now	2
SC - Progress - natural consequence/function of humanity	10
SC - Progress - other comment	5
SC - Progress - possibility does not mean it should happen automatically	6
SC - Progress - reducing MD is good/positive	91
SC - Progress - requires caution	6
SC - Regulation - can't guarantee limits	1
SC - Regulation - international considerations	6
SC - Regulation - needed	10
SC - Regulation - other comment	8
SC - Regulation - specifics	3
SC - Regulation - would prevent slippery slope	4
SC - Safety - other comment	13
SE - Ethical - benefits small number	4
SE - Ethical - consent/choice concern	38
SE - Ethical - consent/choice no concern	4
SE - Ethical - consent/choice other	8
SE - Ethical - embryo rights/usage concern	158
SE - Ethical - embryo rights/usage no concern	4
SE - Ethical - embryo rights/usage other	16
SE - Ethical - end does not justify means	2
SE - Ethical - equity of provision	6
SE - Ethical - ethical imperative to intervene	39
SE - Ethical - genetic modification of human embryos	10
SE - Ethical - implications	8
SE - Ethical - implications minimal/insignificant	1
SE - Ethical - interfering with evolution/playing god	73
SE - Ethical - interfering/playing god already happens	17
SE - Ethical - interfering/playing god is ok	8
SE - Ethical - judging value/worth of life	3
SE - Ethical - limitation of use	13
SE - Ethical - no implications/concerns	29
SE - Ethical - no right to healthy/genetically related child	10
SE - Ethical - no slippery slope/not crossing boundary	29

Code	Count
SE - Ethical - not genetic modification	2
SE - Ethical - other comment	15
SE - Ethical - right to healthy/genetically related child	4
SE - Ethical - sanctity/dignity of human life	67
SE - Ethical - slippery slope generally/crossing boundary	141
SE - Ethical - slippery slope other comment	30
SE - Ethical - slippery slope to designer babies/commoditisation	150
SE - Ethical - slippery slope to eugenics	70
SE - Ethical - slippery slope/similar to cloning	72
SE - Ethical - UK first in crossing ethical boundary	4
SE - Ethical tradeoffs - MST vs PNT	7
SE - Ethical tradeoffs - society vs individual	1
SE - General - benefits outweigh issues	68
SE - General - comment on MST specifically	6
SE - General - comment on PNT specifically	14
SE - General - current social/ethical expectations	4
SE - General - implications (Yes)	301
SE - General - implications all/largely positive	10
SE - General - implications based on personal beliefs	8
SE - General - implications minimal/insignificant	13
SE - General - issues outweigh benefits	8
SE - General - no different to current breeding habits	5
SE - General - no implications/concerns (No)	158
SE - General - not sure	2
SE - General - other comment on implications	27
SE - General - other procedures acceptable/better	12
SE - General - preferable to other procedures	12
SE - General - similar to other procedures	29
SE - General - unforeseen problems/impacts/health issues	232
SE - Social - attitudes towards disabled people/MD sufferers	53
SE - Social - attitudes towards those not treated/and their parents	27
SE - Social - attitudes towards those treated	56
SE - Social - availability of counselling/testing/support	2
SE - Social - benefit to future generations	30
SE - Social - benefits to potential parents/families/relationships	25

Code	Count
SE - Social - child awareness not necessary	1
SE - Social - child awareness/understanding	19
SE - Social - child emotional/psychological impact	74
SE - Social - child health/wellbeing improved	59
SE - Social - child health/wellbeing other	7
SE - Social - child ID/mixed genetic make-up	87
SE - Social - child impacts/damage (other/general)	30
SE - Social - child rights	22
SE - Social - cost/resources	6
SE - Social - donor considerations	31
SE - Social - hardship is natural/contributes to strength of society	3
SE - Social - impact on family relationships (not third parent)	24
SE - Social - impact on future generations	175
SE - Social - impact on lineage/traceability	30
SE - Social - implications	4
SE - Social - implications all/largely positive	1
SE - Social - implications minimal/insignificant	3
SE - Social - implications subjective/time-bound	2
SE - Social - increased burden on NHS	5
SE - Social - issues from having MD/disability	7
SE - Social - legal implications/issues	17
SE - Social - minimal family/relationship impacts	2
SE - Social - no ID issues/implications foreseen	7
SE - Social - no implications/concerns	12
SE - Social - no lineage/traceability concerns	2
SE - Social - no third party parentage issues	11
SE - Social - not sure	2
SE - Social - ongoing monitoring/follow-up	29
SE - Social - overall societal benefit/not harmful	11
SE - Social - overall societal impact	10
SE - Social - overpopulation	9
SE - Social - parent awareness/understanding	4
SE - Social - parent psychological impact	10
SE - Social - parent rights/responsibilities	14
SE - Social - parents should not be pressurised	16

Code	Count
SE - Social - public/societal response/fear	17
SE - Social - reduced burden on services/NHS	11
SE - Social - risk losing valuable individuals	7
SE - Social - third party parentage issues	119

### 3. Implications for identity

Considering the possible impact of mitochondria replacement on a person's sense of identity, do you think there are social and ethical implications? If so, what are they?

Code	Count
AC - Not acceptable - MST and PNT/general	11
CO - Criteria - parent/patient choice	2
CO - Labelling of techniques - misleading/misunderstood	7
CO - Patients - information provision/involvement	5
CP - Consultation - comment on question	6
CP - Consultation - comment on response form	1
CP - Consultation - lack of information	1
CP - Consultation - question motivations/bias	2
CP - Consultation - specific information	2
CP - Follow-up - public communication/education	8
CP - Website - general	1
CP - Website - video	4
DS - Donor - responsibility for actions/know what they are getting into	2
DS - Donor function - providing medical solution/repair	10
DS - Donor motivation - other	1
DS - Donor status - is not parent/relation to child	7
DS - Donor status - is parent/relation to child	4
DS - Donor status - is unclear/ambiguous	4
DS - Donor status - no rights/responsibilities to child	4
IN - Age - other comment	1
IN - Child identity - should not be known by donor	1
IN - Child rights - no right/reason to access any information	2
IN - Child rights - to information generally	2
IN - Child rights - to know origins/donor/parents	36
IN - Donor identity - not relevant/necessary	3
IN - Donor identity - other comment	8
IN - Donor identity - should be available (general)	4

Code	Count
IN - Donor identity - should be optional/not mandatory	1
IN - Donor rights - to anonymity/lack of intrusion	1
IN - Donor status - same as blood/tissue/organ donor	7
IN - Donor status - same as egg/sperm donor	2
IN - Logistics - database/infrastructure resourcing	1
IN - Medical info - available for specific reasons/circumstances	1
IN - Medical info - should be available (general)	6
IN - Overall - depends on MtDNA function	1
IN - Overall - other comment	1
IN - Overall decision - flexible/mutual/depends	1
O - potential quote	1
O - Refer to other question	42
RF - Current legislation	1
RF - Current legislation - non UK	6
RF - External document	2
RF - HFEA	5
RF - Historical experience	14
RF - Media coverage	6
RF - Other evidence/examples	8
RF - Participant - friend/relative/child with MD/similar disease	5
RF - Participant - has MD/similar disease	3
RF - Participant - info about	23
RF - Participant - other medical details	5
RF - Politics/government	3
RF - Relevant research	5
RF - Religion	13
RF - Specific individual/organisation/group	5
RF - Views of other people/participants	17
SC - DNA - natural mixing	4
SC - DNA - nuclear DNA/genome not affected	36
SC - DNA - other comment	3
SC - Germ line - other comment	2
SC - Germ line - should not be altered	2
SC - Mitochondria - function/form	31
SC - Mt DNA - does not determine identity/traits	97



Code	Count
SC - Mt DNA - limited amount/types	2
SC - Mt DNA - maternal/female line	4
SC - Mt DNA - may affect identity/traits	19
SC - Mt DNA - origin/not human	3
SC - Mt DNA - other comment	9
SC - Mt DNA - small quantity/impact	63
SC - Other procedures - abortion/termination	3
SC - Other procedures - adoption	68
SC - Other procedures - genetic techniques/gene therapy	2
SC - Other procedures - IVF/egg or sperm donation/surrogacy	112
SC - Other procedures - not conceiving	1
SC - Other procedures - organ/tissue/blood donation	75
SC - Other procedures - other/general	4
SC - Other procedures - stem cell donation	1
SC - Other procedures - timing is different	1
SC - Other procedures - vaccination	1
SC - Overall - addition/alternative suggestions	1
SC - Overall - assessing/managing risk	1
SC - Overall - further research/trials/evidence	7
SC - Overall - invest in other priorities/solutions	8
SC - Overall - motivation of scientists	1
SC - Overall - nature of medicine/science	2
SC - Overall - object to infertility treatment	1
SC - Overall - other comment	8
SC - Overall - question about application	2
SC - Overall - trust/mistrust of scientists	6
SC - Overall - understanding is limited	6
SC - Progress - natural consequence/function of humanity	1
SC - Progress - possibility does not mean it should happen automatically	1
SC - Progress - reducing MD is good/positive	12
SC - Regulation - other comment	3
SC - Regulation - specifics	1
SC - Regulation - would prevent slippery slope	1
SC - Safety - other comment	1
SE - Ethical - benefits small number	1

Code	Count
SE - Ethical - consent/choice concern	11
SE - Ethical - consent/choice no concern	4
SE - Ethical - consent/choice other	1
SE - Ethical - embryo rights/usage concern	53
SE - Ethical - end does not justify means	2
SE - Ethical - ethical imperative to intervene	7
SE - Ethical - implications	4
SE - Ethical - interfering with evolution/playing god	37
SE - Ethical - interfering/playing god is ok	3
SE - Ethical - judging value/worth of life	2
SE - Ethical - no implications/concerns	3
SE - Ethical - no right to healthy/genetically related child	3
SE - Ethical - no slippery slope/not crossing boundary	2
SE - Ethical - other comment	5
SE - Ethical - right to healthy/genetically related child	2
SE - Ethical - sanctity/dignity of human life	8
SE - Ethical - slippery slope generally/crossing boundary	22
SE - Ethical - slippery slope to designer babies/commoditisation	11
SE - Ethical - slippery slope to eugenics	7
SE - Ethical - slippery slope/similar to cloning	10
SE - Ethical - UK first in crossing ethical boundary	1
SE - Ethical tradeoffs - health vs identity	18
SE - Ethical tradeoffs - society vs individual	1
SE - General - benefits outweigh issues	53
SE - General - comment on MST specifically	25
SE - General - comment on PNT specifically	35
SE - General - current social/ethical expectations	6
SE - General - implications (Yes)	174
SE - General - implications all/largely positive	1
SE - General - implications based on personal beliefs	2
SE - General - implications cannot be understood	4
SE - General - implications minimal/insignificant	6
SE - General - issues outweigh benefits	3
SE - General - no different to current breeding habits	1
SE - General - no implications/concerns (No)	134

Code	Count
SE - General - not sure	3
SE - General - other comment on implications	7
SE - General - other procedures acceptable/better	1
SE - General - similar to other procedures	11
SE - General - unforeseen problems/impacts/health issues	68
SE - Social - attitudes towards disabled people/MD sufferers	4
SE - Social - attitudes towards those not treated	3
SE - Social - attitudes towards those treated	41
SE - Social - availability of counselling/testing/support	10
SE - Social - benefit to future generations	6
SE - Social - benefits to potential parents/families/relationships	6
SE - Social - child awareness not necessary	2
SE - Social - child awareness/understanding	105
SE - Social - child emotional/psychological impact	228
SE - Social - child health/wellbeing improved	37
SE - Social - child health/wellbeing other	4
SE - Social - child ID/mixed genetic make-up	368
SE - Social - child impacts/damage (other/general)	13
SE - Social - child may want to meet donor	3
SE - Social - child rights (non-information related)	5
SE - Social - cost/resources	2
SE - Social - donor considerations (other)	16
SE - Social - donor/child bond OR lack of bond	39
SE - Social - donor/child relationship difficulties	21
SE - Social - ethnic/historical ID issues	3
SE - Social - everyone has identity issues	4
SE - Social - ID from nature/genes	10
SE - Social - ID from nurture/upbringing/beyond genetics	71
SE - Social - ID is a changing/evolving concept	4
SE - Social - ID is increasing focus for society	2
SE - Social - ID issues (other)	22
SE - Social - ID issues cannot be known yet	17
SE - Social - ID issues depend on donor status	2
SE - Social - ID issues depend on MtDNA function	2
SE - Social - ID issues for matrilineal societies	3

Code	Count
SE - Social - ID issues less than other procedures	42
SE - Social - ID issues moot/not relevant	3
SE - Social - ID issues more than other procedures	15
SE - Social - ID issues possible	27
SE - Social - ID issues similar/no different to other procedures	131
SE - Social - ID will become fluid/clouded/less clear	5
SE - Social - ID/issues complex/different for everyone	25
SE - Social - impact on family relationships (not third parent)	32
SE - Social - impact on future generations	23
SE - Social - impact on lineage/traceability	25
SE - Social - issues from having MD/disability	7
SE - Social - legal implications/issues	20
SE - Social - lineage/traceability other issues	14
SE - Social - minimal/insignificant ID issues	34
SE - Social - no ID issues/implications foreseen	100
SE - Social - no implications/concerns	4
SE - Social - no lineage/traceability concerns	4
SE - Social - no third party parentage issues	26
SE - Social - ongoing monitoring/follow-up	7
SE - Social - overall societal benefit/not harmful	2
SE - Social - overall societal impact	12
SE - Social - parent psychological impact	27
SE - Social - parent rights/responsibilities	49
SE - Social - parents should not be pressurised	1
SE - Social - positive impact on ID/other	23
SE - Social - public/societal response/fear	9
SE - Social - third party parentage issues	232
SE - Social - who should know the details	5

#### 4. The status of the mitochondria donor

a) In your view how does the donation of mitochondria compare to existing types of donation?  
Please specify what you think this means for the status of a mitochondria donor.

Code	Count
AC - Acceptable - MST	2
AC - Acceptable - MST and PNT/general	10
AC - Acceptable with caveat - MST	1

Code	Count
AC - Not acceptable - MST and PNT/general	47
AC - Not acceptable - PNT	2
AC - Not sure - MST and PNT/general	1
AC - Overall - understand issue/have sympathy	2
CO - Alternatives - other comment	6
CO - Availability - NHS should not cover/fund privately	1
CO - Labelling of techniques - misleading/misunderstood	11
CO - MST and PNT - see no/little difference	2
CO - Patients - information provision/involvement	1
CP - Consultation - challenge information/data	1
CP - Consultation - comment on question	11
CP - Consultation - other comment	3
CP - Consultation - participants not qualified	1
CP - Consultation - question motivations/bias	1
CP - Consultation - specific information	1
CP - Follow-up - further info on specific topic/s	1
CP - Follow-up - public communication/education	1
CP - Website - general	2
CP - Website - video	1
DS - Donor - availability issues/considerations	20
DS - Donor - is important/should be recognised	17
DS - Donor - may have emotional investment/impact	12
DS - Donor - no emotional investment	2
DS - Donor - payment	11
DS - Donor - responsibility for actions/know what they are getting into	22
DS - Donor - risks/exploitation/health considerations	86
DS - Donor function - contributing to life	15
DS - Donor function - not providing reproductive function	5
DS - Donor function - providing medical solution/repair	36
DS - Donor motivation - gift/altruism	32
DS - Donor motivation - other	2
DS - Donor status - does have rights/responsibilities to child	8
DS - Donor status - is clear/unambiguous	3
DS - Donor status - is not parent/relation to child	39
DS - Donor status - is parent/relation to child/partial parent	47

Code	Count
DS - Donor status - is subjective	6
DS - Donor status - is unclear/ambiguous	27
DS - Donor status - legal considerations	31
DS - Donor status - may change/open to review	7
DS - Donor status - no rights/responsibilities to child	37
DS - Donor status - no status	8
DS - Donor status - not primary concern	2
DS - Donor status - other considerations	17
DS - Mitochondria - 'above' blood	10
DS - Mitochondria - 'above' bone marrow	8
DS - Mitochondria - 'above' egg/sperm/embryo	3
DS - Mitochondria - 'above' organ	6
DS - Mitochondria - 'above' tissue	3
DS - Mitochondria - 'below' donation (general)	2
DS - Mitochondria - 'below' egg/sperm/embryo	33
DS - Mitochondria - 'below' face transplant	1
DS - Mitochondria - 'below' organ	4
DS - Mitochondria - 'below' surrogacy	1
DS - Mitochondria - complex/uncomfortable donation	7
DS - Mitochondria - depends on MST/PNT	30
DS - Mitochondria - depends on MtDNA function	5
DS - Mitochondria - depends on sex of child	2
DS - Mitochondria - difference in choice/consent	5
DS - Mitochondria - difference in longevity of impact	16
DS - Mitochondria - difference in method of donation	3
DS - Mitochondria - difference in perception/ethics	2
DS - Mitochondria - difference in timing	8
DS - Mitochondria - difference is third person DNA/genetic information	94
DS - Mitochondria - different to blood	96
DS - Mitochondria - different to bone marrow	27
DS - Mitochondria - different to donation (general)	77
DS - Mitochondria - different to egg/sperm/embryo	121
DS - Mitochondria - different to organ	102
DS - Mitochondria - different to stem cells	1
DS - Mitochondria - different to surrogacy	3

Code	Count
DS - Mitochondria - different to tissue	12
DS - Mitochondria - envelope/carrier/overcoat	3
DS - Mitochondria - less pervasive	2
DS - Mitochondria - minor/uncomplicated donation	3
DS - Mitochondria - mixed comparison	27
DS - Mitochondria - more pervasive	12
DS - Mitochondria - similar to adoption	2
DS - Mitochondria - similar to biopsy	1
DS - Mitochondria - similar to blood	92
DS - Mitochondria - similar to bone marrow	51
DS - Mitochondria - similar to donation (general)	72
DS - Mitochondria - similar to egg/sperm/embryo/IVF	113
DS - Mitochondria - similar to organ	68
DS - Mitochondria - similar to stem cells	4
DS - Mitochondria - similar to surrogacy	5
DS - Mitochondria - similar to tissue	33
DS - Mitochondria - unessential donation	2
DS - Mitochondria - unique type of donation	10
DS - Origin - allow choice	1
DS - Origin - makes no difference	1
DS - Origin - mitochondria bank/anonymous	3
DS - Origin - should be family member/close relative	2
DS - Origin - should be relative/friend	3
DS - Origin - should be same haplogroup	1
DS - Origin - should be unconnected to family	1
DS - Origin - should not be maternal relative	1
DS - Overall - not sure/no view	8
DS - Overall - oppose donation of all/any kind	10
DS - Overall - other comment	7
DS - Overall - support donation of all/any kind	2
DS - Overall - varied views on donation types	6
IN - Age - 18/when reaching adulthood	10
IN - Age - before 18	1
IN - Age - other comment	1
IN - Child identity - should not be known by donor	7

Code	Count
IN - Child rights - no right to contact donor	2
IN - Child rights - other comment	2
IN - Child rights - should take priority	5
IN - Child rights - to information generally	11
IN - Child rights - to know origins/donor/parents	25
IN - Child rights - to understand process/implications	6
IN - Donor identity - available for specific reasons	1
IN - Donor identity - depends on who the donor is	3
IN - Donor identity - not known by parents	1
IN - Donor identity - not relevant/necessary	6
IN - Donor identity - other comment	7
IN - Donor identity - should be available (general)	17
IN - Donor identity - should be optional/not mandatory	27
IN - Donor identity - should not be available (other/general)	26
IN - Donor rights - not to have relationship with child	1
IN - Donor rights - other comment	5
IN - Donor rights - to anonymity/lack of intrusion	22
IN - Donor rights - to know success of treatment	3
IN - Donor rights - to understand procedure	13
IN - Logistics - donor screening	10
IN - Logistics - information storage/records	11
IN - Medical info - available for specific reasons/circumstances	12
IN - Medical info - not relevant/necessary	1
IN - Medical info - should be available (general)	6
IN - Overall - depends on other factor	1
IN - Overall - legal considerations	3
IN - Overall - no information needed	3
IN - Overall - other comment	6
IN - Overall decision - flexible/mutual/depends	3
IN - Overall decision - parents'/family's	4
IN - Personal info - not relevant/necessary	2
IN - Personal info - should be available (general)	1
IN - Personal info - should not be available (other/general)	1
O - Blank response/no comment	17
O - Refer to other question	18



Code	Count
O - Refer to other response	2
RF - Current legislation	4
RF - Current legislation - non UK	4
RF - External document	2
RF - HFEA	3
RF - Historical experience	2
RF - Media coverage	4
RF - Other evidence/examples	2
RF - Participant - friend/relative/child with MD/similar disease	4
RF - Participant - has MD/similar disease	1
RF - Participant - info about	14
RF - Participant - other medical details	1
RF - Politics/government	4
RF - Relevant research	2
RF - Religion	6
RF - Specific individual/organisation/group	5
RF - Views of other people/participants	10
SC - DNA - nuclear DNA/genome not affected	29
SC - DNA - other comment	6
SC - Germ line - should not be altered	1
SC - Mitochondria - function/form	29
SC - Mt DNA - does not determine identity/traits	56
SC - Mt DNA - limited amount/types	5
SC - Mt DNA - may affect identity/traits	10
SC - Mt DNA - origin/not human	2
SC - Mt DNA - other comment	6
SC - Mt DNA - small quantity/impact	64
SC - Other procedures - adoption	2
SC - Other procedures - IVF/egg or sperm donation/surrogacy	5
SC - Overall - addition/alternative suggestions	1
SC - Overall - further research/trials/evidence	3
SC - Overall - invest in other priorities/solutions	11
SC - Overall - motivation of scientists	1
SC - Overall - need more research/don't know enough	7
SC - Overall - object to infertility treatment	4

Code	Count
SC - Overall - question about application	2
SC - Overall - trust/mistrust of scientists	2
SC - Overall - understanding is limited	5
SC - Progress - reducing MD is good/positive	3
SC - Progress - requires caution	1
SC - Regulation - other comment	3
SC - Regulation - specifics	3
SC - Safety - other comment	1
SE - Ethical - comparison with other donations	4
SE - Ethical - consent/choice concern	5
SE - Ethical - embryo rights/usage concern	157
SE - Ethical - embryo rights/usage other	9
SE - Ethical - end does not justify means	1
SE - Ethical - equity of provision	2
SE - Ethical - implications	4
SE - Ethical - interfering with evolution/playing god	22
SE - Ethical - judging value/worth of life	3
SE - Ethical - no implications/concerns	2
SE - Ethical - no right to healthy/genetically related child	3
SE - Ethical - other comment	5
SE - Ethical - right to healthy/genetically related child	1
SE - Ethical - sanctity/dignity of human life	19
SE - Ethical - slippery slope generally/crossing boundary	12
SE - Ethical - slippery slope to designer babies/commoditisation	6
SE - Ethical - slippery slope to eugenics	2
SE - Ethical - slippery slope/similar to cloning	9
SE - General - benefits outweigh issues	3
SE - General - current social/ethical expectations	3
SE - General - implications (Yes)	3
SE - General - implications minimal/insignificant	1
SE - General - other procedures acceptable/better	4
SE - General - preferable to other procedures	4
SE - General - unforeseen problems/impacts/health issues	28
SE - Social - attitudes towards disabled people/MD sufferers	1
SE - Social - attitudes towards those treated	2

Code	Count
SE - Social - availability of counselling/testing/support	1
SE - Social - benefit to future generations	3
SE - Social - benefits to potential parents/families/relationships	5
SE - Social - child emotional/psychological impact	8
SE - Social - child health/wellbeing improved	4
SE - Social - child ID/mixed genetic make-up	24
SE - Social - child rights	1
SE - Social - donor considerations (other)	3
SE - Social - donor/child bond OR lack of bond	12
SE - Social - donor/child relationship difficulties	2
SE - Social - ID from nurture/upbringing/beyond genetics	1
SE - Social - ID issues (other)	2
SE - Social - ID issues cannot be known yet	1
SE - Social - ID/issues complex/different for everyone	2
SE - Social - impact on family relationships (not third parent)	1
SE - Social - impact on future generations	10
SE - Social - impact on lineage/traceability	3
SE - Social - minimal/insignificant ID issues	1
SE - Social - no ID issues/implications foreseen	4
SE - Social - ongoing monitoring/follow-up	3
SE - Social - overpopulation	1
SE - Social - parent psychological impact	1
SE - Social - parent rights/responsibilities	5
SE - Social - risk losing valuable individuals	1
SE - Social - third party parentage issues	13

b) Thinking about your response to 4a, what information about the mitochondria donor do you think a child should have? (Choose one response only)

- The child should get no information
- The child should be able to get medical and personal information about the mitochondria donor, but never know their identity
- The child should be able to get medical and personal information about the mitochondria donor and be able to contact them once the child reaches the age of 18
- Other
- I do not think mitochondria replacement should be permitted in treatment at all

Please explain your choice.

Code	Count
AC - Acceptable - MST	1
AC - Acceptable - MST and PNT/general	2
AC - Not acceptable - MST and PNT/general	103
AC - Not acceptable - PNT	1
AC - Not sure - MST and PNT/general	1
AC - Overall - understand issue/have sympathy	6
AC - Overall - unsure/no strong view	2
AG - Altering DNA - cloning/hybridisation	3
AG - Altering DNA - impact on germ line/lineage	13
AG - Altering DNA - not acceptable	7
AG - Cost - too much/cannot be justified	2
AG - Costs/risks - outweigh benefits	7
AG - Disease - will not be eradicated/not a cure	2
AG - Donation - risk/exploitation	5
AG - Ethics - creation/destruction of egg/embryo	84
AG - Ethics - general/too many ethical issues	39
AG - Ethics - interfering with evolution/playing god	30
AG - Ethics - judging value/worth of life (particularly PNT)	2
AG - Ethics - lack of consent/choice	3
AG - Ethics - no right to healthy/genetically related child	6
AG - Ethics - other comment	1
AG - Ethics - sanctity/dignity of human life	27
AG - Ethics - UK first in crossing ethical boundary	2
AG - Future - risks/impacts/unintended consequences	47
AG - MST - could be more emotionally difficult	1
AG - Population - too big/would increase	1
AG - Preferable alternative - adoption	5
AG - Preferable alternative - decide not to conceive	3
AG - Preferable alternative - IVF	1
AG - Preferable alternative - other treatment/cure of MD	29
AG - Preferable alternative - other/general	1
AG - Regulation - can't guarantee limits	1
AG - Regulation - may not be consistent across the board	2
AG - Science - false hope/may not work	2
AG - Science - just because it is possible does not mean it should be done	4

Code	Count
AG - Science - role/motivation of scientists	4
AG - Science - understanding is limited	2
AG - Slippery slope - cloning	6
AG - Slippery slope - concerns	18
AG - Slippery slope - designer babies/commoditisation	5
AG - Slippery slope - eugenics	7
AG - Social - general/too many social issues	1
AG - Social - impact on child/identity/psychology	45
AG - Social - impact on donor/donor considerations	3
AG - Social - impact on family relationships	2
AG - Social - impact on parents	3
AG - Social - legal implications/scenarios	7
AG - Social - prioritise other issues/solutions	5
AG - Social - third person as parent/donor	23
AG - Social - worth of MD sufferers/disabled people	3
AG - Wider issue - against artificial fertilisation	5
CO - Labelling of techniques - misleading/misunderstood	11
CP - Consultation - comment on question	30
CP - Consultation - cost concern	1
CP - Consultation - other negative comment	2
CP - Consultation - other positive comment	1
CP - Consultation - question motivations/bias	3
CP - Consultation - question process	2
CP - Consultation - specific information	1
CP - Consultation - suspect foregone conclusion	1
CP - Follow-up - public communication/education	1
CP - Follow-up - wider debate	1
CP - Website - general	1
DS - Donor - availability issues/considerations	53
DS - Donor - responsibility for actions/know what they are getting into	10
DS - Donor function - providing medical solution/repair	8
DS - Donor motivation - gift/altruism	14
DS - Donor motivation - other	2
DS - Donor status - does have rights/responsibilities to child	2
DS - Donor status - is not parent/relation to child	29

Code	Count
DS - Donor status - is parent/relation to child	8
DS - Donor status - is part of child's make-up	2
DS - Donor status - is relation but not parent	1
DS - Donor status - is unclear/ambiguous	3
DS - Donor status - no rights/responsibilities to child	5
DS - Origin - makes no difference	1
IN - Age - 18 is too young	1
IN - Age - 18/when reaching adulthood	32
IN - Age - no minimum/from the start	5
IN - Age - no minimum/other factors	2
IN - Age - other comment	9
IN - Child - understand curiosity	13
IN - Child identity - should not be known by donor	3
IN - Child rights - may want to thank donor	17
IN - Child rights - no right to contact donor	7
IN - Child rights - no right/reason to access any information	13
IN - Child rights - not to feel obligated	2
IN - Child rights - other comment	18
IN - Child rights - should take priority	2
IN - Child rights - to information generally	28
IN - Child rights - to know origins/donor/parents	90
IN - Child rights - to understand process/implications	44
IN - Donor identity - depends on who the donor is	5
IN - Donor identity - family likely to know donor	1
IN - Donor identity - not relevant/necessary	44
IN - Donor identity - other comment	2
IN - Donor identity - should be available (general)	12
IN - Donor identity - should be optional/not mandatory	42
IN - Donor identity - should not be available (other/general)	17
IN - Donor identity - would not benefit child	3
IN - Donor identity/info - misrepresents contribution	16
IN - Donor rights - not to have relationship with child	3
IN - Donor rights - other comment	4
IN - Donor rights - to anonymity/lack of intrusion	36
IN - Donor rights - to know/contact family/child	4

Code	Count
IN - Donor status - different to adoption/surrogacy	4
IN - Donor status - different to blood/tissue/organ donor	2
IN - Donor status - different to donation (non specific)	1
IN - Donor status - different to egg/sperm donor	23
IN - Donor status - same as adoption/surrogacy	5
IN - Donor status - same as blood/tissue/organ donor	79
IN - Donor status - same as donation (non specific)	2
IN - Donor status - same as egg/sperm donor	42
IN - Logistics - database/infrastructure resourcing	1
IN - Logistics - donor screening	6
IN - Logistics - information storage/records	9
IN - Medical info - available for specific reasons/circumstances	82
IN - Medical info - not relevant/necessary	3
IN - Medical info - should be available (general)	45
IN - Option - between 1 and 2	2
IN - Option 1 - would be other choice	3
IN - Option 2 - for male children	1
IN - Option 2 - other comment	8
IN - Option 2 - preferred/if have to choose	3
IN - Option 2 - would be other choice	8
IN - Option 3 - for female children	1
IN - Option 3 - opposing comment	1
IN - Option 3 - other comment	8
IN - Option 3 - preferred/if have to choose	12
IN - Option 3 - would be other choice	7
IN - Option 5 - against/but if I have to choose	9
IN - Option 5 - would be other choice	3
IN - Overall - all/any information (option 3)	14
IN - Overall - balancing interests of parties	6
IN - Overall - depends on MST/PNT	17
IN - Overall - depends on other factor	2
IN - Overall - legal considerations	11
IN - Overall - minimum/only in some circumstances	2
IN - Overall - misuse of information	1
IN - Overall - more information than these options provide	4

Code	Count
IN - Overall - no information needed (option 1)	18
IN - Overall - not sure	5
IN - Overall - other comment	11
IN - Overall - rethink if/when research/knowledge progresses	9
IN - Overall - some/limited information (option 1)	1
IN - Overall - some/limited information (option 2)	4
IN - Overall decision - child's	13
IN - Overall decision - donor's	15
IN - Overall decision - flexible/mutual/depends	21
IN - Overall decision - parents'/family's	11
IN - Personal info - available for specific reasons/circumstances	12
IN - Personal info - not relevant/necessary	7
IN - Personal info - not sure	1
IN - Personal info - should be available (general)	25
IN - Personal info - should be optional/not mandatory	1
IN - Personal info - should not be available (other/general)	7
IN - Selected - no answer	6
IN - Selected - none selected	142
IN - Selected - option 1	111
IN - Selected - option 2	153
IN - Selected - option 3	153
IN - Selected - option 4	83
IN - Selected - option 5	514
O - Blank response/no comment	257
O - Other/general comment	2
O - Refer to other question	157
RF - Current legislation	1
RF - Current legislation - non UK	9
RF - External document	1
RF - HFEA	2
RF - Historical experience	7
RF - Other evidence/examples	2
RF - Participant - friend/relative/child with MD/similar disease	1
RF - Participant - info about	11
RF - Participant - other medical details	4



Code	Count
RF - Politics/government	1
RF - Relevant research	2
RF - Religion	17
RF - Specific individual/organisation/group	8
RF - Views of other people/participants	2
SC - DNA - nuclear DNA/genome not affected	15
SC - Mitochondria - function/form	9
SC - Mt DNA - does not determine identity/traits	60
SC - Mt DNA - maternal/female line	4
SC - Mt DNA - may affect identity/traits	2
SC - Mt DNA - other comment	4
SC - Mt DNA - small quantity/impact	39
SC - Mt DNA - suggested source for donation	1
SC - Other procedures - IVF/egg or sperm donation/surrogacy	3
SC - Other procedures - organ/tissue/blood donation	1
SC - Other procedures - stem cell donation	1
SC - Other procedures - vaccination	1
SC - Overall - assessing/managing risk	1
SC - Overall - balancing science/ethics/religion/society	1
SC - Overall - further research/trials/evidence	5
SC - Overall - new procedure/knowledge will grow	2
SC - Overall - other comment	2
SC - Overall - question about application	1
SC - Overall - understanding is limited	3
SC - Regulation - needed	1
SC - Regulation - other comment	1
SC - Regulation - specifics	1
SE - Ethical - consent/choice concern	1
SE - Ethical - consent/choice other	1
SE - General - current social/ethical expectations	3
SE - General - unforeseen problems/impacts/health issues	1
SE - Social - attitudes towards those treated	1
SE - Social - availability of counselling/testing/support	2
SE - Social - child emotional/psychological impact	13
SE - Social - child health/wellbeing improved	1

Code	Count
SE - Social - child health/wellbeing other	1
SE - Social - child ID/mixed genetic make-up	12
SE - Social - ID issues similar/no different to other procedures	1
SE - Social - impact on family relationships (not third parent)	1
SE - Social - impact on future generations	1
SE - Social - impact on lineage/traceability	2
SE - Social - legal implications/issues	1
SE - Social - no ID issues/implications foreseen	2
SE - Social - ongoing monitoring/follow-up	1
SE - Social - parent psychological impact	2
SE - Social - parent rights/responsibilities	10
SE - Social - third party parentage issues	4

## 5. Regulation of mitochondria replacement

If the law changed to allow mitochondria replacement to take place in a specialist clinic regulated by the HFEA, how should decisions be made on who can access this treatment? (Choose one response only)

- Clinics and their patients should decide when mitochondria replacement is appropriate in individual cases
- The regulator should decide which mitochondrial diseases are serious enough to require mitochondria replacement and, just for these diseases, permit clinics and patients to decide when it is appropriate in individual cases
- The regulator should decide which mitochondrial diseases are serious enough to require mitochondria replacement and also decide, just for these diseases, when it is appropriate in individual cases
- I do not think mitochondria replacement should be permitted in treatment at all

Please explain your choice.

Code	Count
AC - Acceptable - MST and PNT/general	5
AC - Not acceptable - MST and PNT/general	114
AC - Not acceptable - PNT	3
AC - Overall - unsure/no strong view	1
AG - Altering DNA - cloning/hybridisation	6
AG - Altering DNA - impact on germ line/lineage	10
AG - Altering DNA - not acceptable	3
AG - Costs/risks - outweigh benefits	7
AG - Disease - will not be eradicated/not a cure	2

Code	Count
AG - Donation - risk/exploitation	4
AG - Ethics - creation/destruction of egg/embryo	50
AG - Ethics - end does not justify means	3
AG - Ethics - general/too many ethical issues	13
AG - Ethics - interfering with evolution/playing god	27
AG - Ethics - judging value/worth of life (particularly PNT)	8
AG - Ethics - lack of consent/choice	1
AG - Ethics - no right to healthy/genetically related child	7
AG - Ethics - sanctity/dignity of human life	25
AG - Ethics - UK first in crossing ethical boundary	8
AG - Future - risks/impacts/unintended consequences	26
AG - Other - other comment	5
AG - Population - too big/would increase	1
AG - Preferable alternative - adoption	4
AG - Preferable alternative - decide not to conceive	4
AG - Preferable alternative - other treatment/cure of MD	20
AG - Preferable alternative - other/general	4
AG - Science - false hope/may not work	6
AG - Science - just because it is possible does not mean it should be done	6
AG - Science - role/motivation of scientists	4
AG - Science - understanding is limited	3
AG - Slippery slope - attitudes to euthanasia	1
AG - Slippery slope - cloning	6
AG - Slippery slope - concerns	27
AG - Slippery slope - designer babies/commoditisation	6
AG - Slippery slope - eugenics	10
AG - Social - general/too many social issues	1
AG - Social - impact on child/identity/psychology	13
AG - Social - impact on family relationships	4
AG - Social - legal implications/scenarios	3
AG - Social - prioritise other issues/solutions	2
AG - Social - third person as parent/donor	11
AG - Social - worth of MD sufferers/disabled people	4
AG - Wider issue - against artificial fertilisation	4
CO - Labelling of techniques - misleading/misunderstood	9

Code	Count
CP - Consultation - comment on question	19
CP - Consultation - outcomes	2
CP - Consultation - question motivations/bias	1
CP - Consultation - question process	6
DM - Clinicians - advise/recommend/input into decision	33
DM - Clinicians - are professional/should be trusted	3
DM - Clinicians - business interest/other motivation	28
DM - Clinicians - have closest knowledge	16
DM - Clinicians - other comment	7
DM - Clinicians - self-regulation/autonomy	6
DM - Clinicians - should decide	12
DM - Clinicians - should decide within boundaries set by regulator	25
DM - Criteria - base on science/facts	9
DM - Criteria - ensure safety	8
DM - Criteria - last resort only	3
DM - Criteria - medical/psychological considerations	4
DM - Criteria - none/any application should be allowed	8
DM - Criteria - none/treat all diseases/individuals	23
DM - Criteria - other	4
DM - Criteria - patient need/want/case by case	45
DM - Criteria - process/difficulty in setting criteria	15
DM - Criteria - seriousness of diseases/impacts	35
DM - Option 1 - could be introduced later	4
DM - Option 1 - opposing comment	4
DM - Option 1 - other comment	3
DM - Option 1 - would be other choice	2
DM - Option 2 - could be introduced later	2
DM - Option 2 - for MST only	1
DM - Option 2 - if shortage of donors	1
DM - Option 2 - opposing comment	3
DM - Option 2 - other comment	5
DM - Option 2 - preferred/if have to choose	11
DM - Option 3 - for MST only	1
DM - Option 3 - in specific/less clear cases	1
DM - Option 3 - opposing comment	9

Code	Count
DM - Option 3 - other comment	2
DM - Option 3 - preferred/if have to choose	18
DM - Option 4 - opposing comment	1
DM - Overall - alternative approach	3
DM - Overall - consider rare/new/uncategorised diseases	14
DM - Overall - different to other procedures	1
DM - Overall - lack of trust in government/regulator	5
DM - Overall - no/minimal risk of abuse/overuse	8
DM - Overall - not sure	1
DM - Overall - other comment	19
DM - Overall - rethink if needed/after set time	8
DM - Overall - risk of abuse/overuse	9
DM - Overall - similar/no different to other procedures	14
DM - Overall - this is workable/sensible option	9
DM - Parliament - should have ultimate control	32
DM - Patient/clinician - able to influence decision	1
DM - Patient/clinician - have closest knowledge	10
DM - Patient/clinician - joint decision	49
DM - Patient/clinician - joint decision within boundaries set by regulator	47
DM - Patient/clinician - self-regulation	3
DM - Patients - have closest knowledge	10
DM - Patients - involvement in decision/choice	20
DM - Patients - may go elsewhere/abroad	2
DM - Patients - other comment	2
DM - Patients - question motivation	7
DM - Patients - should decide	32
DM - Patients - should decide within boundaries set by regulator	8
DM - Regulator - adds bureaucracy/cost/distress	25
DM - Regulator - appeals process	4
DM - Regulator - closer involvement upfront/early on	19
DM - Regulator - doesn't make it OK/ethical	40
DM - Regulator - helps ensure clinic performance/quality	19
DM - Regulator - helps ensure safety/quality	5
DM - Regulator - helps limit cost/distribute limited resource	8
DM - Regulator - helps prevent abuse/overuse/ensure legality	35

Code	Count
DM - Regulator - helps public acceptability	7
DM - Regulator - impartial/independent/trusted	8
DM - Regulator - international implications	5
DM - Regulator - involvement is necessary (general/other)	30
DM - Regulator - makes decisions on individual cases (option 3)	13
DM - Regulator - must be accountable/trustworthy	4
DM - Regulator - not appropriate to involve	20
DM - Regulator - not necessary to involve	8
DM - Regulator - other comment	20
DM - Regulator - oversight/review role	26
DM - Regulator - politically/financially driven	9
DM - Regulator - reference existing PGD approach	12
DM - Regulator - sets boundaries not individual cases (option 2)	66
DM - Regulator - should not be overburdened	5
DM - Regulator - strict/stringent rules needed	20
DM - Regulator - too distant/generalist/lacking in knowledge	27
DM - Regulator - will not be effective	36
DM - Resourcing - concern over NHS resource	2
DM - Resourcing - other comment	5
DM - Resourcing - should be from patients/privately	4
DM - Resourcing - should not take precedence	2
DM - Selected - no answer	12
DM - Selected - none selected	12
DM - Selected - option 1	232
DM - Selected - option 2	185
DM - Selected - option 3	55
DM - Selected - option 4	547
DM - Timescales - should be fast/efficient	4
O - Blank response/no comment	204
O - Refer to other question	178
RF - Current legislation	8
RF - Current legislation - non UK	11
RF - HFEA	37
RF - Historical experience	29
RF - Media coverage	1

Code	Count
RF - Participant - friend/relative/child with MD/similar disease	4
RF - Participant - has MD/similar disease	1
RF - Participant - info about	6
RF - Participant - other medical details	2
RF - Politics/government	19
RF - Relevant research	2
RF - Religion	9
RF - Views of other people/participants	4
SC - Germ line - could reduce in diversity	1
SC - MD - testing mothers	2
SC - MD - variety of forms/impacts	22
SC - Mitochondria - function/form	3
SC - Mt DNA - does not determine identity/traits	1
SC - Other procedures - abortion/termination	9
SC - Other procedures - adoption	1
SC - Other procedures - genetic techniques/gene therapy	6
SC - Other procedures - IVF/egg or sperm donation/surrogacy	3
SC - Other procedures - organ/tissue/blood donation	6
SC - Other procedures - other/general	4
SC - Overall - nature of medicine/science	4
SC - Overall - new procedure/knowledge will grow	7
SC - Overall - other comment	3
SC - Overall - question about application	2
SC - Overall - understanding is limited	3
SC - Progress - has gone too far to stop now	2
SC - Progress - reducing MD is good/positive	3
SC - Safety - other comment	3
SE - Ethical - benefits small number	3
SE - Ethical - embryo rights/usage other	3
SE - Ethical - equity of provision	16
SE - Ethical - ethical imperative to intervene	4
SE - Ethical - having healthy children is a right	2
SE - Ethical - having healthy children not a right/essential	1
SE - Ethical - implications	1
SE - Ethical - no slippery slope/not crossing boundary	2

Code	Count
SE - Ethical - slippery slope generally/crossing boundary	5
SE - Ethical - slippery slope to designer babies/commoditisation	6
SE - Ethical tradeoffs - evolution vs familial distress	1
SE - Ethical tradeoffs - safety vs progress	1
SE - Ethical tradeoffs - society vs individual	1
SE - General - benefits outweigh issues	1
SE - General - current social/ethical expectations	4
SE - General - no implications/concerns (No)	1
SE - General - unforeseen problems/impacts/health issues	4
SE - Social - benefits to potential parents/families/relationships	4
SE - Social - child awareness/understanding	1
SE - Social - child health/wellbeing improved	5
SE - Social - child health/wellbeing other	6
SE - Social - child rights	5
SE - Social - donor considerations	2
SE - Social - impact on future generations	1
SE - Social - issues from having MD/disability	3
SE - Social - legal implications/issues	1
SE - Social - ongoing monitoring/follow-up	2
SE - Social - overpopulation	1
SE - Social - parent rights/responsibilities	1
SE - Social - parents should not be pressurised	1

## 6. Should the law be changed?

In Question 1, we asked for your views on the mitochondria replacement techniques MST and PNT. Please could you now tell us if you think the law should be changed to allow (one or both of) these techniques to be made available to people who are at risk of passing on mitochondrial disease to their child?

Code	Count
AC - Acceptable - MST and PNT/general	5
AC - Not acceptable - MST and PNT/general	114
AC - Not acceptable - PNT	3
AC - Overall - unsure/no strong view	1
AG - Altering DNA - cloning/hybridisation	6
AG - Altering DNA - impact on germ line/lineage	10
AG - Altering DNA - not acceptable	3



Code	Count
AG - Costs/risks - outweigh benefits	7
AG - Disease - will not be eradicated/not a cure	2
AG - Donation - risk/exploitation	4
AG - Ethics - creation/destruction of egg/embryo	50
AG - Ethics - end does not justify means	3
AG - Ethics - general/too many ethical issues	13
AG - Ethics - interfering with evolution/playing god	27
AG - Ethics - judging value/worth of life (particularly PNT)	8
AG - Ethics - lack of consent/choice	1
AG - Ethics - no right to healthy/genetically related child	7
AG - Ethics - sanctity/dignity of human life	25
AG - Ethics - UK first in crossing ethical boundary	8
AG - Future - risks/impacts/unintended consequences	26
AG - Other - other comment	5
AG - Population - too big/would increase	1
AG - Preferable alternative - adoption	4
AG - Preferable alternative - decide not to conceive	4
AG - Preferable alternative - other treatment/cure of MD	20
AG - Preferable alternative - other/general	4
AG - Science - false hope/may not work	6
AG - Science - just because it is possible does not mean it should be done	6
AG - Science - role/motivation of scientists	4
AG - Science - understanding is limited	3
AG - Slippery slope - attitudes to euthanasia	1
AG - Slippery slope - cloning	6
AG - Slippery slope - concerns	27
AG - Slippery slope - designer babies/commoditisation	6
AG - Slippery slope - eugenics	10
AG - Social - general/too many social issues	1
AG - Social - impact on child/identity/psychology	13
AG - Social - impact on family relationships	4
AG - Social - legal implications/scenarios	3
AG - Social - prioritise other issues/solutions	2
AG - Social - third person as parent/donor	11
AG - Social - worth of MD sufferers/disabled people	4

Code	Count
AG - Wider issue - against artificial fertilisation	4
CO - Labelling of techniques - misleading/misunderstood	9
CP - Consultation - comment on question	19
CP - Consultation - outcomes	2
CP - Consultation - question motivations/bias	1
CP - Consultation - question process	6
DM - Clinicians - advise/recommend/input into decision	33
DM - Clinicians - are professional/should be trusted	3
DM - Clinicians - business interest/other motivation	28
DM - Clinicians - have closest knowledge	16
DM - Clinicians - other comment	7
DM - Clinicians - self-regulation/autonomy	6
DM - Clinicians - should decide	12
DM - Clinicians - should decide within boundaries set by regulator	25
DM - Criteria - base on science/facts	9
DM - Criteria - ensure safety	8
DM - Criteria - last resort only	3
DM - Criteria - medical/psychological considerations	4
DM - Criteria - none/any application should be allowed	8
DM - Criteria - none/treat all diseases/individuals	23
DM - Criteria - other	4
DM - Criteria - patient need/want/case by case	45
DM - Criteria - process/difficulty in setting criteria	15
DM - Criteria - seriousness of diseases/impacts	35
DM - Option 1 - could be introduced later	4
DM - Option 1 - opposing comment	4
DM - Option 1 - other comment	3
DM - Option 1 - would be other choice	2
DM - Option 2 - could be introduced later	2
DM - Option 2 - for MST only	1
DM - Option 2 - if shortage of donors	1
DM - Option 2 - opposing comment	3
DM - Option 2 - other comment	5
DM - Option 2 - preferred/if have to choose	11
DM - Option 3 - for MST only	1

Code	Count
DM - Option 3 - in specific/less clear cases	1
DM - Option 3 - opposing comment	9
DM - Option 3 - other comment	2
DM - Option 3 - preferred/if have to choose	18
DM - Option 4 - opposing comment	1
DM - Overall - alternative approach	3
DM - Overall - consider rare/new/uncategorised diseases	14
DM - Overall - different to other procedures	1
DM - Overall - lack of trust in government/regulator	5
DM - Overall - no/minimal risk of abuse/overuse	8
DM - Overall - not sure	1
DM - Overall - other comment	19
DM - Overall - rethink if needed/after set time	8
DM - Overall - risk of abuse/overuse	9
DM - Overall - similar/no different to other procedures	14
DM - Overall - this is workable/sensible option	9
DM - Parliament - should have ultimate control	32
DM - Patient/clinician - able to influence decision	1
DM - Patient/clinician - have closest knowledge	10
DM - Patient/clinician - joint decision	49
DM - Patient/clinician - joint decision within boundaries set by regulator	47
DM - Patient/clinician - self-regulation	3
DM - Patients - have closest knowledge	10
DM - Patients - involvement in decision/choice	20
DM - Patients - may go elsewhere/abroad	2
DM - Patients - other comment	2
DM - Patients - question motivation	7
DM - Patients - should decide	32
DM - Patients - should decide within boundaries set by regulator	8
DM - Regulator - adds bureaucracy/cost/distress	25
DM - Regulator - appeals process	4
DM - Regulator - closer involvement upfront/early on	19
DM - Regulator - doesn't make it OK/ethical	40
DM - Regulator - helps ensure clinic performance/quality	19
DM - Regulator - helps ensure safety/quality	5

Code	Count
DM - Regulator - helps limit cost/distribute limited resource	8
DM - Regulator - helps prevent abuse/overuse/ensure legality	35
DM - Regulator - helps public acceptability	7
DM - Regulator - impartial/independent/trusted	8
DM - Regulator - international implications	5
DM - Regulator - involvement is necessary (general/other)	30
DM - Regulator - makes decisions on individual cases (option 3)	13
DM - Regulator - must be accountable/trustworthy	4
DM - Regulator - not appropriate to involve	20
DM - Regulator - not necessary to involve	8
DM - Regulator - other comment	20
DM - Regulator - oversight/review role	26
DM - Regulator - politically/financially driven	9
DM - Regulator - reference existing PGD approach	12
DM - Regulator - sets boundaries not individual cases (option 2)	66
DM - Regulator - should not be overburdened	5
DM - Regulator - strict/stringent rules needed	20
DM - Regulator - too distant/generalist/lacking in knowledge	27
DM - Regulator - will not be effective	36
DM - Resourcing - concern over NHS resource	2
DM - Resourcing - other comment	5
DM - Resourcing - should be from patients/privately	4
DM - Resourcing - should not take precedence	2
DM - Selected - no answer	12
DM - Selected - none selected	12
DM - Selected - option 1	232
DM - Selected - option 2	185
DM - Selected - option 3	55
DM - Selected - option 4	547
DM - Timescales - should be fast/efficient	4
Holding	1
O - Blank response/no comment	204
O - Refer to other question	178
RF - Current legislation	8
RF - Current legislation - non UK	11

Code	Count
RF - HFEA	37
RF - Historical experience	29
RF - Media coverage	1
RF - Participant - friend/relative/child with MD/similar disease	4
RF - Participant - has MD/similar disease	1
RF - Participant - info about	6
RF - Participant - other medical details	2
RF - Politics/government	19
RF - Relevant research	2
RF - Religion	9
RF - Views of other people/participants	4
SC - Germ line - could reduce in diversity	1
SC - MD - testing mothers	2
SC - MD - variety of forms/impacts	22
SC - Mitochondria - function/form	3
SC - Mt DNA - does not determine identity/traits	1
SC - Other procedures - abortion/termination	9
SC - Other procedures - adoption	1
SC - Other procedures - genetic techniques/gene therapy	6
SC - Other procedures - IVF/egg or sperm donation/surrogacy	3
SC - Other procedures - organ/tissue/blood donation	6
SC - Other procedures - other/general	4
SC - Overall - nature of medicine/science	4
SC - Overall - new procedure/knowledge will grow	7
SC - Overall - other comment	3
SC - Overall - question about application	2
SC - Overall - understanding is limited	3
SC - Progress - has gone too far to stop now	2
SC - Progress - reducing MD is good/positive	3
SC - Safety - other comment	3
SE - Ethical - benefits small number	3
SE - Ethical - embryo rights/usage other	3
SE - Ethical - equity of provision	16
SE - Ethical - ethical imperative to intervene	4
SE - Ethical - having healthy children is a right	2

Code	Count
SE - Ethical - having healthy children not a right/essential	1
SE - Ethical - implications	1
SE - Ethical - no slippery slope/not crossing boundary	2
SE - Ethical - slippery slope generally/crossing boundary	5
SE - Ethical - slippery slope to designer babies/commoditisation	6
SE - Ethical tradeoffs - evolution vs familial distress	1
SE - Ethical tradeoffs - safety vs progress	1
SE - Ethical tradeoffs - society vs individual	1
SE - General - benefits outweigh issues	1
SE - General - current social/ethical expectations	4
SE - General - no implications/concerns (No)	1
SE - General - unforeseen problems/impacts/health issues	4
SE - Social - benefits to potential parents/families/relationships	4
SE - Social - child awareness/understanding	1
SE - Social - child health/wellbeing improved	5
SE - Social - child health/wellbeing other	6
SE - Social - child rights	5
SE - Social - donor considerations	2
SE - Social - impact on future generations	1
SE - Social - issues from having MD/disability	3
SE - Social - legal implications/issues	1
SE - Social - ongoing monitoring/follow-up	2
SE - Social - overpopulation	1
SE - Social - parent rights/responsibilities	1
SE - Social - parents should not be pressurised	1

## 7. Further considerations

Are there any other considerations you think decision makers should take into account when deciding whether or not to permit mitochondria replacement?

Code	Count
AC - Acceptable - MST	2
AC - Acceptable - MST and PNT/general	6
AC - Acceptable with caveat - MST and PNT/general	4
AC - Not acceptable - MST and PNT/general	21
AC - Not acceptable - PNT	2

Code	Count
AC - Overall - understand issue/have sympathy	11
AC - Preference - MST over PNT	1
AG - Altering DNA - cloning/hybridisation	35
AG - Altering DNA - impact on germ line/lineage	36
AG - Altering DNA - not acceptable	28
AG - Cost - too much/cannot be justified	5
AG - Costs/risks - outweigh benefits	2
AG - Disease - will not be eradicated/not a cure	8
AG - Donation - risk/exploitation	9
AG - Ethics - creation/destruction of egg/embryo	10
AG - Ethics - embryo (mainly PNT) creation/destruction	100
AG - Ethics - end does not justify means	34
AG - Ethics - general/too many ethical issues	23
AG - Ethics - interfering with evolution/playing god	66
AG - Ethics - lack of consent/choice	1
AG - Ethics - no right to healthy/genetically related child	38
AG - Ethics - sanctity/dignity of human life	43
AG - Ethics - UK first in crossing ethical boundary	15
AG - Future - risks/impacts/unintended consequences	59
AG - Overall - not our decision to make/no right	6
AG - Population - too big/would increase	4
AG - Preferable alternative - adoption	16
AG - Preferable alternative - counselling/support	2
AG - Preferable alternative - decide not to conceive	2
AG - Preferable alternative - donor eggs	26
AG - Preferable alternative - donor embryo	2
AG - Preferable alternative - IVF	2
AG - Preferable alternative - other treatment/cure of MD	75
AG - Preferable alternative - other/general	16
AG - Preferable alternative - screening eggs/embryos	1
AG - Regulation - can't guarantee limits	5
AG - Regulation - may not be consistent across the board	3
AG - Science - false hope/may not work	70
AG - Science - just because it is possible does not mean it should be done	11
AG - Science - other comment	2

Code	Count
AG - Science - role/motivation of scientists	37
AG - Science - understanding is limited	3
AG - Slippery slope - attitudes to euthanasia	1
AG - Slippery slope - cloning	20
AG - Slippery slope - concerns	38
AG - Slippery slope - designer babies/commoditisation	18
AG - Slippery slope - eugenics	15
AG - Social - general/too many social issues	4
AG - Social - impact on child/identity/psychology	58
AG - Social - impact on donor/donor considerations	7
AG - Social - impact on family relationships	4
AG - Social - impact on parents	5
AG - Social - legal implications/scenarios	1
AG - Social - prioritise other issues/solutions	8
AG - Social - third person as parent/donor	52
AG - Social - will never be able to tackle all diseases	1
AG - Wider issue - against artificial fertilisation	3
CO - Alternatives - other comment	2
CO - Availability - NHS cover	3
CO - Availability - NHS should not cover/fund privately	1
CO - Business interest/involvement	4
CO - Cost/funding - general/who pays	18
CO - Criteria - cost/value	4
CO - Criteria - family situation/ability to provide	2
CO - Criteria - identifying those in need	4
CO - Criteria - medical evidence/advice	3
CO - Criteria - other	6
CO - Criteria - parent/patient choice	10
CO - Criteria - patient need/appropriateness	1
CO - Criteria - patient/clinician joint decision	7
CO - Criteria - regulator should decide	1
CO - Criteria - safety	21
CO - Criteria - seriousness of diseases/impacts	6
CO - Criteria - success rate/efficacy/efficiency	12
CO - Criteria - where proven risk to offspring	3



Code	Count
CO - Donation - availability/origin	4
CO - Donation - risk/exploitation	1
CO - Embryo or egg rights/life - concern	1
CO - Embryo or egg rights/life - general/other	3
CO - Ethics - different to designer embryos/cloning	6
CO - Ethics - interfering with evolution/playing god	3
CO - Ethics - other comment	7
CO - Ethics - should prevail	6
CO - Identity - concerns	1
CO - Labelling of techniques - misleading/misunderstood	7
CO - MST - could be more publically/ethically acceptable	4
CO - MST & PNT - other comparative comment	1
CO - Other priorities - concept of family	1
CO - Other priorities - MD diagnosis	1
CO - Other priorities - other health issues	2
CO - Other priorities - other MD treatment/cure	1
CO - Other priorities - poverty	1
CO - Other priorities - psychological/psychiatric care	1
CO - Overall - complex/unique decision/new territory	9
CO - Overall - needs 'humanising'	1
CO - Overall - needs rational/objective consideration	5
CO - Overall - no further considerations	29
CO - Overall - other comment	3
CO - Overall - same as other IVF/fertility treatment	6
CO - Overall - similar to other existing treatments/techniques	5
CO - Overall - speed of introduction	4
CO - Overall - weigh risks vs benefits/net gain	3
CO - Patients - follow up studies/monitoring	21
CO - Patients - information provision/involvement	16
CO - Patients - may go elsewhere/abroad	2
CO - Patients - support/counselling	9
CO - Population - growth/general	2
CO - Regulation - international considerations	6
CO - Regulation - limitation of use	10
CO - Regulation - needed	6

Code	Count
CO - Regulation - not needed	1
CO - Regulation - other comment	1
CO - Regulation - specifics	22
CO - Regulation - would prevent slippery slope	1
CO - Safety - risks is always present with medical procedures	2
CO - Safety - risks vs benefits	2
CO - Science - further research/trials/evidence	18
CO - Science - other comment	2
CO - Science - should prevail	9
CO - Slippery slope - designer babies/commoditisation	7
CO - Slippery slope - general	10
CO - Social - number of cases	11
CO - Social - parents should not be pressurised	3
CP - Consultation - comment on question	2
CP - Consultation - comment on response form	3
CP - Consultation - cost concern	1
CP - Consultation - lack of information	1
CP - Consultation - other negative comment	2
CP - Consultation - other positive comment	3
CP - Consultation - outcomes	1
CP - Consultation - poor publicity/lack of response	4
CP - Consultation - question motivations/bias	8
CP - Consultation - timing	3
CP - Consultation - welcomed	12
CP - Follow-up - further info on specific topic/s	3
CP - Follow-up - offer of help/further info	3
CP - Follow-up - other	2
CP - Follow-up - public communication/education	16
CP - Follow-up - role of specific sector/group	4
CP - Follow-up - wider debate	5
CP - Respondents - bear in mind experience/knowledge	3
CP - Respondents - comment on response rate	1
CP - Specific groups/views - disregard/do not give undue weight	23
CP - Specific groups/views - other comment	4
CP - Specific groups/views - talk to/consider	35

Code	Count
CP - Website - difficulty	1
CP - Website - lack of information	1
CP - Website - positive comment	1
CP - Website - video	1
CP - Wider issues - fertility treatment overall	2
CP - Wider issues - genetic disease	1
CP - Wider issues - pre-implantation techniques	1
CP - Wider issues - use of animals in research	1
DM - Clinicians - other comment	1
DM - Overall - consider rare/new/uncategorised diseases	1
DM - Overall - other comment	10
DM - Regulator - doesn't make it OK/ethical	1
DM - Regulator - sets boundaries not individual cases (option 2)	1
DS - Donor - payment	3
DS - Donor - responsibility for actions/know what they are getting into	1
DS - Donor function - providing medical solution/repair	2
DS - Donor status - no rights/responsibilities to child	1
DS - Mitochondria - complex/uncomfortable donation	1
DS - Mitochondria - similar to blood	1
DS - Mitochondria - similar to bone marrow	2
DS - Mitochondria - similar to organ	1
DS - Origin - allow choice	1
DS - Origin - should be family member/close relative	1
DS - Parents - payment	1
DS - Parents - responsibility for actions/know what they are getting into	2
FA - Benefits - outweigh cost/other considerations	7
FA - Disease - avoidance important/positive	9
FA - Disease - eradicate	9
FA - Disease - impact on families/sufferers	49
FA - Disease - scale of suffering underestimated	2
FA - Ethics - ethical imperative to intervene	17
FA - Ethics - no concerns	3
FA - Ethics - right to healthy/genetically related child	6
FA - MST - does not destroy embryos	2
FA - Overall - better than other techniques	5

Code	Count
FA - Overall - no reason not to allow	4
FA - Safety - changing law allow techniques to developed safely/responsibly	1
FA - Safety - these techniques are safe/risks acceptable	8
FA - Science - allow to progress as far as it can	2
FA - Science - could lead to new treatments (MD or other diseases)	6
FA - Science - important/positive	9
FA - Science - natural progress	2
FA - Science - other comment	3
FA - Science - UK as a leader in new techniques	5
FA - Slippery slope - not a concern	6
FA - Social - benefits to potential parents/families	24
FA - Social - health/wellbeing of the child	34
FA - Social - reduces burden on services/NHS	17
HOLDING	1
IN - Age - 18/when reaching adulthood	1
IN - Donor identity - should be available (general)	1
IN - Donor rights - other comment	2
IN - Logistics - donor screening	6
IN - Logistics - information storage/records	4
IN - Medical info - available for specific reasons/circumstances	1
IN - Medical info - should be available (general)	1
IN - Overall - conflicts of rights/interests	1
IN - Personal info - should be available (general)	1
LS - Comparison - like IVF/egg/sperm donation	1
LS - Conditions - allow testing/trials only at first	1
LS - Law should change - MD only	3
LS - Law should change - MST&PNT/general	23
LS - Law should change - quickly/asap	7
LS - Law should change w caveats - MST	1
LS - Law should change w caveats - MST&PNT/general	5
LS - Law should NOT change - MST&PNT/general	24
LS - Other - international impetus/influence/implications	7
LS - Other - other comment on law/legal system	5
LS - Other - punishment for undertaking techniques	10
LS - Other - re-examine if needed/after set period	1

Code	Count
LS - Other - specific related laws/legislation	7
LS - Other - specific suggestions for detail	3
O - Blank response/no comment	68
O - Not sure/do not know	4
O - Other/general comment	3
O - Refer to other question	21
O - Refer to other response	2
RF - Current legislation	5
RF - Current legislation - non UK	33
RF - External document	9
RF - External website	4
RF - HFEA	12
RF - Historical experience	69
RF - Media coverage	16
RF - NICE	1
RF - Other evidence/examples	7
RF - Participant - friend/relative/child with MD/similar disease	19
RF - Participant - has MD/similar disease	10
RF - Participant - info about	22
RF - Participant - other medical details	6
RF - Participant - personal details	2
RF - Politics/government	26
RF - Relevant research	12
RF - Religion	45
RF - Specific individual/organisation/group	23
RF - Views of other people/participants	46
SC - DNA - natural mixing	1
SC - DNA - nuclear DNA/genome not affected	2
SC - DNA - other comment	3
SC - Germ line - other comment	1
SC - MD - variety of forms/impacts	7
SC - Mitochondria - function/form	3
SC - Mt DNA - does not determine identity/traits	3
SC - Mt DNA - limited amount/types	1
SC - Mt DNA - origin/not human	1

Code	Count
SC - Mt DNA - other comment	8
SC - Mt DNA - small quantity/impact	2
SC - Mt DNA - suggested source for donation	2
SC - Other procedures - abortion/termination	2
SC - Other procedures - donor cytoplasm	1
SC - Other procedures - IVF/egg or sperm donation/surrogacy	6
SC - Other procedures - organ/tissue/blood donation	4
SC - Other procedures - other/general	1
SC - Overall - balancing science/ethics/religion/society	1
SC - Overall - further research/trials/evidence	1
SC - Overall - invest in other priorities/solutions	2
SC - Overall - motivation of scientists	2
SC - Overall - other comment	7
SC - Overall - question about application	3
SC - Overall - specific consideration for PNT	1
SC - Overall - trust/mistrust of scientists	2
SC - Progress - natural consequence/function of humanity	1
SC - Progress - other comment	2
SC - Progress - requires caution	3
SC - Safety - other comment	1
SE - Ethical - benefits small number	2
SE - Ethical - consent/choice concern	3
SE - Ethical - consent/choice other	1
SE - Ethical - end justifies means	1
SE - Ethical - equity of provision	8
SE - Ethical - interfering/playing god already happens	1
SE - Ethical - judging value/worth of life	1
SE - Ethical - no right to healthy/genetically related child	2
SE - Ethical - slippery slope generally/crossing boundary	1
SE - Ethical - society vs individual	4
SE - General - current social/ethical expectations	2
SE - General - implications	1
SE - General - implications cannot be understood	1
SE - General - unforeseen problems/impacts/health issues	6
SE - Social - attitudes towards disabled people/MD sufferers	10

Code	Count
SE - Social - attitudes towards those not treated	3
SE - Social - attitudes towards those treated	2
SE - Social - availability of counselling/testing/support	1
SE - Social - benefit to future generations	2
SE - Social - child awareness/understanding	3
SE - Social - child emotional/psychological impact	4
SE - Social - child health/wellbeing other	4
SE - Social - child ID/mixed genetic make-up	2
SE - Social - child impacts/damage (other/general)	1
SE - Social - child rights	5
SE - Social - donor considerations	1
SE - Social - ID issues less than other procedures	1
SE - Social - ID/issues complex/different for everyone	1
SE - Social - impact on family relationships (not third parent)	3
SE - Social - impact on future generations	11
SE - Social - issues from having MD/disability	1
SE - Social - legal implications/issues	2
SE - Social - no ID issues/implications foreseen	2
SE - Social - no third party parentage issues	5
SE - Social - overall societal benefit/not harmful	2
SE - Social - overall societal impact	12
SE - Social - parent rights/responsibilities	4
SE - Social - public/societal response/fear	2
SE - Social - risk losing valuable individuals	3
SE - Social - third party parentage issues	3
SE - Social - who should know the details	1

## 8. Non-questionnaire responses

Code	Count
AC - Acceptable - MST and PNT/general	38
AC - Acceptable with caveat - MST and PNT/general	1
AC - Not acceptable - MST	1
AC - Not acceptable - MST and PNT/general	297
AC - Not acceptable - PNT	1
AC - Overall - understand issue/have sympathy	20

Code	Count
AG - Altering DNA - cloning/hybridisation	17
AG - Altering DNA - impact on germ line/lineage	100
AG - Altering DNA - not acceptable	24
AG - Cost - too much/cannot be justified	3
AG - Costs/risks - outweigh benefits	20
AG - Donation - risk/exploitation	5
AG - Ethics - embryo (mainly PNT) creation/destruction	229
AG - Ethics - end does not justify means	13
AG - Ethics - general/too many ethical issues	29
AG - Ethics - interfering with evolution/playing god	91
AG - Ethics - lack of consent/choice	13
AG - Ethics - no right to healthy/genetically related child	3
AG - Ethics - other comment	7
AG - Ethics - sanctity/dignity of human life	181
AG - Ethics - UK first in crossing ethical boundary	109
AG - Future - risks/impacts/unintended consequences	173
AG - MST & PNT - both involve IVF/embryo destruction	4
AG - Population - too big/would increase	2
AG - Preferable alternative - adoption	6
AG - Preferable alternative - counselling/support	1
AG - Preferable alternative - IVF	1
AG - Preferable alternative - other treatment/cure of MD	118
AG - Preferable alternative - other/general	103
AG - Preferable alternative - screening eggs/embryos	2
AG - Regulation - can't guarantee limits	2
AG - Science - false hope/may not work	3
AG - Science - just because it is possible does not mean it should be done	11
AG - Science - other comment	5
AG - Science - role/motivation of scientists	31
AG - Science - understanding is limited	18
AG - Slippery slope - cloning	92
AG - Slippery slope - concerns	17
AG - Slippery slope - designer babies/commoditisation	99
AG - Slippery slope - eugenics	28
AG - Slippery slope - normalising GM	10



Code	Count
AG - Social - hardship is natural/contributes to strength of society	5
AG - Social - impact on child/identity/psychology	198
AG - Social - impact on donor/donor considerations	4
AG - Social - impact on family relationships	33
AG - Social - impact on parents	8
AG - Social - legal implications/scenarios	3
AG - Social - other comment	7
AG - Social - prioritise other issues/solutions	2
AG - Social - third person as parent/donor	249
AG - Social - worth of MD sufferers/disabled people	7
AG - Wider issue - against artificial fertilisation	1
CO - Embryo or egg rights/life - concern	2
CO - Embryo or egg rights/life - not a concern	1
CO - Ethics - different to designer embryos/cloning	3
CO - Ethics - other comment	3
CO - Identity - child should know about conception	1
CO - Identity - concerns	1
CO - Patients - information provision/involvement	2
CO - Regulation - international considerations	1
CO - Safety - risks vs benefits	4
CO - Science - further research/trials/evidence	6
CO - Science - mitochondrial function	4
CO - Science - other comment	4
CO - Science - participant understanding	7
CO - Slippery slope - designer babies/commoditisation	1
CO - Social - number of cases	4
CO - Social - parents should not be pressurised	2
CO - Social - risk losing valuable individuals	1
CP - Consultation - comment on question	2
CP - Consultation - other comment	11
CP - Consultation - other negative comment	6
CP - Consultation - other positive comment	5
CP - Consultation - poor publicity/lack of response	3
CP - Consultation - timing	4
CP - Consultation - welcomed	4

Code	Count
CP - Specific groups/views - disregard/do not give undue weight	2
CP - Specific groups/views - talk to/consider	1
CP - Website - difficulty	6
CP - Website - general	2
DM - Regulator - helps public acceptability	1
DM - Regulator - involvement is necessary (general/other)	3
DS - Donor status - is parent/relation to child	2
DS - Donor status - is unclear/ambiguous	1
DS - Donor status - legal considerations	1
DS - Mitochondria - different to blood	1
DS - Mitochondria - similar to egg/sperm/embryo/IVF	2
DS - Parents - responsibility for actions/know what they are getting into	1
FA - Benefits - outweigh cost/other considerations	2
FA - Disease - avoidance important/positive	6
FA - Disease - eradicate	6
FA - Disease - impact on families/sufferers	18
FA - Disease - scale of suffering underestimated	1
FA - Ethics - ethical imperative to intervene	2
FA - Ethics - right to healthy/genetically related child	2
FA - Identity - no concerns	1
FA - MST and PNT - better/alternative to current options	1
FA - Science - important/positive	4
FA - Science - nuclear DNA not altered	1
FA - Social - benefits to potential parents/families	7
FA - Social - general benefit to society/public health	1
FA - Social - health/wellbeing of the child	8
LS - Comparison - like IVF/egg/sperm donation	1
LS - Comparison - like organ/blood/tissue	1
LS - Further exploration needed - general/both	3
LS - International - impetus/influence/implications	1
LS - Law should change - MST&PNT/general	5
LS - Law should NOT change - MST&PNT/general	222
LS - Other - international impetus/influence/implications	12
LS - Other - lack of trust in government/regulators	2
LS - Other - punishment for undertaking techniques	56

Code	Count
LS - Other - specific related laws/legislation	2
LS - Punishment for undertaking techniques	1
O - Additional attachment	1
O - Other/general comment	43
O - Refer to other response	1
RF - Culture/literature	3
RF - Current legislation	7
RF - Current legislation - non UK	145
RF - External event/discussion	4
RF - HFEA	7
RF - Historical experience	19
RF - Participant - friend/relative/child with MD/similar disease	36
RF - Participant - has MD/similar disease	7
RF - Participant - info about	60
RF - Participant - personal details	11
RF - Politics/government	10
RF - Relevant research	37
RF - Religion	105
RF - Scientific review panel	1
RF - Specific individual/organisation/group	18
RF - Views of other people/participants	9
SC - DNA - nuclear DNA/genome not affected	1
SC - DNA - other comment	2
SC - MD - diagnosis	2
SC - Mt DNA - does not determine identity/traits	1
SC - Mt DNA - may affect identity/traits	1
SC - Mt DNA - other comment	1
SC - Other procedures - adoption	1
SC - Other procedures - IVF/egg or sperm donation/surrogacy	1
SC - Other procedures - organ/tissue/blood donation	2
SC - Overall - other comment	3
SC - Overall - trust/mistrust of scientists	1
SC - Progress - other comment	2
SC - Progress - reducing MD is good/positive	1
SC - Safety - other comment	3

Code	Count
SE - Ethical - consent/choice other	1
SE - Ethical - embryo rights/usage other	1
SE - Ethical - slippery slope generally/crossing boundary	1
SE - Ethical - slippery slope/similar to cloning	2
SE - Ethical - UK first in crossing ethical boundary	2
SE - General - implications	2
SE - General - other procedures acceptable/better	1
SE - Social - child rights	1
SE - Social - cost/resources	1
SE - Social - donor/child relationship difficulties	1
SE - Social - issues from having MD/disability	2
SE - Social - public/societal response/fear	1
SE - Social - third party parentage issues	1



# Medical Frontiers: Debating mitochondria replacement

## Annex V: Open consultation meetings: London and Manchester

Report to HFEA

February 2013

OPM  
252B Gray's Inn Road,  
London WC1X 8XG

tel: 0845 055 3900  
fax: 0845 055 1700  
email: [info@opm.co.uk](mailto:info@opm.co.uk)  
web: [www.opm.co.uk](http://www.opm.co.uk)

Client	HFEA
Document title	Medical Frontiers: Debating Mitochondria Replacement: open consultation meetings: London and Manchester
Date modified	15 March 2013
Classification	Final
OPM project code	8984
Author	Grace Trevelyan
Quality assurance by	Tim Vanson
<b>Contact details</b>	
Main point of contact	Robin Clarke
Telephone	0207 239 7871
Email	<a href="mailto:RClarke@opm.co.uk">RClarke@opm.co.uk</a>

If you would like a large text version of this document, please contact us.



---

# Contents

Executive Summary .....	1
1. Introduction .....	3
2. Meeting design .....	4
3. Small group discussions .....	7
a) Avoiding mitochondrial disease .....	7
b) Affecting future generations: changing the germ line .....	8
c) Implications for identity: DNA from three people .....	9
d) The status of the mitochondria donor:.....	10
e) Regulation of mitochondria replacement.....	11
4. Whole room debate .....	12
a) Modifying and using embryos .....	12
b) Concepts of identity .....	14
c) Safety .....	15
d) Affecting future generations .....	17
e) The status of the mitochondria donor:.....	17
f) Regulation and Choice: Who decides? .....	18
g) Putting the issues in context .....	20
Appendix 1 – Discussion handouts.....	22
Appendix 2 – Agenda .....	27

## Executive Summary

The Office for Public Management (OPM), in partnership with Forster and Dialogue by Design, was commissioned by the Human Fertilisation and Embryology Authority (HFEA) to conduct a multi-method research and engagement project looking at the possible social and ethical issues relating to two techniques for the avoidance of mitochondrial disease: pronuclear transfer (PNT)<sup>1</sup> and maternal spindle transfer (MST)<sup>2</sup>.

As part of this research and engagement, OPM ran two open consultation meetings which were held in November 2012 in London and Manchester. A broad range of channels were used to promote the meetings and participants were self selecting. A total of 53 people attended the London meeting and 39 people attended the Manchester meeting.

The meetings were designed to expose participants to the full spectrum of possible views about mitochondria replacement techniques and to provide a forum for informed debate about the issues. After being provided with an overview of the scientific and contextual details, participants had the chance to engage in small group discussions structured around the broad social and ethical themes, before posing questions to an invited panel in a whole group debate.

### Key messages from London

The London meeting was characterised by a dynamic exchange of views on a range of social and ethical issues. The diverse set of perspectives and reference points that the audience members drew on to illustrate their points made for an animated and often heated debate. However, in terms of the balance of opinion throughout the discussions, there were more comments from people who were supportive of the techniques compared to those who opposed them.

Participants expressed different views around matters such as the moral status of embryos. While it was pointed out by several participants that the destruction of embryos already routinely takes place in IVF treatments, for some members of the audience the need to treat embryos with respect played a crucial role in determining their attitude towards mitochondria replacement. In the light of this, the feeling that embryos were being used as '*building blocks*' to create '*better*' embryos was viewed as particularly contentious. At several points during the meeting mitochondria replacement was likened to cloning. This fed into discussion of a potential slippery slope effect, a prospect which was a prominent concern for some but dismissed as highly unlikely by others.

There was also a great deal of discussion about the relative importance of '*genetic relatedness*', with some identifying this outcome as a tangible advantage of the new techniques deemed important from the patients' and parents' perspective, while others put forward the view that it was a '*relatively minor*' benefit when compared with the potential risks

---

<sup>1</sup> Pronuclear transfer involves transferring the pronuclei from an embryo with unhealthy mitochondria and placing them into a donor embryo which contains healthy mitochondria and has had its pronuclei removed. A pronucleus is a small round structure containing nuclear DNA seen within an embryo following fertilisation. A normal embryo should contain two pronuclei, one from the egg (maternal pronucleus) and one from the sperm (paternal pronucleus).

<sup>2</sup> The maternal spindle is a structure within the egg containing the mother's nuclear DNA. Maternal spindle transfer involves transferring the spindle from the intended mother's egg, with unhealthy mitochondria, and placing it into a donor egg with healthy mitochondria.



and consequences which may not currently be understood. A number of different ways of conceptualising the role of the mitochondria donor were put forward at the London meeting. Some members of the audience spoke about the '*insignificance*' of the tiny amount of genetic material that any child born following the use of mitochondria replacement techniques would inherit from the donor. This line of argument was backed up with reference to distinctions between mitochondrial and nuclear DNA, with the former being seen playing no role in determining identity. Others complained that this DNA centric approach was reductionist and contended that the role of the donor should not be down played. A number of participants supported the techniques in principle but suggested that any children born following mitochondria replacement should have the right to access information about the mitochondria donor.

### Key messages from Manchester

While a diversity of perspectives were aired at the London meeting, the Manchester meeting was characterised by a strongly 'pro' mitochondria replacement tone. Throughout the proceedings, particular weight was given to the views expressed by those who had been personally affected by mitochondrial disease. For the participants who expressed their support for the techniques, two important and recurring themes underscored many of the arguments:

- There is an ethical imperative to intervene to prevent suffering where the capability to do so exists.
- Individual families should be empowered to make an informed choice about whether or not mitochondria replacement is right for them.

A great deal of floor time was devoted to safety considerations and scientific details, particularly in relation to mitochondrial function and its perceived lack of significance in determining characteristics. For many participants the balance and role of mitochondrial and nuclear DNA appeared to be fundamental when reflecting on and discussing the ethical significance of the new techniques. Having considered the available scientific evidence many participants concluded that terms such as 'three parent families', which have sometimes been associated with mitochondria replacement, were highly misleading. Most of the participants did not feel that mitochondria replacement would have a significant negative effect on a child's sense of identity, and some suggested that from a child's point of view it would present less identity issues than egg donation. The participants were also very influenced by the findings of a relevant report by the Nuffield Council on Bioethics<sup>3</sup>. Many agreed with the report's conclusion that if mitochondria replacement techniques can be proved to be safe then they do not present any significant ethical concerns.

---

<sup>3</sup> Nuffield Council on Bioethics, 2012. *Novel Techniques for the prevention of mitochondrial DNA disorders: an ethical review*. London: Nuffield Council on Bioethics on Bioethics

Available at: <http://www.nuffieldbioethics.org>

# 1. Introduction

Mitochondria are present in almost all human cells. They are often referred to as the cell's 'batteries' as they generate the majority of a cell's energy supply. For any cell to work properly, the mitochondria need to be healthy. Unhealthy mitochondria can cause genetic disorders known as mitochondrial disease.

There are many different conditions that are linked to mitochondrial disease. They can range from mild to severe or life threatening, and can have devastating effects on the families that carry them. Currently there is no known cure and treatment options are limited. For many patients with mitochondrial disease preventing the transmission of the disease to their children is a key concern.

Mitochondrial disease can be caused by faults in the genes within a cell's nucleus that are required for mitochondrial function or by faults within the small amount of DNA that exists within the mitochondria themselves. It is the latter form of mitochondrial disease that could be avoided using two new medical techniques, termed pro-nuclear transfer (PNT)<sup>1</sup> and maternal spindle transfer (MST)<sup>2</sup> which UK researchers are working on.

These techniques are at the cutting edge, both of science and ethics and are currently only permitted in research. They involve removing the nuclear DNA from an egg or embryo with unhealthy mitochondria, and transferring it into an enucleated donor egg or embryo with healthy mitochondria.

The Human Fertilisation and Embryology Act (1990) (as amended) ('the Act') governs research and treatment involving human embryos and related clinical practices in the UK. The Act currently prevents the clinical use of these techniques (or any other technique that involves genetic modification of gametes and embryos to treat patients). However, in 2008 the Act was amended, introducing new powers which enable the Secretary of State for Health to permit techniques which prevent the transmission of serious mitochondrial disease. The Secretary of State for Health and the Secretary of State for Business, Innovation and Skills asked the Human Fertilisation and Embryology Authority (HFEA) to seek public views on these emerging techniques. On considering advice from the HFEA the Government will decide whether to propose regulations legalising one or both of the procedures for treatment.

The HFEA, together with the Sciencewise Expert Resource Centre<sup>4</sup>, therefore commissioned OPM (in partnership with Forster and Dialogue by Design) to conduct a multi-method research and engagement project looking at the possible social and ethical issues and arguments relating to the techniques. The project consisted of five strands:

1. Deliberative public workshops
2. Public representative survey
3. Patient focus group
4. Open consultation meetings
5. Open consultation questionnaire

This research provides the evidence base that will inform the HFEA's advice to the Secretary of State.

The two **open consultation meetings** were held in November 2012 in London and Manchester. The objectives of the meetings were:

---

<sup>4</sup> The Sciencewise Expert Resource Centre (Sciencewise-ERC) is the UK's national centre for public dialogue in policy making involving science and technology issues

1. To provide participants with detailed information about the context and science behind the development of mitochondria replacement techniques.
2. To highlight some of the key issues which have been raised in support of and in opposition to the proposed procedures, thereby exposing participants to a range of different perspectives.
3. To provide a forum for informed debate about key social and ethical issues associated with mitochondria replacement techniques.
4. To allow the HFEA to gather information about people's views on the matter, and to observe the ways in which they respond to particular arguments.

This report provides an overview of the themes and issues that were raised by the panellists and audience members at each of the meetings.

## 2. Meeting design

The open consultation meetings were designed to engage a wide range of different stakeholders and members of the public. At each of the events the audience was made up of a group of self selecting people. The meetings were widely promoted and interested parties were targeted through the following channels:

- Email invitations were sent to the HFEA stakeholder database (patient groups, government departments, relevant charities, foundations and trusts, academics, scientists and research groups).
- Meetings listings were placed on the main HFEA website, the mitochondria consultation website and an independent meetings websites.
- The HFEA's Twitter account was used to promote the meetings. Others who followed the HFEA then spread the word by retweeting the invitation.
- Email invitations were sent to people who had registered to complete the online consultation, to people who had signed up to receive email alerts about the consultation, and to people who had attended the Deliberative public workshops in London, Cardiff and Newcastle.
- Oversight group members and panellists were asked to make the members of their relevant networks aware of the open invitation for the event.
- The meetings were promoted in HFEA publications and during speaking slots at public meetings.
- The press were informed about the consultation and meeting dates.

Participants were asked to state any affiliations when they registered to attend the meeting. This information was used to allocate participants with a mix of backgrounds and areas of expertise to each table.

A panel of speakers was invited to both consultation meetings to share their knowledge and views on mitochondria replacement with the audience and answer specific questions from participants. As mentioned above, one of the key objectives of the open consultation meetings was to highlight the most contentious issues surrounding mitochondria replacement and expose audience members to the full range of views. The panellists in both Manchester and London were therefore carefully selected for the range of different perspectives and areas of expertise that they brought. It was hoped that their divergent outlooks would help to

stimulate discussion from members of the audience. It should be noted that the HFEA did not endorse any of the views put forward by the panellists.

## Format and structure of the meetings

Each of the meetings began with a short animated film that introduced audience members to the background and science behind the two techniques; this film had also been used at the Deliberative public workshops and was available on the consultation website. The scientific information was complemented by brief presentations from each of the panellists explaining the science and outlining some of the issues and views that exist in order to trigger discussion and elicit participants' views. This was followed by an opportunity for participants to discuss the key issues in small groups for approximately 30 minutes. The discussions were structured around five pre-identified themes<sup>5</sup> and participants were provided with handouts for each (see Appendix 1). The themes discussed were:

- a. Avoiding mitochondrial disease
- b. Affecting future generations: changing the germ line
- c. Implications for identity: DNA from three people
- d. The status of the mitochondria donor
- e. Regulation of mitochondria replacement

So as to ensure that each of the themes was covered, each table began by discussing a particular theme before being invited to choose a remaining theme, or themes, that they would like to cover. Most of the small groups discussed two themes within the allocated time. An audio recorder captured the dialogue on each table, and key points were recorded by a self-selected 'scribe'. The key points to emerge in this part of the meeting are discussed in the 'Small group discussion' section below.

The third and final part of the open consultation meetings was a 55 minute 'question time' style debate, where audience members were able to air their own views, seek clarification on particular issues and direct questions or comments at panellists. The content of this third section has been thematically discussed. The agenda for both meetings can be found in Appendix 2.

## Meeting summaries

### London

The London meeting took place on 13<sup>th</sup> November 2012 and was held at Hamilton House in Euston. It was chaired by **Professor Bobbie Farsides**, professor of Clinical and Biomedical Ethics at Brighton and Sussex Medical School.

The panel was comprised of:

**Dr Helen Watt:** Senior Research Fellow at the Anscombe Bioethics Centre. The Anscombe Bioethics Centre, an independent charity, is a Roman Catholic academic institute that engages with moral questions arising in clinical practice and biomedical research.

---

<sup>5</sup> The five themes used to structure table discussions are broadly in line with the themes and questions that were used in the other strands of the consultation and deliberative public workshops.

**Alison Maguire:** Research Director at The Lily Foundation. The Lily Foundation is a patient charity set up to support those affected by mitochondrial disease and supports research into such disorders. Alison provided a patient perspective having had a child who suffered from a mitochondrial disease.

**Professor Mike Parker:** Professor of Bioethics and Director of the Ethox Centre at the University of Oxford.<sup>6</sup>

**Hannah Darby:** Senior Policy Manager at the HFEA with an understanding of the scientific underpinnings of mitochondria replacement techniques.

The London meeting was attended by **53** people. This included a broad mix of stakeholders many of whom were highly engaged and knowledgeable about the key issues. This included:

- Representatives from research and medical charities
- Students of law and healthcare ethics
- Patients directly affected by mitochondrial disease and their parents
- Clinicians and academics working in relevant fields.

A wide range of topics were discussed in great detail, and the conversations which took place throughout the evening aired many of the pertinent social and ethical arguments for and against the use of two new mitochondria replacement techniques.

## **Manchester**

The Manchester meeting was held on 22<sup>nd</sup> November 2012 at The Studio, a conference venue located in central Manchester. The proceedings were chaired by **Professor Margot Brazier**, a Professor of Law at the University of Manchester.

The panel was comprised of:

**Dr Shamima Rahman** – Reader in Paediatric Metabolic Medicine at the UCL Institute of Child Health within the Department of Clinical & Molecular Genetics.

**Josephine Quintavalle:** The Founder of ‘Comment on Reproductive Ethics’ (CORE), a public interest group focusing on ethical dilemmas surrounding human reproduction.

**Dr Marita Pohlschmidt:** Director of Research at the Muscular Dystrophy Campaign. The Muscular Dystrophy Campaign (MDC) is the leading UK charity focusing on muscular dystrophy and other related conditions. MDC have supported the scientific community to develop treatments and cures.

The Manchester meeting was attended by **39** people including a number of participants who were learning about mitochondria replacement for the first time.

---

<sup>6</sup> Arrangements had been made for a geneticist to sit on the panel but due to unforeseen circumstances she was unable to attend on the day. For this reason, Mike Parker and Hannah Darby stepped in to add to the range of knowledge on the panel.

As well as several clinicians and academics working in relevant fields, at the Manchester meeting there was good representation from:

- Families affected by mitochondrial disease
- Sixth form and university students - including several from a nearby sixth form as well as students on the Healthcare Ethics and Law MSc course at Manchester University.

In terms of the balance of opinion, the large majority of views expressed were supportive of the techniques and the mood in the room was more consensual when compared with the London meeting. For this reason the chair and panel played a role in encouraging participants to consider and debate the range of social and ethical issues around the introduction of the new techniques.

## 3. Small group discussions

### a) Avoiding mitochondrial disease

#### London

The participants in London used the small group discussion time to debate the ethical implications of the science behind mitochondria replacement. Questions were asked about whether eggs would be “*cloned*” in the first technique (MST) and embryos “*killed*” in the second (PNT). Some participants expressed greater reservations about the latter techniques and explained that they had more concerns about manipulating an embryo than an egg.

The participants expressed a range of views about the extent to which the proposed mitochondria replacement techniques differ from existing approaches such as pre-implantation genetic diagnosis (PGD) and prenatal diagnosis (PND). In addition to this, a number of participants were insistent that options such as adoption and IVF with a donor egg were ‘*perfectly good*’ ways for carriers to avoid passing mitochondrial disease onto their children. Some put forward the view that it would be “*better to focus on treatment for children who have already been born with mitochondrial disease*”. It was also suggested that there were ‘*perfectly valid*’ forms of treatment available to sufferers, but no specific examples of these were given.

The conversations also revealed contrasting interpretations of the ‘*benefits*’ that would be brought about by the introduction of mitochondria replacement techniques. The chance to offer a greater degree of choice to “*traumatised*” families with a history of the disease was put forward by some participants as a progressive step forward. Others, however, were not convinced by this argument and suggested that while the risks to children born as a result of the “*invasive manipulation of embryos*” would be high, the associated “*social*” benefits of allowing genetic parenthood were “*relatively minor*.” This line of argument was also to find expression during the debate.

#### Manchester

Many of the participants in Manchester felt that the lack of an available cure for mitochondrial disease created an imperative for exploring other options. It was noted that one course of action available to affected families was to “*just have a child and see*” but it was felt that this option was “*not a particularly good one*.”



The participants attributed particular significance to the fact many affected families appeared to support the introduction of mitochondria replacement techniques. It was suggested, for example, that the “voices” of those who have been “*most affected*” ought to be listened to. One participant who had lost a child to mitochondrial disease gave a rationale for his own perspective on the matter explaining “*I do not want any parent to go through what we have been through.*”

The idea that affected families should have the right to make a personal judgement about whether or not to take advantage of mitochondria replacement techniques was repeated several times. On one table, for example, it was argued that:

*“It is question of choice. A sufferer should not have to wait for postnatal options if prenatal choices are in development.”*

Participants also wondered about the efficacy of gamete donation and questioned whether donors were screened for mitochondrial disease themselves. The possibility that mitochondria replacement techniques are “*just about scientists wanting to push boundaries*” was raised, but this point was closely followed by the suggestion that scientific curiosity is not a problem as long as it ultimately helps people. There was also repetition of the argument that the severity of the disease meant that there is a clear case for permitting the new techniques:

*“There is a compelling reason why so much time and energy has been invested in these new techniques.”*

## **b) Affecting future generations: changing the germ line**

### **London**

This issue elicited a number of strong responses which can be grouped into three broad categories.

The first type of response took the view that the germ line would not be significantly changed. It was argued that parents could “*ideally*” choose a mitochondria donor with a very similar mitochondrial DNA sequence to the intended mother. This line of argument was backed up with reference to scientific evidence that mitochondrial DNA variation is limited, particularly in individuals of the same ancestral origin (e.g. European, sub-Saharan African).

The second type of response was based on the idea that the intergenerational effects of mitochondria replacement techniques would be significant and negative. It was argued, for example, that mitochondria replacement *posed “serious risks to societies and individuals.”* There was some concern about the “*unforeseen*” effects of mitochondria replacement, with participants on one table concluding that “*we are playing with something unknown and the full risks need to be understood.*” On a separate table, meanwhile, statements were made about the danger of “*taking human embryos lightly.*” Terms such as “*unnatural*”, “*genetic manipulation*” and “*violating the integrity of nature*” were also used.

A third type of response came from individuals who felt that mitochondria replacement techniques would have a significant but positive impact on future generations. These respondents felt that it would be “*more irresponsible*” for society to allow families with a history of the disease “*to have more children and face the risk of more affected children being born.*”

A variety of views were recorded in response to the question of whether parents have the right to make a decision that will impact their child's future. Participants on one table felt that parents have a *"full right"* to make such a decision since the alternative is to risk their children *"suffering and living a short life."* Others agreed and argued that any child born following mitochondria replacement would be *"unlikely to think what their parents had done was wrong"*. Reference was made to the fact that parents are commonly expected to make decisions that will affect their children's future health and development, and it was suggested that there is *"little difference"* between mitochondria replacement and the choice to vaccinate a child. Others, however, claimed to disagree with the concept of making a life changing choice on behalf of an unborn child and suggested that there was some tension between the best interests of the child and the best interests of the parents.

## Manchester

In Manchester this theme attracted less discussion. Those participants who did cover the subject felt that the new techniques would be changing the germ line *"for the better"* by creating a *"healthy cell."* They focussed on the fact that mitochondria replacement would not change characteristics and while they acknowledged that the impact on future families would be huge, they felt that the impact would be entirely positive: *"the child will go on to pass on healthy mitochondria and children will be free from mitochondrial disease."*

## c) Implications for identity: DNA from three people

### London

Many of the participants were comfortable with the concept of a child having genetic information from three people. On a number of tables the discussion dwelt on mitochondrial DNA's perceived lack of relevance in determining identity, with some participants concluding *"it's just like changing the battery in your laptop."* A participant at a separate table expressed a similar sentiment, explaining *"I don't think of my mitochondrial DNA in the same way as my nuclear DNA."* Others, however, suggested that genetic science may *'change'* and mitochondria may be discovered to have a greater impact on determining characteristics than has hitherto been assumed.

When discussing alternatives such as using a donor egg it was suggested that children born following mitochondria replacement may be *"happier"* in the knowledge that they are genetically related to both their parents. This comment introduced the possibility that mitochondria replacement techniques could raise fewer identity issues than existing procedures.

### Manchester

Three tables used the small group discussions as an opportunity to debate the role played by genetics in determining identity. One table posed the question *"what do we mean by parents?"* On another table participants asked *"what is identity?"* and suggested that in the light of practices such as adoption, our concepts of family are socially constructed. On a third table, however, it was argued that while *"ideas about the significance of genetics"* may vary, genetic relatedness still holds great weight in society. A related area of concern was the influence of the media. The view that *"sensationalised headlines"* surrounding the technique might themselves have an impact on the way children thought about their identity was expressed.



Several references to the Nuffield report<sup>3</sup> were made and these were linked to the view that mitochondria replacement poses “*no ethical problems*” with regards to identity. As was the case in London, it was hypothesised by some participants that egg donation, where all maternal DNA is sourced from a donor, would result in “*greater implications on a sense of identity*” than mitochondria replacement, where most of a child’s maternal DNA would be inherited from their mother. This point was developed further in the debate section of the Manchester meeting. On one table, however, it was claimed that adopted children ‘*crave*’ information about their natural parents, a statement which could be interpreted as suggesting that children born following the use of the techniques would be at risk of experiencing a similar sense of curiosity about their mitochondria donor.

One participant whose son had been affected by mitochondrial disease shared the belief that the child’s mitochondrial DNA had shaped his life but had not affected who he was. The implicit suggestion was that if he had had healthy mitochondria he would have been the exactly the same person but would simply not have been forced to cope with the debilitating symptoms of the disease.

Some participants explained their views by drawing comparisons between the new techniques and more familiar medical procedures such as blood transfusions and organ transplants, neither of which are commonly thought to have a significant impact on identity. It was noted that one potential counter to the argument that mitochondria can be likened to other transferable human tissue is the fact that mitochondria are present in every human cell. This point, however, was balanced by repetition of the accepted view that mitochondrial DNA does not play a role in determining an individual’s identity or phenotype. Indeed, discussion about mitochondrial function emerged as an important theme and appeared to be of paramount importance in determining an individual’s ethical stance on the matter. Some participants identified clear communication as a priority, arguing that explaining the science would help to distinguish mitochondria replacement from separate areas of genetics, such as cloning. They felt that the impact of mitochondrial disease on patients and their families should also be widely articulated.

## **d) The status of the mitochondria donor:**

### **London**

A number of participants in London expressed the view that records should be kept about mitochondria donors. This was linked to a suggestion that although there is currently no scientific indication that mitochondrial DNA has a determining influence of characteristics, this area of genetic science is “*new and could change*”. Some indicated that those willing to donate their mitochondria were “*making a choice to be a part of a child’s life*” and referenced the importance of being “*upfront about what donor-ship means*.”

It was claimed that having access to information about “*where you come from*” is recognised as a fundamental human right. This observation was followed up by one suggestion that any individual born following mitochondria replacement should be able to find out about their “*third parent*” and their “*genetic origins*” in the same way that children born from egg donors are able to access donor information once they reach the age of 18.

### **Manchester**

While the participants in Manchester agreed that ‘three parent’ terminology was confusing, they had different views of exactly how the status of the mitochondria donor should be

understood. Most were emphatic that there *“is no relationship”* between the child and the donor, while a minority maintained that mitochondria donors were making a huge commitment.

A number of the participants acknowledged that people may want to know the *“origin of their mitochondria”*, but the general consensus within the small groups was that donors should be *“non-traceable.”* There was concern that if mitochondria donors could be contacted it would not only *‘limit donation’* but it would alter the public’s perception of the process by fuelling the misleading notion of ‘three parents’.

The opportunity for donors to give informed consent based on honest information about what would happen to their eggs was considered to be essential. Participants acknowledged that this was *“uncharted territory”*, and some followed up on earlier points by suggesting that mitochondria donation could not be satisfactorily compared with either tissue or egg donation, but should instead seen as existing in a category of its own.

## e) Regulation of mitochondria replacement

### London

The theme of the regulation of mitochondria replacement attracted less detailed and varied discussion compared with others however some clear messages emerged. Participants in London attributed a high degree of importance to regulation and felt that strict controls should be put in place to safeguard against illegal use of the techniques. Some felt that regulation was necessary because of a potential slippery slope effect and warned that *“once you breach a principle such as allowing hybrids it creates a precedent.”*

On one table there was a reference to *“a lack of confidence in the HFEA”* as a result of unspecified cases in which licences were granted to clinics where research wasn’t *“up to scratch”*. In light of this it was deemed essential that any regulator should earn a reputation as being trustworthy.

There was also some suggestion that mitochondria replacement programmes should be structured in a way that ensured treatment priority would be given to those at risk of passing on the most severe forms of mitochondrial disease.

### Manchester

As in the London meeting this theme attracted less detailed discussion. Participants in Manchester again argued that regulation was essential within experimental science. It was suggested that mitochondria replacement should be administered and monitored in a similar way to egg donation and that licenses should be reserved for special HFEA approved centres.

The participants also recognised the need to regulate spending on clinical trials since it was felt that healthcare budgets could not absorb unlimited costs.

## 4. Whole room debate

### a) Modifying and using embryos

#### London

A number of audience members and panellists at the London meeting held strong and opposing views about the ethical implications attached to the modification and use of human embryos. As such, this issue constituted an important and recurring theme which surfaced at a number of different points during the debate session.

The belief that human embryos must be treated with respect was forcefully articulated by one audience member:

*“The HFEA is here because we believe there is something special about human embryos and sperm which we don’t accord to mouse or monkey sperm and embryos... The important thing which we, as a society, have got to be very careful about, is not to begin treating embryos as instruments for us to do to what we like.”*

The suggestion that there is a need for the HFEA to take into account ‘*important moral differences*’ between the two proposed mitochondria replacement techniques (MST and PNT) was voiced early on in the debate. The implicit suggestion was that PNT, which relies on the creation of embryos that will never be implanted, is more ethically objectionable than MST, where the egg containing unhealthy mitochondria is not fertilised.

One of the strongest objections to PNT was the argument that embryos were being created and destroyed to provide ‘spare parts’. Dr Helen Watt referred to the embryo as a ‘child’ and expressed grave concerns about the fact that one embryo is “*deliberately conceived solely to extract its pro-nuclei*.” She used the following metaphor to elaborate on this point:

*“This is no more prevention than killing a 20 year old with a condition so that 20 year old can’t have children or grandchildren with that condition. That is not prevention but is eliminating someone.”*

The above statement rests on the assumption that human embryos share the same human worth as adult human individuals. This line of argument prompted Alison Maguire of the Lily foundation to point out that “*we already destroy embryos in IVF, it is common place*.” Dr. Watt’s response was that “*two wrongs don’t make a right*.” She expressed further objections to the PNT technique, in terms of the deployment of embryos it would involve whenever it was used:

*“It is bad enough that we destroy embryos through IVF but here the embryos are building blocks for new embryos.”*

The discussion of embryo modification acted as a catalyst for a subsequent exchange of ideas about the likelihood that mitochondria replacement would leave other areas of genetic science more vulnerable by creating a ‘slippery slope’ effect. One audience member captured this concern by commenting that:

*“In society we get used to certain things happening and we say, we are doing that already, so it would be alright to do this.”*

Another participant voiced their disquiet at the wording of the 2008 amendment to the Human Fertilisation and Embryology Act, which they felt had created a “*loophole*” which “*could allow changes in nuclear DNA*” as part of future efforts to prevent other varieties of mitochondrial

disease. However, a fellow audience member offered a degree of reassurance on this matter by pointing out that such techniques wouldn't be needed because there are other legal diagnosis options available to people with the type of mitochondrial disease which is caused by mutations in the nuclear DNA.

Others at the meeting were keen to challenge the 'slippery slope' argument altogether by pointing out that the techniques would have a very specific application. One audience member who identified themselves as belonging to a patient campaign group explained:

*"We are trying to tackle human suffering and misery in a way that has an ethical basis with carefully tested scientific research which might benefit no more than a few thousand people who may wish to choose to take advantage of this."*

Another audience member then attempted to demonstrate holes in the 'slippery slope' argument by pointing out that:

*"The difference between these proposed techniques and other forms of genetic manipulation, is that in this instance the DNA molecules are intact, they are transferred whole – they are not interfered with."*

This prompted a response from Dr Watt who contended that:

*"The same argument could be given in a few years time for Dolly style cloning. Where we are not doing anything to the nucleus, we are leaving it completely intact."*

The above comment led to a member of the audience to accuse Dr Watt of *"making pejorative statements all the time"* and complained that she was not paying due attention to *"the suffering of the children who are affected by this."*

## Manchester

The use of embryos proved to be a less contentious issue at the Manchester meeting than it had been in London. For example, the logic behind 'slippery slope' arguments were swiftly dismissed by an audience member who contended that *"the same has been [been argued about] IVF, the same has been done with pretty much anything."*

Josephine Quintavalle voiced a number of concerns about the new techniques. For example, she implied that she had greater ethical objections to PNT than MST, when she announced:

*"I've got a statement here from Professor Herbert where she is clearly opting for the embryo rather than the egg... It does seem that egg manipulation is being put into the back ground now."*

Dr Rahman confirmed that while experts were continuing to work on developing both techniques, in her view it did appear that PNT was the safer option. No follow up comments were made in relation to this matter.

Josephine later returned to this issue and described PNT as the *"disaggregation"* of one embryo to create a *"better"* embryo:

*"Some will argue that when you are combining two embryos you have to accept that both of those individual embryos could have been implanted and developed into children so you're sort of getting into a big identity question for any offspring of 'who am I?'"*

However, no similar sentiments were expressed by any audience members. This suggests that this particular line of argument did not achieve a great deal of traction with the Manchester audience.

## b) Concepts of identity

### London

A large section of the London audience was keen to learn more about the properties of mitochondrial DNA. Early on in the proceedings the panellists were asked how confident scientists are able to be about the role played by this genetic material. An answer to this question was provided by Hannah Darby of the HFEA, who spoke of a *“body of evidence”* which has informed the widely accepted scientific view that the function of mitochondrial DNA is to encode cell structures involved in energy production. She did acknowledge, however, that there are other [unknown] factors to take into account including the interaction between the mitochondrial and nuclear DNA. A number of audience members went on to add to this discussion by providing contextual scientific detail. For example, one participant ventured that the reason mitochondria replacement feels *“new”* and *“difficult”* is *“the DNA-centric and reductionist way we understand things.”* They expanded on this point by suggesting that phenomena such as the human genome project and the widely known importance of DNA to forensic identification processes have helped to promote a *“fairly simplistic account of the role of DNA”*:

*“We were all taught that it is a very special thing and... it’s very important for our personality... but mitochondria are not really part of that story.”*

Later on another audience member explained that while nuclear DNA sequences are unique to each individual, people of similar ancestry often have mitochondrial DNA sequences that are *‘essentially identical.’*

This scientific interpretation, however, was not popular with everyone in the room. Dr Helen Watt reminded audience members that *“mitochondria... do help us trace our maternal life history.”* She drew on this fact to suggest that mitochondria play a *“very important social role”*, adding *“this is how we know about people thousands of years ago to whom we are connected by this maternal line.”*

Indeed, Dr Watt went on to posit the view that mitochondria replacement could have wide reaching implications for identity. She made the suggestions that a child conceived using PNT, where two original embryos were used as ‘building blocks’, would not be the true genetic child of the couple but would be constructed artificially from two separate *‘children’* – the couple’s embryo and the donor embryo – whose genes the *“PNT child”* would inherit:

*“Is that helping a parent conceive their own child? You are using their child and another woman’s child to produce another child entirely.”*

Some sympathy for this kind of thinking was expressed by other members of the audience (see sections on the modification of embryos above and the role of the donor below). Dr Watt also described PNT as a form of cloning, by which she meant cloning from an earlier embryo, where the resulting embryo would *“have no genetic parents in the normal sense.”* She argued that *“we need to look at whether we are replacing parenthood by these techniques.”*

## Manchester

At Manchester there appeared to be a broader degree of consensus amongst audience members about the function of mitochondrial DNA. For example, the following statement from an audience member went entirely unchallenged:

*“We are not changing characteristics, we are not changing those things that make you, ‘you’ what we are changing is energy metabolism.”*

It is important to note that a great deal of weight was attributed to the views of this particular participant (Participant A) who identified herself as *“one of these young women”* at risk of passing mitochondrial disease onto their children. Throughout the meeting she spoke eloquently about the dilemmas she faced and her personal experience of living with mitochondrial disease. She made a broader point about identity by referring to a newspaper article which had previously been referenced by Josephine Quintavalle and which recounted the stories of sufferers under headlines such as ‘My Mother Loves Me the way I Am’:

*“Well, my mother loves me the way I am...but would she love it if I didn’t have the disease? Of course she would! And would I love to have a child who didn’t have this disease? More than anything”*

This statement achieved wide spread expressions of approval and was followed by enthusiastic applause.

Later on in the debate a Josephine Quintavalle’s suggested that it would be morally preferable to accept a healthy embryo created using a donor egg (see discussion in regulation and choice section below) by echoing a point that had been made by several participants during the small group discussions:

*“Doesn’t that just leave the child with identity issues? ... Don’t they know their identity better if their DNA is from their parents who are going to raise them, rather than a donor egg?”*

A large portion of the audience seemed to agree that mitochondria replacement would actually *“resolve”* rather than *“generate”* identity dilemmas by making it possible for children who would otherwise have been born using donor eggs to be genetically related to both their parents. In fact, a number of questions from the floor were accompanied by laughter and phrased in a way that poked fun at the assumed irrationality of identity-based objections. One participant, for example, made the following point:

*“There is talk of three parents, but the alternative is to have a debilitating illness. Why is that such a problem of mixed identity? Can you not explain to them that its not that you’ve got three parents, your main identity is your mum and dad, we’ve just altered a little bit of how the process works, your body works, and we’ve stopped you having a debilitating illness.”*

Against this back drop Josephine Quintavalle found little support from the floor for her view that *“this is about creating human life. It’s considerably different from blood donation.”*

## c) Safety

### London

Safety was a prominent concern amongst audience members in London. Indeed, the very first question to the panellists was a request for more detail about the safety implications of



the proposed techniques. Hannah Darby of the HFEA responded by telling the audience members that there were robust tests being conducted. However, as she pointed out, this has to be balanced with the reality that *“we won’t be sure [that the techniques are safe] until the first child is born.”*

Some participants would go on to draw the conclusion that the potential health risk to *“the child”* and any subsequent decedents, combined with the broader notion of *“risks to society”* were so great as to outweigh any of the associated ‘social’ benefits (see discussion of this issue in the Regulation section below).

## Manchester

A considerable portion of the debate section at Manchester was devoted to safety matters. Much of this was instigated by Josephine Quintavalle, who structured her safety related concerns around a *“similar”* American experiment which, she explained, had also involved an *“egg to egg kind of process.”* She pointed out that this research was ultimately shut down due to a poor safety record and used this to argue that the process of combining genetic material from two different women *“is potentially very complicated and dangerous.”* She added that *“to find that a process that we think is going to cure mitochondrial disease is actually causing other problems”* would be *“the last thing we would want to do.”*

Dr Rahman later provided some more information about the experiments that had taken place in America, which had been designed to help *“older women”* have their own children. She agreed with Josephine that those procedures had not been safe but then went on to explain that the abnormalities in that case had been a consequence of duplication of mitochondria populations. She reassured the audience that when it came to developing the proposed techniques, the UK experts were carrying out rigorous tests to *“make sure there is as little carry over of the mitochondrial DNA from the genetic mother’s structure, the nucleus, as possible”* and that they did not believe this would pose a problem.

Participant A contributed to this part of the discussion by arguing:

*“Of course there are risks...this is what happened with the first organ transplant. This is what happened with the first egg donation. More information should be found. More research should be done, but that doesn’t mean that it shouldn’t move forward.”*

She then added that she would be prepared to take on some of that risk herself:

*“If they need to do an experiment, fine, I’ll sign up. If people need to be aware of it, fine, I’ll be aware of it and go for it.”*

Dr Pohlschmidt agreed that a safe, regulated environment was very important, especially to the patients who she was there to represent. However, she argued that there is always going to be *“that scary step towards doing it in a human being.”* This, she felt, was necessary for progress. For this reason she insisted that it remained imperative that individuals who volunteer for clinical trials *“are given the right information in a language that they understand.”*

The chair of the debate summed up by concluding that while all could agree that it was necessary to identify a threshold of acceptable risk, it was unlikely that they were ever going to agree about where the line should be drawn.

## d) Affecting future generations

### London

At the London meeting this issue was tackled head on by an audience member who asked *“Are we experimenting with future generations and is this ethical?”*

Dr Watt responded in the affirmative to the first part of the question and in the negative to the latter part. She expressed a concern that *“this will go on and on and on if we make a mistake.”*

It was also Dr Watt who introduced the matter of couples using new means of creating children who might then have moral objections to those means; *“There could be moral questions asked by a child conceived this way.”*

This point prompted a strong response from one audience member who argued that *“as parents we are making decisions for our children all the time, some of which they may not agree with.”* This audience member went on to express the view that *“as long as we did it in their best interest, fine. We can do no more than that.”*

Alison Maguire concluded this part of the debate by drawing on her personal experience:

*“I think it would be very easy, in the context of an affected family, for a child who was conceived this way to understand why this happened.”*

### Manchester

The impact that mitochondria replacement could have on future generations was very much the focus of the arguments put forward by Josephine Quintavalle at the Manchester meeting. She pointed out, for example, that *“there will be a lot of invasive charting of their health and their wellbeing etc... we need to look at the issue of children’s rights from this perspective.”*

She also expressed a concern that if something were to go wrong the child would have *“every right”* to ask:

*“Why did this happen to me?” and “Why have I got a slightly different type of genome from everybody else which I’m going to be passing on to my children as well?”*

Participant A strongly objected to this suggestion and argued:

*“I have no problem saying to my child ‘because I love you’... and why has this happened to you? So you could live a long, healthy, fulfilling life without the obstacles that I’ve had to deal with.”*

Other audience members agreed that the affect on future generations would be positive based on the potential for *“stopping next generations coming through with this illness.”*

## e) The status of the mitochondria donor:

### London

In London a number of audience members took the opportunity to speak about the role of the mitochondria donor. Their comments highlighted some interesting and diverse perspectives.

The first participant to ask a donor-related question enquired whether the terminology surrounding the donation process is accurate:



*“Is it fair to call healthy mitochondria “donated” if the majority of mitochondrial proteins are encoded by the nuclear genome?”*

An answer to this question was provided by a fellow audience member who agreed that *“the mitochondria are not really donated it is just the mitochondrial DNA”* since mitochondria are made up of about 1500 different proteins *“of which all but 13 are coming from the mother who is going to give birth to these embryos.”*

The second audience member who raised the issue of donor status took specific objection to the type of reasoning seen above. This participant complained that *“The discussions we are hearing are about DNA, DNA, DNA!”* and warned that such a narrow focus amounted to one of the *“classic pitfalls of reductionist biology”* adding *“they are not just a mitochondria donor, they are donating the body of the embryo.”*

A third audience member spoke out in support of the formation of an HFEA mitochondria donor register. They acknowledged that many children will not wish to find out information about the person who had donated mitochondrial DNA but felt that those who did wish to learn this information should have the option to do so.

## Manchester

This issue did not feature in the Manchester debates apart from in passing. Participant A mentioned that donors should be protected and respected, while Josephine Quintavalle expressed the view that any children born following this procedure should have access to detailed information about how they were conceived.

## f) Regulation and Choice: Who decides?

### London

In relation to the question of ‘who decides?’ Mike Parker, who was sitting on the London panel in his capacity as an ethicist, suggested that consideration ought to be given to the interdependencies between choice, cost and justice. Patient-centredness and autonomy are morally important, he argued, but this cannot be separate from the *“ethics of who should be paying for this.”* He suggested that if the technique was to be privately funded then its use could legitimately be seen as matter of individual choice in a rather limited sense. He did point out, however, that a solely private funding structure would create an unjust situation whereby a potentially valuable preventative tool was only available to wealthy, well-resourced individuals or those willing to go into debt.

Some members of the London audience, however, were sceptical about the suggestion that individual parents should be given the power to choose whether or not to use the techniques. They questioned the motivations behind using mitochondria replacement as opposed to other options including adoption and egg donation. For example, one participant asked the panel whether *“genetic relatedness”* should be considered a medical or social benefit. This point was picked up on by another audience member who identified himself as a biologist and argued that if you were to take a rigidly scientific risk-benefit analysis approach to the problem, according to which medical benefits are granted a greater degree of significance, then the answer was self-evident:

*“The unknown risks [to the child and future generations] are not justified by a relatively minor [social] benefit [genetic parenthood].”*

It was Mike Parker who provided a counter-narrative to this. He pointed out that *“genetic relatedness matters to many people. It is not trivial for everyone.”* Later in the debate he built on this point by arguing that *“medicine is about providing social benefits as well as physical benefits.”* He argued that *“the question of whether such interventions should be available cannot be ‘dodged’ by the use of the label ‘social’.”*

## Manchester

As had been the case in the small group discussions, the notion that individual families should have the right to make a choice about whether or not to take advantage of the techniques was very influential throughout the Manchester debate. Participant A persuasively argued that:

*“What we are saying is that there is the potential to have a different choice, and I think that if you don’t agree with it then you don’t have to have it, nobody would force you... If you do, and these techniques do exist, well then I think it’s unethical not to offer them. In my opinion, that is where there is a real ethical question.”*

At one point Josephine Quintavalle challenged the notion that the ultimate decision should rest with prospective parents by suggesting that the desire for parents to be genetically related to their children *“at all costs”* was overshadowing the welfare of the child. This comment was followed by some expressions of disagreement from members the audience.

She went on to suggest

*“If the idea is to have ‘my child’ but we want it healthy, I’m suggesting we look to cure it afterwards.”*

This prompted a number of comments to the effect that developing preventative techniques and continuing to search for treatments are not mutually exclusive endeavours. Josephine Quintavalle maintained that it is worth posing the following question:

*“Why sacrifice a perfectly healthy embryo....why not simply use that embryo without manipulation?”*

Dr Rahman pointed – to signs of agreement around the room – that for many of the patients that she sees genetic parenthood remains a very important issue, meaning that using a donor egg would be unacceptable.

Dr Pohlschmidt built on her fellow panellists point by explaining that for many women with mitochondrial disease one of the hardest things to reconcile themselves to is the decision not to have their ‘own’ child for fear of passing on the mutation, even though they are in fact fertile. She ventured that this scenario was quite different from that faced by women who accept egg donation because *“they have come to terms with the fact that they are infertile.”*

The issue of *international* regulation was raised by Josephine Quintavalle. She pointed to the United Nations Educational, Scientific and Cultural Organisation’s Universal Declaration on the Human Genome and Human Rights and referred to *“considerable concern worldwide”* about mitochondria replacement. One audience member dismissed these points: *“They’re only laws, they’re only words; they can be changed”*, adding *“we need to change in order to move forward.”*

It was suggested by another audience member that it would helpful to hear the wording of the international legislation that allegedly prohibited mitochondria replacement. This was provided, and was followed by a point from the chair about the ambiguity of the wording in

such declarations, an observation which was repeated by an audience member who went on to explain:

*“I also don’t believe that because there is a diversity of international opinion that should change our opinions and what our progress with this is.”*

## g) Putting the issues in context

### London

At the London meeting there was a desire to gauge the scale of potential uptake if mitochondria replacement techniques were to be made available. The question of whether the ‘1 in 5000’ incidence statistic<sup>7</sup> represented too many people to treat was put to the panellists. Alison Maguire predicted that there would not be a huge flood of people coming forward because not everyone who has access to the technique will want to use it.

Following a further question from the audience member, Alison Maguire confirmed that many families do not find out that a mother is a carrier of the mutation until they have a child who is affected by the disease. Indeed, this is exactly the scenario that had confronted her. Alison added that a screening programme for all women of child bearing age would be a *“huge expense for a disease which is relatively rare”* and suggested it was therefore unlikely to take place. Certain sections of the audience found this difficult to accept and several follow up points were made in support of a wider screening programme: *“One affected person can highlight that many people are carrying the gene because you can just look at the maternal line.”*

Alison Maguire responded to subsequent questions about treatment options by explaining that there were a number of projects looking for ways to treat mitochondrial disease, but that the complexity of the conditions posed significant obstacles. She concluded by saying that: *“treatment options are not forthcoming so prevention is the way forward.”*

### Manchester

Similar queries about the scale of the problem were raised in Manchester. Dr Rahman explained that the ‘1 in 5000’ statistic had been derived from a number of separate epidemiological studies which had corroborated each other, and confirmed that this number related to people who were already aware that they had the disease.

An impassioned question about screening was put to the panellists:

*“What have we got in place that is going to identify these young women that don’t even know they’ve got the disease? How are we going to find these people? We have to find them otherwise we can’t stop it.”*

Whereas cost had been identified as the main prohibiting factor in London, Dr Rahman explained that a broad screening of the population was not an option because of sociological considerations:

*“It is not felt to be ethical to screen for a disease for which we have no treatment.”*

---

<sup>7</sup> As set out in the HFEA’s open consultation website <http://mitochondria.hfea.gov.uk/mitochondria/>

This prompted a strong response from an audience member who had lost his son to the disease:

*“But for these young women who become pregnant, unwittingly, there is another life that’s ruined.”*

Participant A spoke up at this point, explaining:

*“I understand why you can’t do wide screening but for me that is why these developments are truly so amazing.”*

## Appendix 1 – Discussion handouts

Participants were provided with one to two page information handouts for each of the five discussion areas.

### Handout 1 - Implications for identity: DNA from three people

#### What is this?

Children born from these techniques will have inherited nuclear DNA from their parents and mitochondrial DNA from a donor. This is a first for medical science and some people may have concerns that it raises the question of whether it will impact on the future child's sense of identity.

#### Why is this potentially an issue?

It is our genes, together with environmental factors, that shape our physical characteristics and are therefore important to identity. Genes are long interlinked chains of our nuclear DNA. Mitochondrial DNA, which comprises a very small proportion of total DNA, is thought only to play a role in energy production and is not responsible for any personal characteristics or traits. So, on the one hand a mitochondria donor might be thought to be similar to a bone marrow or blood donor. Donors could be seen as contributing to the recipient's health and wellbeing while not influencing the recipient's sense of identity.

On the other hand, some people feel that although mitochondrial DNA comprises a very small portion of genes, this is still vital to our genetic makeup. After all, mitochondria can have a devastating effect on health if they do not function normally. Also, as mitochondria are passed down through generations they can be used to trace maternal ancestry. Some people therefore have concerns about the effect mitochondria replacement may have on a person's sense of self and what makes them who they are.

#### Questions for consideration:

- How do you feel about this issue? Why?
- What do you think are the most important points raised in relation to this issue?
- To what extent do these issues impact on your views on whether these new techniques should be used in treatment? Why?

### Handout 2 - Regulation of mitochondria replacement

#### What is this?

Mitochondria replacement would only ever be legalized in the UK if it were deemed safe enough by expert consensus. The HFEA as the regulating body, would need to decide how to monitor and regulate use. They would only allow specialist clinics to offer these treatments if they had the relevant expertise and equipment to do so. They would also need to consider the following questions:

- When and how should patients be able to access mitochondria replacement?
- Who should decide when mitochondria replacement is used?

#### Why is this potentially an issue?

There are a number of options for how treatment is offered. For example, clinics and their patients could decide when mitochondria replacement is appropriate in individual cases.

Another alternative is that HFEA could decide which mitochondrial diseases are serious enough to require mitochondria replacement and, just for these diseases, permit clinics and patients to decide when it is appropriate in individual cases.

Yet another option is that HFEA could decide which mitochondrial diseases are serious enough to require mitochondria replacement and also decide, just for these diseases, when it is appropriate in individual cases.

Factors which may affect which mitochondria replacement technique (PNT or MST) is used include whether couples have an ethical preference for one technique over the other and whether one technique is shown to be safer or more efficient than the other.

#### Questions for consideration:

- How do you feel about this issue? Why?
- What do you think are the most important points raised in relation to this issue?
- Who do you think should decide whether and when patients can use mitochondria replacement techniques? Why?

To what extent does this issue impact on your views on whether these new techniques should be used in treatment? Why?

### Handout 3 - Affecting future generations: Changing the germline

#### What is this?

Any changes to a person's mitochondria will be passed down to the next generation, and if the child is a daughter, to the one after that and so on. This is referred to as affecting the female germ line.

Germ line modifications have never been permitted on embryos before and this may raise important social and ethical questions.

#### Why is this potentially an issue?

Some people are concerned that modifying the germ line would affect the child's right to an 'open' future. This means that a decision is made, on a future child's behalf. In this case, the decision would be to ensure the future child and their future children are free from disease.

Many people think that a life free from disease is a more 'open' one than a life with mitochondrial disease. However, the decision to perform mitochondria replacement is an irreversible choice not just for the future child, but future generations too.

Because of this some people are concerned that mitochondria replacement is tampering with nature. They feel that germ line modification is a step too far. Others feel that, because we already intervene in other areas of reproduction and medicine (for example, in vitro fertilisation) it doesn't make sense to apply this argument to mitochondria replacement.

#### Questions for consideration:

- How do you feel about this issue? Why?
- What do you think are the most important points raised in relation to this issue?
- To what extent do you think that parents have the right to make a decision that will impact on their child's future like this? Why?

- To what extent does this issue impact on your views on whether these new techniques should be used in treatment? Why?

## Handout 4 - Avoiding mitochondrial disease

### What are current options for avoiding mitochondrial disease?

If a woman has mitochondrial disease, there is a risk that when she tries to conceive naturally the disease may be passed onto her child. This is because mitochondrial DNA is inherited from the mother. People in this situation have a number of options available to reduce the chance of this happening. However, there are advantages and disadvantages associated with each option:

**Adoption:** A woman, or couple, may choose to adopt a child rather than conceiving naturally. This will mean that they do not risk passing on mitochondrial disease to their child. However, the child will not be genetically related to either of the intended adoptive parents.

**IVF with donor eggs:** In vitro fertilisation (IVF) is a process in which an egg is surgically removed from a woman's ovaries and fertilised with her partner's sperm outside the body. The subsequent embryo is later placed in the woman's womb. People affected by mitochondrial disease may choose to have a child through IVF with eggs donated by a woman who does not have mitochondrial disease. However, the child will not be genetically related to the intended mother.

**Testing embryos:** An alternative to IVF with egg donation or to adoption is to create embryos using IVF and then test them to see if mitochondrial disease is present. Any embryos without the disease would then be transferred to the intended mother. This technique is called preimplantation genetic diagnosis (PGD). PGD gives people the opportunity to reduce the chance of having a child with mitochondrial disease. However, it cannot guarantee a child free from disease. This is because an egg can either contain mitochondria that are all unhealthy, or it can contain some healthy and some unhealthy mitochondria. When choosing an embryo using PGD, embryos with the lowest number of unhealthy mitochondria can be chosen, which reduces the chance of having an affected child. However, there is still a chance of the disease developing.

**Testing of foetuses:** Another option is to have a child naturally, and then to test the foetus during the pregnancy to find out whether the child will be born with a particular disease. This technique is called prenatal diagnosis (PND). If a foetus is diagnosed with mitochondrial disease, the prospective parents could decide to continue the pregnancy or could opt for a termination of the pregnancy. Parents could be offered IVF with PGD (pre-implantation genetic diagnosis) followed up by PND to confirm if the child will be born free of the disease. As with PGD, it cannot guarantee that the baby born will be unaffected. Even if a girl is born and appears healthy, she may herself carry a proportion of unhealthy mitochondria, which could lead to her children being affected by mitochondrial disease.

### What are the new techniques for avoiding mitochondrial disease?

Scientists have developed two new methods that could help to preventing mothers from passing on mitochondrial disease to their children (and their children's children and so on). If approved, these techniques would take place within licensed clinics and may allow children to be born free from mitochondrial disease. These techniques would be preventing mitochondrial diseases caused by faults in mitochondrial DNA, but not those caused by faults



in nuclear DNA. Scientists are still working on these techniques to find out which will be the safest and most effective.

**Pro-Nuclear Transfer (PNT):** Immediately after fertilisation, an embryo has two pro-nuclei. These are the parts of the egg and sperm that hold the nuclear DNA. Pro-nuclear transfer (PNT) involves removing pro-nuclei from an embryo with unhealthy mitochondria immediately after fertilisation. The pro-nuclei, are then transferred into a donated embryo. This donor embryo contains healthy mitochondria, but has had its own pro-nuclei removed.

**Maternal Spindle Transfer:** A maternal spindle is a structure within a woman's egg that contains only the mother's half of a child's nuclear DNA. The father's half of the nuclear DNA comes from the sperm. Maternal spindle transfer (MST) involves removing the spindle from the mother's egg before it is fertilised by the father's sperm. The spindle is then placed into a healthy donor egg with healthy mitochondria (from which the donor's spindle, and therefore the nuclear DNA, has been removed).

### How are the new techniques different from the current options?

At the moment, modifying an embryo is allowed in scientific research, if that research has been deemed to advance knowledge and treatment into fertility or serious diseases. Embryos created for research are discarded before they reach 14 days old and are never transferred into a woman. If these techniques were to be made available for treatment, it would be the first time that modified embryos were used to make a child.

The proposed treatments are limited to mitochondrial DNA replacement and would not involve modifying the nuclear DNA.

Some people have concerns that modifying embryos for health reasons is the first step on a slippery slope towards designer babies. The concern is that, once modifying embryos to avoid mitochondrial disease is accepted, this will be extended to approving embryo modification for more minor conditions or for cosmetic traits such as height, hair and eye colour. Others however argue that is not the case, since these further steps would require new research, techniques and further changes to the law before they were possible.

Some people are not concerned at all about a slippery slope if this means that more genetic diseases can be avoided or treated before birth. They suggest that it is a slope worth sliding down. Others consider that slippery slope arguments are meaningless because almost all forms of technology can be used for good or bad and that we solve this through adopting social norms and regulations.

### Questions for consideration:

- How do you feel about the current options available to avoid mitochondrial disease? What are their benefits? And drawbacks?
- How do you think the new techniques are different from those that are currently being used? How are they better? How are they worse?
- How do you feel about the fact that the new techniques involve the modification of embryos? Why?



## Handout 5 - Status of the mitochondria donor

### What is this?

If mitochondria replacement techniques become legal, law makers would have to decide how to classify the mitochondria donor. They would need to consider the status of the donor and what, if any, information about the donor (e.g., personal, medical or contact details) should be available to the future child.

### Why is this potentially an issue?

Currently, people donate many different types of tissue for medical purposes. Each one of these donation processes has very specific regulations regarding the rights of the donor.

People who donate their sperm or eggs can only do so if they agree to be identifiable to any future child. A donor conceived child can also get medical and personal information about the donor and is able to contact them once the child reaches the age of 18. This is based on the idea that donor conceived children have a legitimate interest in the person or people who contributed to their genetic makeup through supplying half of their nuclear DNA.

On the other hand, people who wish to donate blood, bone marrow or other tissue do so anonymously. This is partly because donation of non-reproductive tissue is not seen as key to a person's sense of identity – although in bone marrow donation, some donor DNA is also transferred to the recipient.

People's views on how mitochondria contribute to a person's identity, or sense of identity, may affect what they think about the status of the donor. Some people may feel that the child should have the option of accessing as much information as they like about the donors. Others may feel there is no obligation on the donor to reveal their identity and that forcing donors to do so may put them off donating.

### Questions for consideration:

- How do you feel about this issue? Why?
- What do you think are the most important points raised in relation to this issue?
- How should we think of the relationship between the child and the mitochondria donor? What kind of role or status should the donor have?
- To what extent does this issue impact on your views on whether these new techniques should be used in treatment? Why?

## Appendix 2 – Agenda

### Medical Frontiers: Debating mitochondria replacement

Time	Session
18.00 – 18.30	<b>Arrival and registration</b> Tea, coffee and finger food available
18.30 – 19.00	<b>Introductions from the Chair and HFEA/OPM</b>  <b>Mitochondria replacement: Some facts</b>  <b>Introductions from the panel</b> Having been introduced by the Chair, each panel member will outline some of the issues and views, in order to trigger discussion.
19.00 – 19.30	<b>Explore the key social and ethical issues</b> Group discussions, where each group will have the opportunity to discuss two of the following sets of issues: <ol style="list-style-type: none"> <li>1. Avoiding mitochondrial disease</li> <li>2. Affecting future generations: Changing the germline</li> <li>3. Implications for identity: DNA from three people</li> <li>4. The status of the mitochondria donor</li> <li>5. Regulation of mitochondria replacement</li> </ol>
19.30 – 20.25	<b>Ask a question; debate the issues</b> The final session will take the form of a lively debate using a Question Time format. Panel members will field questions that emerge from the group discussions before opening up discussion to the floor.
20.25 – 20.30	<b>Thank-you and next steps from the Chair</b>



# Medical frontier: Debating mitochondria replacement

## Annex VI: Patient focus group

Report to HFEA

February 2013

OPM  
252B Gray's Inn Road,  
London WC1X 8XG

tel: 0845 055 3900  
fax: 0845 055 1700  
email: [info@opm.co.uk](mailto:info@opm.co.uk)  
web: [www.opm.co.uk](http://www.opm.co.uk)

Client	HFEA
Document title	Medical Frontiers: Debating mitochondria replacement: Patient focus group
Date modified	22/02/2013
Status	Final
OPM project code	8984
Author	Sanah Sheikh
Quality assurance by	Robin Clarke
<b>Contact details</b>	
Main point of contact	Tim Vanson
Telephone	020 7239 7806
Email	tvanson@opm.co.uk

If you would like a large text version of this document, please contact us.



---

# Contents

Executive summary .....	1
1. Introduction .....	3
2. Overview of participants' backgrounds .....	4
3. Views on the existing options .....	5
4. Understanding of and views on new techniques .....	7
5. Potential social and ethical issues .....	9
5.1 Affecting future generations .....	9
5.2 DNA from three people .....	9
5.3 Status of the mitochondrial donor .....	10
6. Key messages.....	11

## Executive summary

The Office for Public Management (OPM), in partnership with Forster and Dialogue by Design, was commissioned by the Human Fertilisation and Embryology Authority (HFEA) to conduct a multi-method research and engagement project looking at the possible social and ethical issues relating to two techniques for the avoidance of mitochondrial disease: pronuclear transfer (PNT)<sup>1</sup> and maternal spindle transfer (MST)<sup>2</sup>.

As part of this research and engagement, OPM conducted a focus group in London in December 2012 with six participants, all of whom had been affected by mitochondrial disease in different ways. We also conducted one telephone interview, in January 2013, with a participant who was unable to attend the focus group. Participants reported having spent long periods of time in hospital under the care of doctors, and a great deal of time worrying about having children. Understandably the topic was quite difficult for some participants and they were therefore often overcome with emotion.

The importance of being able to have a healthy child that is genetically their own underpinned participants' attitudes towards **the existing options** available to couples who would like to avoid passing on mitochondrial disease to their children. For example, with regards to preimplantation genetic diagnosis (PGD) and prenatal diagnosis (PND), participants were quick to point out that neither of these techniques guaranteed that children born from using them would be free from mitochondrial disease. With respect to adoption and IVF with donor eggs, many participants felt that whilst these were suitable for some people, they wanted to have children that were genetically related to them.

Participants were overwhelmingly positive about the **new techniques**, particularly because, unlike most of the current options, they could potentially eliminate mitochondrial disease not only for the child, but also from the germ line. They also appreciated that the techniques would enable them to have children that were genetically their own. Those participants that had a less clear understanding of the techniques had some questions and concerns that they were keen to have clarified, for example about the safety and uncertainty of the techniques. In general, all participants emphasised the importance of individual choice in deciding whether to use these new techniques.

Participants were not particularly concerned that the new techniques would result in changing the female **germ line**. They felt that the techniques only changed the germ line in so far as they were 'preventing disease' and that this was essentially a good thing. Participants were also comfortable with parents making this decision on the behalf of children, because again it was about ensuring that the child would be healthy. Participants were very familiar with the potential issue relating to these new techniques employing **DNA from three people**. They rejected the '3 parent family' label - drawing on their knowledge of the science to argue that since no nuclear DNA would be used from a third party, the

---

<sup>1</sup> Pronuclear transfer involves transferring the pronuclei from an embryo with unhealthy mitochondria and placing them into a donor embryo which contains healthy mitochondria and has had its pronuclei removed. A pronucleus is a small round structure containing nuclear DNA seen within an embryo following fertilisation. A normal embryo should contain two pronuclei, one from the egg (maternal pronucleus) and one from the sperm (paternal pronucleus).

<sup>2</sup> The maternal spindle is a structure within the egg containing the mother's nuclear DNA. Maternal spindle transfer involves transferring the spindle from the intended mother's egg, with unhealthy mitochondria, and placing it into a donor egg with healthy mitochondria.

techniques were more akin to blood or tissue donation and that a child's sense of self would therefore still be inherited from the parents. Participants also felt quite strongly that **donors** should remain anonymous. They also felt that donors would *and* should want to remain anonymous as this would mean that they were doing it for the right reasons. They felt that this was because unlike with sperm or egg donation there was no nuclear DNA that was being donated. Participants identified a number of **key messages** for government about the new techniques:

- The potential for the new techniques to relieve suffering
- The potential for the new techniques to reduce costs to the health system
- The potential for the new techniques, unlike current options, to prevent mitochondrial disease

# 1. Introduction

Mitochondria are present in almost all human cells. They are often referred to as the cell's 'batteries' as they generate the majority of a cell's energy supply. For any cell to work properly, the mitochondria need to be healthy. Unhealthy mitochondria can cause genetic disorders known as mitochondrial disease.

There are many different conditions that are linked to mitochondrial disease. They can range from mild to severe or life threatening, and can have devastating effects on the families that carry them. Currently there is no known cure and treatment options are limited. For many patients with mitochondrial disease preventing the transmission of the disease to their children is a key concern.

Mitochondrial disease can be caused by faults in the genes within a cell's nucleus that are required for mitochondrial function or by faults within the small amount of DNA that exists within the mitochondria themselves. It is the latter form of mitochondrial disease that could be avoided using two new medical techniques, termed pro-nuclear transfer (PNT)<sup>1</sup> and maternal spindle transfer (MST)<sup>2</sup> which UK researchers are working on.

These techniques are at the cutting edge, both of science and ethics and are currently only permitted in research. They involve removing the nuclear DNA from an egg or embryo with unhealthy mitochondria, and transferring it into an enucleated donor egg or embryo with healthy mitochondria.

The Human Fertilisation and Embryology Act (1990) (as amended) ('the Act') governs research and treatment involving human embryos and related clinical practices in the UK. The Act currently prevents the clinical use of these techniques (or any other technique that involves genetic modification of gametes and embryos to treat patients). However, in 2008 the Act was amended, introducing new powers which enable the Secretary of State for Health to permit techniques which prevent the transmission of serious mitochondrial disease. The Secretary of State for Health and the Secretary of State for Business, Innovation and Skills asked the Human Fertilisation and Embryology Authority (HFEA) to seek public views on these emerging techniques. On considering advice from the HFEA the Government will decide whether to propose regulations legalising one or both of the procedures for treatment.

The HFEA, together with the Sciencewise Expert Resource Centre<sup>3</sup>, therefore commissioned OPM (in partnership with Forster and Dialogue by Design) to conduct a multi-method research and engagement project looking at the possible social and ethical issues and arguments relating to the techniques. The project consisted of five strands:

1. Deliberative public workshops
2. Public representative survey
3. Patient focus group
4. Open consultation meetings
5. Open consultation questionnaire

This research provides the evidence base that will inform the HFEA's advice to the secretary of state.

---

<sup>3</sup> The Sciencewise Expert Resource Centre (Sciencewise-ERC) is the UK's national centre for public dialogue in policy making involving science and technology issues



The **patient focus group** aimed to provide a dedicated safe space where a small number of those affected by mitochondrial disease could make in-depth contributions about their views and experiences. Rather than attempting to highlight the full range of patient and family views and experiences, the focus group and additional interview provides a small scale qualitative 'snapshot' of the varying views of those affected by mitochondria diseases.

This report provides an overview of the key themes and issues that were raised by participants.

## 2. Overview of participants' backgrounds

OPM conducted one focus group in December 2012 which was attended by six participants, all of whom had been affected by mitochondrial disease in different ways<sup>4</sup>. We also conducted one telephone interview, in January 2013, with a participant who was unable to attend the focus group. Participants were recruited through contacts at patient groups and charities and at the open consultation meetings which were run as part of the project.

A brief background of the participants is provided below.

- **Participants A and B:** A couple who had a daughter with Leigh's syndrome who had passed away last year. They reported that the doctors had informed them that their daughter had acquired the disease not as a result of maternally inherited mitochondrial DNA, but as a result of a combination of the couple's DNA. However, the woman (Participant A) also reported that she had not been tested for mitochondrial disease. The couple are in the process of trying to have a child through IVF with donor eggs, but have been on the waiting list for a year and a half.
- **Participant C:** A mother of five who reported having five children with varying degrees of Mito Partial Complex 1, all of whom were only diagnosed quite recently. She is particularly concerned for her three daughters who are in their late teens/early twenties and whom she worries will not be able to have children without passing on the disease.
- **Participant D:** A woman, who reported having two grandchildren with Mito Complex 1 which had been maternally inherited from her foster daughter. She reported that her foster daughter would not want to have any more children because she does not want to pass on the disease.

---

<sup>4</sup> Mitochondrial disease can be caused by one of two problems within a cell. Firstly, by faults in the genes within a cell's nucleus that are required for mitochondrial function. This type of mitochondrial disease can be inherited from the father or mother as nuclear DNA is inherited from both parents. Secondly, by faults within the small amount of DNA that exists within the mitochondria themselves. Mitochondrial DNA is only inherited from the mother and helps produce a cell's energy. It is this form of mitochondrial disease that could be avoided using the new techniques.

Mitochondrial diseases vary in terms of severity, depending on the type and extent of DNA defect and the specific gene affected. It also depends on the proportion of healthy versus unhealthy mitochondria within a cell and what type of cell is affected.

Diseases caused by faults in mitochondria may appear at birth or develop later in life. They are usually degenerative and can affect the functioning of muscles and major organs as well as the nervous system and the cardio-vascular system. There are many different conditions that are linked to mitochondrial disease.

- **Participants E and F:** A young woman (Participant E) who reported that she had been diagnosed with MELAS when her maternal aunt had passed away as a result of mitochondrial disease. She felt strongly that she would not want to risk passing the disease on to her children. Her mother (Participant F) also attended the focus group.
- **Interview participant:** A mother who has a son with mitochondrial neuro-gastrointestinal encephalopathy, who was misdiagnosed for many years before the above diagnosis was confirmed at the age of 26. He has had numerous major operations over the years and has been in intensive care and nearly died a few times. A bone marrow transplant from his sister has helped with his recovery, although this recovery is very slow. There is no history of mitochondrial disease in the family. She reported the pain, suffering and disruption experienced by the whole family when a family member is so ill for so long.

Participants reported having spent long periods of time in hospital and under the care of doctors. They also all reported having spent a great deal of time thinking and worrying about having children. Some participants were quite keen to share their experiences and talk about how their lives had been affected by mitochondrial disease from the start of the discussion. Others were initially more reserved but opened up once the discussion progressed and the participants had bonded well as a group. Understandably the topic was quite difficult for the participants and they were therefore often overcome with emotion.

### 3. Views on the existing options

At the beginning of the focus group participants had the chance to learn about the techniques and the science. This involved reading and discussing a one page briefing paper and watching an animated video<sup>5</sup>.

Next, participants were invited to share their views on and experiences of the current options available to couples who would like to avoid passing on mitochondrial disease to their children.

As mentioned above, one couple reported that they were in fact trying to have **IVF with a donor egg**. They had been told by doctors that they had a 25% chance of having another child with mitochondrial disease and felt very strongly that this was not a risk worth taking:

*“We wouldn’t take that risk, it’s too high, it’s too cruel a disease...to have another child and watch that child die.” Participant A*

However they had been unsuccessful so far because of the lack of availability of egg donors. They had been on a waiting list for a year and a half and were both frustrated and disappointed about not having been more successful. They reported having been advised to find their own egg donor, but felt quite strongly that they wanted the donor to be anonymous.

They also reported that given that they are only entitled to one round of IVF on the NHS, they couldn’t afford to pay for the treatment privately if the first round failed, as many people tend to do. They therefore felt that this option was better suited to people that were well off and could afford private treatment. Other participants felt that this was not an option they would

---

<sup>5</sup> As part of the research and engagement project, a short participant briefing video was produced. The video was about 5 minutes long and introduced the science and the new techniques.

consider because, although it may be acceptable and suitable for some people, they were keen to have children that were genetically related to them. The same drawback was also associated with **adoption**, which none of the participants had considered as yet, and about which there was little discussion. The interview participant felt that adoption is really the ‘final straw’ for families that can’t have children by any other means.

With regards to **preimplantation genetic diagnosis** (PGD) and **prenatal diagnosis** (PND), participants were quick to point out that neither of these techniques guaranteed that children born would be free of mitochondrial disease. Some participants also reported that they had been told by doctors or read online that these techniques were only able to identify some types of mitochondrial disease and not others. The interview participant noted that the experience of PND could be very traumatic as it could result in parents having to choose whether or not to terminate a pregnancy if a fetus is diagnosed with mitochondrial disease. No participants had considered using these techniques as yet. Participants reported being “*too terrified*” to try these two techniques. They felt that there was “*too high a risk*” that their children would still also have mitochondrial disease and therefore suffer greatly, as would the rest of the family.

*“As somebody who has had symptoms and has seen it at its worst...I couldn’t do that.”*  
Participant E

*“The trauma, the upset, the total disruption to normal family life when you have someone in family that is seriously ill.”* Interview participant

Furthermore, the two participants (C and D) reported that these two options would not be available to their daughters because embryo screening is not currently permitted in Ireland.

The importance of being able to have a healthy child that is genetically their own therefore underpinned participants’ attitudes towards the existing options. The young woman with MELAS (Participant E) felt quite strongly that “*these are not treatments, these are not cures...none of them.*” The interview participant agreed with her that these techniques do not represent ‘reproductive choice’, particularly in light of the fact that there are techniques being developed that can potentially eliminate the disease and allow people to have children that are genetically their own.

*“They can be right for certain people but it’s a matter of choice and if the techniques exist...if there is a way that women can have their own children, if there is a way that can eliminate the disease...then it should be available.”* Participant E

*“If you can guarantee it with another procedure then you would go for that option. Parents want to give child the best opportunities in life, to give them a normal life.”* Interview participant

Some participants also reported that most patients are not “*at this stage yet*”, and are still struggling to get confirmed diagnoses and come to terms with the implications. Others drew on their own long and often drawn out experiences of uncertainty to report that all the current options are available only to those who know they have mitochondrial disease. They expressed great concern about people who are likely to have the disease and do not know it.

## 4. Understanding of and views on new techniques

There were varied levels of understanding about the new techniques amongst the participants, with some having a very detailed understanding of the science involved, and others having a basic understanding as well as lots of questions for clarification. The majority had heard about the techniques online as part of their own research about one year ago. One participant reported that her consultant had in fact told her that the new techniques were in development about three years ago. The interview participant reported that she had heard about the techniques at an event that was part of the HFEA's public dialogue events.

Participants were **overwhelmingly positive** about the new techniques, particularly because, unlike most of the current options, they could eliminate mitochondrial disease not only for the child, but also from the germ line.

*"Anything that could eliminate even part of mitochondria disease is a wonderful thing..."*  
Participant C

*"If either can eliminate the disease so be it...there is nothing more sad than seeing a child that can't join in with rest of society."* Interview participant

They also appreciated that the techniques would enable them to have children that were genetically their own.

*"It will still be the genes of the mother and father, the child will still look and sound and act like its parents, that's really important."* Interview participant

One participant (Participant E) recognised that the techniques didn't really represent a cure and felt positive that perhaps there would be a cure in the future. However, these new techniques represented the best option available to women now. She remarked that these new techniques *"would change my life."*

*"We're talking about mothers now and what can be done for them...for right now, this is phenomenal."* Participant E

Participants also felt that the new techniques would save the health system a great deal of money, given how expensive it currently is to care for patients with mitochondrial disease.

Those participants who had a less clear understanding of the techniques had **some questions and concerns** that they were keen to address. For example, one participant (Participant C) had questions about the **safety and uncertainty** of the techniques. More specifically, she had questions about what needed to happen to refine the techniques and how confident scientists were that the techniques would work. She had concerns that the first babies born from these techniques would be akin to an 'experiment':

*"Imagine being the parents of that first child born this way...it doesn't sit right with me."*  
Participant C

Other participants disagreed and reported that they would be happy to be the first and that *"it is a risk I'm willing to take...for me the risk is lower than the risk of the disease."* Participant E

Some participants argued that there is always a degree of uncertainty with respect to medical innovation and that this is *"a part of all medical progress"* (Participant D). This led the participants to discuss and agree on the importance of **individual choice** in deciding whether to use these new techniques.

Two participants (C and D) reported that when they had presented these new techniques to a group of approximately 170 parents with mitochondrial disease in Ireland, the response had been mixed with half supporting the techniques and the other half having concerns. The participants felt that the latter group held religious and cultural values and for this reason had some discomfort with the involvement of a third person or donor in the construction of embryos. However, the participants reported that the group that initially had concerns was now *'starting to come around'* after they began to understand the techniques better. One participant (Participant C) reported that her daughter (who has mitochondrial disease) had a *"fear that a little bit of her would be missing."* She reported that she herself, being *"an Irish Catholic girl"* had *"a little bit of reservation"* with the concept of third party involvement, but that if her daughter decided to use these techniques she would fully support her. Again, the importance of **individual reproductive choice** was discussed.

*"If this isn't right for you...because of your personal beliefs, because of your culture, because of your background, then you don't have to have it...it's about choice."*

*Participant E*

One participant also wanted to clarify whether the new techniques could only eliminate those types of mitochondrial disease that were a result of mitochondrial DNA mutations and not those that were the result of nuclear mutations. Although the former was claimed to include the vast majority of mitochondrial diseases, it was also recognised that for the latter group of patients, the new techniques were therefore not helpful or applicable.

## 5. Potential social and ethical issues

Participants were asked to consider a number of potential social and ethical issues and to comment on the extent to which these issues had an impact on their views on whether these new techniques should be used in treatment.

### 5.1 Affecting future generations

Participants were not particularly concerned that the new techniques would result in changing the female germ line. They drew on their knowledge of the science of the techniques and argued that the techniques only changed mitochondrial DNA and not nuclear DNA, and that it was the latter that determined inheritable characteristics. They therefore felt that the techniques only changed the germ line in so far as they were 'preventing disease' and that this was, in essence a good thing.

*"It's not changing the child...It's just making sure it's a healthy child." Participant D*

*"I have no problem with removing whatever has to be removed and changing the germ line...I don't care." Participant C*

Participants were also very comfortable with parents making this decision on the behalf of children, because again it was simply about ensuring that the child would be healthy. They felt that it was part of their instincts as 'parents' to want to provide their children with the best opportunities in life. One (Participant E) remarked that she would be *"happy for my mum to make this decision on my behalf"* and another remarked that *"I have it and would want my germ line changed"* (Participant F). Moreover, the interview participant felt that future generations may in fact resent their parents for not having used a technique that could have saved them much pain and suffering.

### 5.2 DNA from three people

Participants were very familiar with the potential issue relating to these new techniques employing DNA from three people. They reported that the media had picked up on this and had reported it in a sensationalist manner. They also felt that the way in which the issue is generally talked about is 'misleading', 'emotive' and 'confusing'. They again drew on their knowledge of the science to argue that since no nuclear DNA would be used from a third party, the techniques were more akin to blood or tissue donation. They stressed that mitochondrial DNA is only involved in energy production and that a child's sense of self would be derived from his/her nuclear DNA which would still be inherited from the parents.

*"Everything that makes you 'you' and that makes your child 'your child' is not touched..." Participant F*

They also felt that the benefits associated with these techniques were also more important than the downside of not being able to trace maternal ancestry.

*"How often do you actually want to trace maternal ancestry...? And is that more important than having a healthy child?" Participant E*

### 5.3 Status of the mitochondrial donor

Discussion about the 'DNA from three people' issue led participants to discuss the status of the donor and whether or not the donor should be able to access information about the child and vice versa. Participants felt quite strongly that donors should remain anonymous. They also felt that donors would *and* should want to remain anonymous as their only motivation should be to help other couples have a healthy child of their own. They felt that this was because, unlike with sperm or egg donation, there was no nuclear DNA that was being donated.

*"I've donated blood and haven't given a thought about where that's going. There has never been in the press that someone wants to know where the blood came from that saved their life." Interview participant*

Participants C and D were quite concerned because they had read online that donors would in fact be able to access information about the child and were relieved to hear that this was not necessarily the case and that the policy on information access had not been decided.

Participants felt that donors should be well informed and should have to sign documentation agreeing to be anonymous.



## 6. Key messages

Participants were asked to take a few minutes to themselves to note down the key messages they would like to give the Government regarding the new techniques. A few common themes emerged<sup>6</sup>:

- **The potential for the new techniques to relieve suffering:**

*“Future children would be spared the awful pain, suffering, constant endless hospital stays and spared having bits of muscle cut from their bodies for testing.”*

*“Parents would not have to watch their children dying slowly, painfully and know that they will not be able to have any more children.”*

- **The potential for the new techniques to reduce costs to the health system:**

*“If mitochondrial disease was eradicated then it would be one less bill the government would have to pay.”*

- **The potential for the new techniques, unlike current options, to prevent mitochondrial disease:**

*“The current options are not cures – PNT and MST will for the first time mean that a cure can be offered.”*

*“Existing options are not treatment or cures. As a matter of preventing transmission of disease and reproductive choice new treatments are ethically acceptable – indeed it would be less ethical and of more risk to prevent further research.”*

Other messages included:

- The importance of these techniques being tested/trialled in a regulated environment
- The anonymity of the donor
- The importance of mitochondrial disease testing/diagnosis

---

<sup>6</sup> The key messages for Government were noted down on to post-it notes and so cannot be attributed to the different participants.



## **Annex VII: A report on regulatory considerations for mitochondria replacement**

**Matthew Watts, Regulatory Policy Manager, HFEA**

## **1. Introduction**

- 1.1. In January 2012, the Secretary of State for Health and the Secretary of State for Business, Innovation and Skills, jointly asked the HFEA to seek public views on emerging IVF-based techniques designed to prevent the transmission of mitochondrial disease<sup>1</sup>. The HFEA was also asked to consider the practical implications of allowing these techniques within the existing regulatory regime.
- 1.2. Such techniques are currently prohibited in clinical practice. However, the Secretary of State for Health can propose Regulations which would allow gametes or embryos created through mitochondria replacement techniques to be classed as 'permitted' under the Human Fertilisation and Embryology Act 1990 (as amended) ('the Act').

## **2. Background**

- 2.1. This report highlights some of the regulatory issues associated with permitting mitochondria replacement. It makes no assessment of the acceptability of mitochondria replacement techniques<sup>2</sup>. Instead the focus is on the practical issues involved. As a result, we consulted with fertility sector staff and other professionals who have direct experience of working with patients and donors in the clinic environment, rather than the general public.
- 2.2. The outcome of the HFEA public engagement work may influence how certain aspects of regulation are approached. We focussed on a small number of key regulatory issues for the Ethics and Law Advisory Committee (ELAC)<sup>3</sup> and the Scientific and Clinical Advances Advisory Committee (SCAAC)<sup>4</sup> to consider and provide initial comments to flesh out some of the issues.
- 2.3. The outcomes of the ELAC and SCAAC discussions fed into a workshop for fertility sector staff and other professionals on 5 February 2013 to allow for further discussion and input<sup>5</sup>. The following sections summarise the topics considered, and explores comments made by stakeholders.

## **3. Licensing and patient eligibility**

- 3.1. The issue examined here was how we might permit the use of mitochondria replacement techniques, and in what circumstances it would be appropriate, bearing in mind how the HFEA regulates comparable activities.
- 3.2. If Government was minded to draft Regulations permitting mitochondria

---

<sup>1</sup> <http://www.hfea.gov.uk/6898.html>

<sup>2</sup> Maternal Spindle Transfer (MST) and Pro-nuclear Transfer (PNT)

<sup>3</sup> <http://www.hfea.gov.uk/ELAC-November-2012.html>

<sup>4</sup> <http://www.hfea.gov.uk/7559.html>

<sup>5</sup> A copy of the discussion document that was circulated to workshop delegates is at Annex A.

replacement, it is likely that there will need to be some criteria to specify when these techniques can or cannot be used. The Act states that Regulations may allow for gametes or embryos to be 'permitted' if:

"...the egg or embryo has had applied to it in prescribed circumstances a prescribed process designed to prevent the transmission of serious mitochondrial disease."

- 3.3. Other comparable techniques have a basis in the Act, in particular, the testing of embryos cannot take place unless the Authority is satisfied:  
"...that there is a significant risk that a person with the abnormality will have or develop a serious physical or mental disability, a serious illness or any other serious medical condition"
- 3.4. To ensure that the Authority is satisfied, authorisation processes are in place for pre-implantation genetic diagnosis (PGD) and pre-implantation tissue typing (PTT).
- 3.5. In the case of PGD, embryo testing clinics apply to the HFEA for permission to test for a particular genetic condition which they believe meets the criteria in the Act as noted above. If approved, any clinic with the appropriate licence can test for this condition in the embryos of patients who they deem appropriate.
- 3.6. For PTT the HFEA approves embryo testing on a case-by-case basis involving a specific patient. Only conditions that have already been approved under the authorisation process for PGD can be considered for PTT. In making its decision, the HFEA will consider a referral from the child's treating clinician to ensure that the treatment is necessary and all other options have been considered.
- 3.7. PGD has already been approved for a number of specific and named mitochondrial diseases and it is a reproductive option for some patients at risk of passing on mitochondrial disease. This might suggest that a useful starting point is that an authorisation process for mitochondria replacement should mirror that for PGD.
- 3.8. Some stakeholders favoured this approach, suggesting that the HFEA should approve conditions, and leave the judgement as to which patients receive the treatment with clinical staff. This would result in a list of approved conditions which fertility clinics would refer to when offering mitochondria replacement techniques. However, others argued that a key trait of mitochondrial disease is its variability, in terms of the severity of the disease itself, and how it can manifest within different patients. Approving a mitochondrial disease for use in these techniques would not necessarily mean that all patients with that condition would go on to develop a serious manifestation of the disease.
- 3.9. To investigate how a disease may manifest in a particular patient, input may be required from mitochondria specialists and genetics teams who would consider the family history to understand how the disease had developed in other family members. The level of mutant load might also be a factor taken into account. Whilst one could be confident that a disease will manifest in patients with homoplasmic cells (ie, all the

mitochondria is unhealthy), for those with heteroplasmic cells (ie, some healthy and some unhealthy mitochondria) the likelihood of being affected will be harder to predict as it will depend on the gene mutation involved, and the proportion of healthy to unhealthy mitochondria as cells develop.

- 3.10. The variability described above might suggest a case-by-case approach to deciding who should receive this treatment. This would determine if mitochondria replacement is suitable, and whether the disease was likely to develop into a serious condition for that particular patient.
- 3.11. Stakeholders agreed, stating that the complexity of the diseases means that fertility clinics would need to liaise with genetics teams and mitochondria specialists before deciding the most appropriate treatment. Currently, there are three NHS mitochondria centres<sup>6</sup> which it was thought could act as a 'gatekeeper' to ensure that only the most appropriate patients are put forward for this treatment. Referral from these centres, or any future expert centres, could be worked into any new authorisation process.
- 3.12. Many stakeholders were of the view that the decision on who should receive the treatment should be made by fertility clinics, rather than the HFEA (as in PTT). This was partially based on a mistaken understanding of the role the HFEA plays in authorising PTT and a desire to avoid administrative systems. In fact, the HFEA's role is clear in that it must be assured that the treatment being proposed is the most suitable option available based on a referral from the child's treating clinician. Systems are in place to ensure such applications and referrals can be considered by the HFEA in a timely manner.
- 3.13. If a case-by-case approach was in place, it might mirror the process for PTT. The HFEA could ensure that a fertility clinic has the expertise to carry out the technique and consider a referral letter (possibly from the NHS mitochondria centres) explaining why this technique is necessary and whether the disease is likely to manifest into a serious condition for that patient.
- 3.14. Past experience suggests that as new techniques are introduced into clinical practice, there is demand for rigorous regulatory oversight to ensure public confidence. This was evident with PGD which was initially only available on a case-by-case basis. Whilst the statutory requirements set out by Parliament in the Act have not changed and must still be met, the HFEA has changed its own authorisation process from a case-by-case decision making process, to a condition by condition approach as the technique became established in clinical practice.
- 3.15. Bearing in mind past experience with comparable techniques, it seems unlikely that Parliament would allow mitochondria replacement techniques to be introduced into clinical practice without some degree of oversight, particularly as the Act currently prohibits gametes or embryos which have had their mitochondrial DNA altered to be used in treatment.
- 3.16. The variability of mitochondrial diseases described earlier suggests a

---

<sup>6</sup> <http://www.mitochondrialncg.nhs.uk/>

case-by-case approach to decision making. Given the assurances of regulatory oversight that Parliament is likely to want, we would suggest that mitochondria replacement techniques should be authorised in a similar way to PTT. To future proof any Regulations, such oversight might be better expressed in HFEA guidance and processes, rather than on the face of the Regulations themselves. This could give the HFEA the flexibility to design an authorisation process, and powers to impose licence conditions on fertility clinics offering mitochondria replacement to ensure that the relevant oversight is in place. For example, an additional licence type could be created, which included a new licensed activity of 'creating embryos through mitochondria replacement', of which MST and PNT might be approved processes. Other assurances that the HFEA could seek include the fertility clinic having the relevant premises, equipment and expertise to carry out mitochondria replacement.

### Summary

- Many stakeholders agreed that a case-by-case approach to decision making is necessary for mitochondria replacement. However, they felt that this decision should rest with fertility clinics rather than the HFEA. That said, bearing in mind past experience with comparable techniques, the variability of mitochondrial diseases and the likely assurances of regulatory oversight that Parliament would want, we would suggest that mitochondria replacement techniques should be authorised in a similar way to PTT.
- Parliament may initially want a high degree of regulatory oversight, but it would be sensible to future proof any Regulations. This could be achieved by expressing such oversight in HFEA guidance and processes.
- The HFEA should be able to impose licence conditions on those fertility clinics wishing to offer mitochondria replacement techniques to ensure that appropriate standards have been met.

## **4. Consent**

- 4.1. Should mitochondria replacement techniques be permitted, it is important that we are satisfied that effective consent is taken. Patients and donors may initially be unaware of what mitochondria replacement involves, or have their own personal view of their acceptability. For example, some donors may not want their nuclear DNA to perish, or alternatively they may only want to donate their mitochondrial DNA (and would therefore prefer this type of donation to 'standard' egg donation).
- 4.2. The Act states that before consent can be given, relevant information must be provided. This includes the nature of the treatment, its consequences and risks. Stakeholders went further and stated that for mitochondria replacement, information should be provided which ensures that the donor is aware of what genetic contribution they are making to the child, and how (possibly) the law surrounding mitochondria donors is

different to normal gamete donors.

- 4.3. Due to the amount and complexity of information to be provided, all stakeholders agreed that it would be appropriate for patients and donors to specifically consent to mitochondria replacement separately from established ART techniques.
- 4.4. Stakeholders highlighted that some donors may wish to specifically donate to mitochondria replacement. It was felt that it may be unreasonable to require all fertility clinics to provide the level of information described above to donors.
- 4.5. This led stakeholders to agree that only a fertility clinic which offers mitochondria replacement should take consent from a mitochondria donor. It was also suggested that such consent should be captured on a specific consent to mitochondria donation form, rather than a standard gamete donation form. This would ensure that consent is properly informed. Whilst stakeholders felt that the novel nature of mitochondria replacement warranted a specific consent form, some felt that donors should not be able to consent to one technique over the other (ie, MST or PNT).
- 4.6. By limiting the taking of consent to those fertility clinics which offer the techniques and capturing consent to donation for mitochondria replacement on a specific consent form, the HFEA can be satisfied that patients and donors are fully aware of what is involved due to the expertise of staff at that fertility clinic.

### Summary

- It is important that consent is taken prior to treatment or donation, and that relevant information is provided. Such consent should only be taken by a fertility clinic which offers mitochondria replacement techniques.
- Consent to donation should be captured on a specific consent to mitochondria donation form, rather than on a standard gamete donation form.

## **5. Follow-up research on children born**

- 5.1. The novel nature of mitochondria replacement techniques means that it is not clear how effective they may be when used outside of a research setting or how any resulting child may feel about the way they were conceived. The Nuffield Council on Bioethics has suggested<sup>7</sup> that, should mitochondria replacement be permitted, there should be long-term follow-up research on children and families.
- 5.2. Whilst mitochondria replacement techniques would take place in an HFEA licensed fertility clinic, the requirement to follow up patients and families following treatment falls outside of our current remit. Instead, we provide

---

<sup>7</sup> <http://www.nuffieldbioethics.org/mitochondrial-dna-disorders>

best practice guidance to clinics which carry out PTT, stating that they should have arrangements in place to allow follow-up studies to take place<sup>8</sup>.

- 5.3. Follow-up studies can be difficult to run as it requires the commitment of patients over a number of years. In this case, it might be that researchers wish to assess both the patient and child. Whilst stakeholders agreed that this group of patients would probably be committed to helping others and take part in such studies, there is no obligation on them or their future children. This issue would be exacerbated should overseas patients use this service.
- 5.4. An area where the HFEA could be involved is through the use of its Register data. Currently, clinics submit information to the HFEA on each treatment cycle that they perform, and in recent years, researchers have been able to link this information with other national data sets, allowing studies which look for long term effects of fertility treatment.
- 5.5. The Register could 'flag' those treatment cycles which involved mitochondria replacement, and ensure that the NHS number of both patient and child are submitted to the HFEA. Researchers could then link those patients, and children born following mitochondria replacement, with other NHS national data sets to understand its success in avoiding mitochondrial disease (providing that the patient consents to the disclosure of their information to researchers).
- 5.6. There was also discussion and some support for having a separate national Register of all mitochondria replacement techniques. Part of this discussion centred on how it would be funded, and what information it would contain. In particular, suggestions were made that the cost of a cycle of treatment with mitochondria replacement (presumably funded by the NHS) could include an amount to cover some follow-up work. Other possibilities included patients only being able to access the treatments as part of a research trial, on the condition of committing to be followed up.
- 5.7. Stakeholders saw the creation of a separate national Register as outside the HFEA's role. However, its exact purpose is not entirely clear. Some of its data might duplicate that which is already required by the HFEA. For example, as part of a cycle of treatment, a fertility clinic would be required to submit information to the HFEA on:
  - Key characteristics of the patient / donor (ie, age, date of birth, ethnicity, medical history)
  - Number of eggs collected from a patient / donor
  - How long embryos were cultured for and if they were subsequently frozen
  - If treatment involved fresh or frozen gametes or embryos
  - What type of treatment took place (ICSI / IVF)
  - Whether a cycle of treatment resulted in a pregnancy and / or a live

---

<sup>8</sup> <http://www.hfea.gov.uk/496.html#guidanceSection4363>

birth

- 5.8. This type of information may also be required if a separate national Register of mitochondria replacement techniques was set up, although its scope might also include information such as:
- Whether there was any carry-over of unhealthy mitochondria into donor eggs or embryos
  - Other observations with regards to embryo development following mitochondria replacement
  - Findings of follow-up studies on patient or child.
- 5.9. Several stakeholders were of the view that no further information about the techniques themselves (other than the fact that a cycle of treatment involved mitochondria replacement) would need to be submitted to the HFEA. However, if additional information were required, we would be well placed to collect and hold such data through submissions to the HFEA Register. Alternatively, any additional information could be held by clinics and reviewed by the HFEA on inspection.
- 5.10. Whilst some stakeholders were of the view that the requirement to promote the follow-up of children and families should be 'best practice' and guidance in the HFEA Code of Practice (as in the case of PTT), there was also some support for a tougher stance. This could be in the form of a licence condition, stating that links must be in place with research groups or mitochondria specialists, ensuring that other professionals in the field were aware of the success of treatment or the procedure itself (although confidentiality provisions in the Act may impact on this).

### Summary

- Follow-up of children born following mitochondria replacement is important, but the HFEA's remit is limited.
- The HFEA can aid follow-up work by flagging those cycles which involved mitochondria replacement on its Register, and through the use of licence conditions and guidance to ensure follow-up plans or links are in place.
- There was some discussion and support for having a separate national Register of mitochondria replacement techniques, although its creation was seen as outside of the HFEA's role. It is not clear what this may contain, although it may duplicate information which fertility clinics are already required to submit to the HFEA. If additional information was required, the HFEA would be well placed to collect this data.

## **6. Access to, and provision of, donor information**

- 6.1. The issue examined here was the extent to which mitochondria donation is comparable to other forms of donation, and whether the same rules that cover gamete donation are applicable.



- 6.2. When considering how mitochondria donation compares with gamete donation, concepts of identity and genetic contribution were discussed. Children born through gamete donation have half their nuclear DNA provided by a donor. Stakeholders described how the genes of a person's nuclear DNA, together with environmental factors, shape their physical characteristics and are important to identity. The removal of donor anonymity in 2005 was partly because of a donor conceived child's right to know who made them who they are. In contrast, some stakeholders mentioned that current scientific evidence suggested that the role of mitochondria is limited to energy production and therefore, in their view, does not impact on a person's physical characteristics or identity.
- 6.3. Stakeholders discussed other forms of donation, such as organ or blood, where patients are given a contribution which can transform their life for the better. Although it was not seen to provide a genetic contribution which could affect identity. Donor anonymity is provided, although in some situations there are mechanisms in place for donor and recipient to exchange information and meet through mutual consent.
- 6.4. The role and function of mitochondria, and how it compares to other types of donation led the majority of stakeholders to the view that the contribution from a mitochondria donor is different from a gamete or embryo donor, that it was less likely to affect a person's identity and that mitochondria donation was more akin to a type of 'tissue' donation. Many stakeholders suggested that this would then infer that anonymity should be provided to a mitochondria donor. They went on to argue that if mitochondria donors were treated on a par with gamete donors, then this could have the perverse effect of de-valuing the status and role of gamete donors.
- 6.5. Some stakeholders thought that children born through mitochondria replacement would still be curious to find out details about their origin, just as the recipient of a tissue donation might. However, views on the difference in function of mitochondrial DNA compared to nuclear DNA led some to consider that curiosity was not enough to warrant providing donor information. A reference was made to how children born via surrogacy, may have the same desires, but no information is provided.
- 6.6. Even if a mitochondria donor were classified differently from a gamete donor, there may be benefit in collecting some donor information. This is based on the principle that the science surrounding the role of mitochondria could change, and that there is a possibility that it may later come to light that a donor suffers from a previously unidentified heritable disorder. Some stakeholders agreed that it is important for fertility clinics to hold some donor information for traceability purposes, and mentioned that it is a requirement of the European Union Tissue and Cells Directive (EUTCD)<sup>9</sup>. This requires a centre to be able to trace all tissues and cells from procurement to use and storage, including being able to identify the donor. Whilst some stakeholders did not see the need to submit such information on mitochondria donors to the HFEA, a system is already in place for fertility clinics to submit gamete donor information to the HFEA.

---

<sup>9</sup> <http://www.hfea.gov.uk/2072.html>

This includes:

- Physical characteristics
- Ethnic group
- Details of medical history and additional screening tests carried out
- Identifying information (such as name and address)
- Good will message and pen portrait (optional)

- 6.7. A donor-conceived child can access non-identifying information from the HFEA at the age of 16, and identifying information at the age 18. If mitochondria donors were classified on a par with gamete donors, then there would not need to be any change to current processes. Whilst this may not be too burdensome on the clinic (except for the potential increase in number of donors), several stakeholders thought that a similar provision of information as in gamete donation would go against the principle (in their view) of mitochondria donation being akin to a type of 'tissue' donation.
- 6.8. However, if mitochondria donors were classified differently from gamete donors, there may be benefit in fertility clinics using the same processes in place to submit information to the HFEA, either to ensure traceability, or to allow the mitochondria-donor conceived child certain identifying or non-identifying information depending on what status the donor is given.
- 6.9. There was also consensus that mitochondria donors should be able to find out the same level of information about their donation as is currently available to gamete donors (ie, the number, sex, and year of birth). However, it is worth noting that when gamete donors were provided anonymity, they were initially unable to find out this type of information about their donation.

### Summary

- The majority of stakeholders considered the role and function of mitochondria to be different from that of other forms of donation, and suggested that it was, in the most part, akin to 'tissue donation'.
- Information about mitochondria donors would be held by clinics to ensure traceability, though the HFEA has a system in place should the status of the mitochondria donor result in certain identifying or non-identifying information being available to mitochondria donor-conceived.

## **7. Other regulatory issues**

- 7.1. ELAC, SCAAC and workshop delegates also mentioned a number of other issues which may require further consideration should mitochondria replacement be permitted in clinical practice. These are summarised below.

Using sex selection to choose male only embryos following mitochondria

### replacement

- 7.2. As a means of avoiding any effects of mitochondria replacement on future generations, it was suggested that only male embryos were used in treatment. However, this was seen as impractical as using sex selection after mitochondria replacement would expose the embryos to additional intervention.

### Assessment of staff competency

- 7.3. This was discussed by SCAAC members who agreed that staff must be competent in the techniques, although further consideration is needed as to how this might be assessed. The HFEA might consider reviewing how fertility clinics had assessed competence when on inspection.

### Family donation

- 7.4. ELAC discussed whether Code of Practice guidance around family donation, which prevents the mixing of gametes of close genetic relatives, should apply in the case of mitochondria donation. For example, it could be envisaged that intended parents may wish the intended father's sister to be the mitochondria donor. It was thought that further consideration should be given to this once the status of the mitochondria donor is agreed.

### Criteria before donating

- 7.5. This was discussed by SCAAC and at the workshop. Delegates questioned what type of screening, or other medical examinations, may be required for mitochondria donors. It was also questioned whether there would need to be an age restriction for mitochondria donors, similar to that for egg donors. This was seen as needing further research and consideration.

## **Annex A: Discussion document used at regulatory workshop**

### **Workshop discussion document**

## **Regulatory considerations for mitochondria replacement techniques**

---

### **Introduction**

The purpose of this workshop is for people working in fertility clinics and other professionals to discuss some of the practical issues that might arise if mitochondria replacement techniques were permitted in clinical practice.

In January 2012, the HFEA was asked to seek the public's view on techniques to avoid mitochondrial disease, and to consider the practical implications of allowing them within Regulations. As well as findings from our public engagement process, we will be providing Government with an idea of some of the issues they may wish to consider should they be minded to draft Regulations allowing mitochondria replacement.

This briefing paper is designed to introduce some of the regulatory issues around mitochondria replacement, preparing delegates for discussion at the workshop on 5 February 2013.

### **Legal context**

Gametes and embryos which have had their nuclear or mitochondrial DNA altered do not fall within the definition of 'permitted' under the Human Fertilisation and Embryology Act 1990 (as amended) (the Act) and cannot be used in treatment. Therefore, techniques to avoid mitochondrial disease are currently only allowed in research.

The Act was amended in 2008, with a provision to allow for Mitochondrial Donation Regulations. These regulations would classify embryos, or eggs, created by a technique designed to avoid mitochondrial disease as permitted embryos or eggs.

Should the law be changed to permit mitochondria replacement in clinical practice, the HFEA is likely to have scope to impose additional requirements on centres performing the technique. These might be in the form of licence conditions or Code of Practice guidance and must be adhered to, either before permission is given to offer mitochondria replacement or through the inspection process.

## Topics for discussion

At the workshop, we want to hear your views on four specific issues. The sections below provide you with a summary of thoughts that we would like to discuss with you. These do not represent our plans, but are presented as a prompt for discussion. At the end of the workshop, there will be an open session where you can raise other points.

### Licensing and eligibility criteria

**We would like to hear your views on the type of authorisation system that may need to be in place for mitochondria replacement techniques, and the diseases they aim to avoid, and what eligibility criteria there might be for patients.**

How might it be decided which mitochondrial diseases are serious enough to warrant using mitochondria replacement? When approving genetic conditions for pre-implantation genetic diagnosis (PGD), the HFEA has to be satisfied that the condition in question meets the 'significant' and 'serious' criteria set out in the Act.

Although some mitochondrial diseases have been authorised for PGD, it may not be straight forward to apply the significance and seriousness test to other mitochondrial diseases. Some types of mitochondrial disease can be linked to a named condition (eg, Leigh's Disease). Other forms of mitochondrial disease, however, have more variable symptoms. Furthermore, the symptoms of these diseases may be hard to predict, depending on the gene mutation involved and the proportion of healthy versus unhealthy mitochondria within a cell.

We would be interested to hear your views on when you think it is appropriate to offer mitochondria replacement, and what eligibility criteria may need to be in place. For example, is there a threshold of unhealthy mitochondria in a patient's gametes or embryos, which means that PGD is not suitable, and mitochondria replacement should be offered immediately?

It could be that the HFEA approves the use of the techniques to avoid certain mitochondrial diseases (on a condition by condition basis), and then the Person Responsible (PR), based on a referral from a specialist genetics team, decides which patients should receive the treatment (as with PGD).

Alternatively, the HFEA could approve the use of mitochondria replacement for patients on a case-by-case basis (as with pre-implantation tissue typing (PTT)). This requires a referral from a patient's treating clinician, stating why the technique is necessary. In the case of mitochondria replacement, it may be that advice would be sought from a mitochondria specialist.

### Key questions to consider

- How might the use of mitochondria replacement techniques be authorised to avoid a particular mitochondrial disease?
- Who should decide when to use mitochondria replacement techniques and for which patients? How might this decision be made?

## Giving consent

**We would like to hear your views on whether donors should be able to opt in to, or out of, their gametes being used in mitochondria replacement techniques, and how to ensure that consent is properly taken.**

Mitochondria replacement techniques are at the cutting edge of science and ethics, involving the manipulation of gametes and embryos. Patients and donors may be unaware of what they involve, or have their own personal view of their acceptability. For example, some donors may not want their nuclear DNA to perish, or alternatively they may only want to donate their mitochondrial DNA (and would therefore prefer this type of donation to 'standard' egg donation).

To address this, it may be desirable for patients and donors to be able to specifically opt in to, or out of, the use of their gametes in mitochondria replacement. In the case of donors, it would mean they could consent to being a gamete donor for 'standard' IVF or donor insemination, but not for mitochondria replacement, or vice versa.

Currently, donors can consent to the use of their gametes, or embryos created *in vitro* with their gametes, in the treatment of others. Whilst there is no option for them to consent to their donation being used in particular procedures such as IVF, ICSI or PGD, they are able to place some restrictions on their donation.

We would be interested to hear whether you think mitochondria replacement techniques justify specific consent, or whether it would suffice to allow donors to note down on their consent that they restrict the use of their donation in mitochondria replacement.

If there was specific consent, allowing donors to opt in to or out of mitochondria replacement, how would centres find taking this consent? There could be a separate consent form specifically for those people donating their gametes to be used in either Maternal Spindle Transfer (MST) or Pro-nuclear Transfer (PNT). If this was not available to donors, there would continue to be a standard consent form to donation. However all potential donors would need to be informed that there is a chance, albeit small, that their donation may be used in mitochondria replacement. Centres may find this a difficult approach as they would be required to provide additional, complex, information prior to donation, about a technique which would affect a very small number of donors.

### Key questions to consider:

- Should donors be able to opt in to, or out of, mitochondria replacement? If so, how?

## Follow-up research on children born

**It has been suggested that if mitochondria replacement is permitted in clinical practice, there should be long-term follow-up research on families and their children. We would like to hear your views on what the HFEA could do to allow this to happen.**

What role should the HFEA and other bodies play in long-term follow-up research of children born through mitochondria replacement? Currently the HFEA acts as a data collector, requiring centres to submit information about each treatment cycle. In recent years, researchers have been able to link this information with other national data sets, allowing studies which look for long term effects of fertility treatment.

If mitochondria replacement is permitted, it is likely that centres will need to send additional information to the HFEA. It might be that a flag is added to forms that clinics submit to the HFEA, stating whether a procedure involved gametes which had mitochondria replacement techniques applied to them, or it may be that additional information is required on the techniques themselves. For example, would it be useful to know if there was any carryover of unhealthy mitochondria in unused eggs or embryos, or if gametes and embryos were damaged when carrying out the treatment? Information such as this might be useful to assess on-going safety and effectiveness.

Alternatively, to aid long-term follow-up research, the role of the HFEA could be to collect basic data on treatment cycles involving mitochondria replacement, but for researchers to go to individual clinics where treatment was carried out for more information. If this was the case, and the HFEA were able to impose a licence condition on centres performing mitochondria replacement, it could state that consent to long-term follow-up studies must be sought from patients. It might also be a requirement that these centres show how they intend to allow researchers to access their data and patients. This, along with specific information on each cycle carried out being held by individual clinics, might allow for suitable follow-up work to take place.

Whilst having long-term follow-up studies on children born would be useful for researchers, it is the choice of the individual couple and child whether they take part in such studies. It might be that the key to aiding follow-up research is being able to link basic HFEA data on treatment cycles, with other NHS information. This kind of linkage study can be done by applying to the HFEA for access to 'Register' data, although since October 2009, this can only be done for patients who have consented to such a use of their data.

### Key questions to consider:

- What mechanisms should be in place to allow for follow-up research to take place?
- What should be the role of the HFEA and fertility clinics to aid follow-up research?
- What information should be submitted to the HFEA about treatment cycles involving mitochondria replacement?

## Access to, and provision of, donor information

**We would like to hear your views on what mechanisms would need to be in place should Parliament decide to classify mitochondria donors differently from gamete donors.**

As part of our engagement work, the public has been asked if mitochondria donation is comparable with other types of donation such as organ, blood or tissue and, consequently, what type of information should be available to the children born. Due to your experience of working with both patients and donors, we would like to hear your views on how mitochondrial donors may be classified, and what issues may arise from this.

At this stage it is not clear whether mitochondria donors will be classified differently from standard gamete donors. It could be argued that they are comparable with tissue donors, providing an important contribution to a person's health. In this scenario, recipients may be grateful for the donor's important contribution, but less interested in knowing personal details about them as they would not be genetically related to the same extent as in standard gamete donation.

Alternatively, they could be classified in a similar way to standard gamete donation as they would be biologically related, and the donation would have resulted in them being born with a highly reduced risk of developing a mitochondrial disease. In either case, any resulting child may be curious to find out details of their donor, although it is common place in other forms of tissue donation (such as blood or organ) not to know details of the donor.

We'd be interested to hear your thoughts on how the mitochondria donor could be classified and what level of information could be collected and possibly provided to any resulting child. Currently, children born through donor conception can find out identifiable information, as well as details of the medical history and physical characteristics of their donor. Should this be an option for mitochondria donor-conceived children? It could be argued that scientific knowledge on the role of mitochondria may develop over the coming years, and it would be useful for a child who was conceived through mitochondria replacement to have some details about their donor (for example, information on their medical history).

We'd also like to hear your views on what type of information a mitochondria donor could access about their donation. This may depend on whether they are given the status of 'tissue' or 'gamete' donor, although currently, gamete donors can find out the number, year of birth, and sex of children born from their donation.

Furthermore, if donors are not told in advance whether their donation will be used for mitochondria replacement, should they be informed of this by the HFEA when they request information? Knowing this could impact on how they tell their families about their donations. Alternatively, this could be the responsibility of fertility clinics.

### Key questions to consider:

- How might mitochondria donors be classified? As a tissue or gamete donor? What issues might arise from either of these classifications?
- What type of information should mitochondria donors be able to access about children born through mitochondria replacement?



## Further Information

This document gives some background to the issues we would like to discuss with you. These, and other issues, were discussed in further detail at the HFEA's Ethics and Law Advisory Committee meeting on 7 November 2012 ([www.hfea.gov.uk/ELAC-November-2012.html](http://www.hfea.gov.uk/ELAC-November-2012.html)) and at the Scientific and Clinical Advances Advisory Committee meeting on 31 October 2012 ([www.hfea.gov.uk/7559.html](http://www.hfea.gov.uk/7559.html)).

### Mitochondria replacement techniques

**Pro-nuclear transfer (PNT):** involves transferring the pronuclei from an embryo with unhealthy mitochondria into a donor embryo which contains healthy mitochondria but has had its pronuclei removed. This new embryo contains nuclear DNA from the intended father and mother and healthy mitochondrial DNA from the donor embryo.

**Maternal spindle transfer (MST):** involves transferring the spindle from the intended mother's egg and placing it into a donor egg with healthy mitochondria (from which the donor's spindle, and therefore the nuclear DNA, has been removed). The mother's egg, now without any nuclear DNA, is destroyed. This creates a healthy egg which can then be fertilised with the intended father's sperm.

Visit our consultation website to find out more about the techniques, and the process involved: <http://mitochondria.hfea.gov.uk/mitochondria/>

# **Annex VIII: Scientific review of the safety and efficacy of methods to avoid mitochondrial disease through assisted conception: update**

Report provided to the Human Fertilisation and Embryology Authority,  
March 2013

Review panel chair: **Professor Neva Haites, University of Aberdeen**



## Contents

	Page
Executive summary	3
1. Introduction, scope and objectives	6
2. Review of maternal spindle transfer and pronuclear transfer to avoid mitochondrial disease	7
3. Further research	19
Annex A: Methodology of review	23
Annex B: Evidence reviewed	25

## Executive summary

Mitochondria are small structures present in cells that produce much of the energy required by the cell. They contain a small amount of DNA that is inherited exclusively from the mother through the mitochondria present in her eggs. Mutations in this mitochondrial DNA can cause a range of rare but serious diseases, which can be fatal. However, there are several novel methods with the potential to reduce the transmission of abnormal mitochondrial DNA from a mother to her child, and thus avoid mitochondrial disease in the child and subsequent generations.

The Human Fertilisation and Embryology (HFE) Act 1990 (as amended) only permits eggs and embryos that have not had their nuclear or mitochondrial DNA altered to be used for treatment. However, the Act allows for regulations to be passed by Parliament that will allow techniques that alter the DNA of an egg or embryo to be used in assisted conception, to prevent the transmission of serious mitochondrial disease.

The Secretary of State for Health asked the Human Fertilisation and Embryology Authority (HFEA), in February 2011, to carry out a scientific review to scope “expert views on the effectiveness and safety of mitochondrial transfer”. In order to carry out this task, the HFEA established a small panel, with broad-ranging scientific and clinical expertise, to collate and summarise the current state of expert understanding on the safety and efficacy of methods to avoid mitochondrial disease through assisted conception. The panel reported its findings in April 2011.<sup>1</sup>

The panel noted that Preimplantation Genetic Diagnosis (PGD)<sup>2</sup> can only reduce, not eliminate, the risk of transmitting abnormal mitochondrial DNA that may lead to a mitochondrial disease. PGD is suitable for some, but not all, patients who suffer from mutations in their mitochondrial DNA. The panel made recommendations for centres carrying out PGD for mitochondrial disease to reduce the level of uncertainty around the diagnosis.

The panel concluded that the techniques of Maternal Spindle Transfer (MST) and Pronuclear Transfer (PNT)<sup>3</sup> are potentially useful for a specific and defined group of patients whose offspring may have severe or lethal genetic disease, due to

---

<sup>1</sup> <http://www.hfea.gov.uk/6372.html>

<sup>2</sup> PGD involves removing and examining one or more cells from an early embryo, in the current context to identify those embryos that are unlikely to develop a mitochondrial disorder in the resulting child. PGD for mitochondrial diseases is licensed in the UK.

<sup>3</sup> Maternal spindle transfer and pronuclear transfer are two techniques, currently at the research stage that would involve transferring the nuclear genetic material from an unfertilised or fertilised egg that contains mitochondria with mutant mtDNA into an unfertilised or fertilised donor egg with normal mitochondria from which its nuclear genetic material has been removed. Neither technique is permitted for treatment under the HFE Act 1990 (as amended) because each replaces (and thereby alters) the mitochondrial DNA of the egg or embryo with that from the donor.

mutations in mitochondrial DNA<sup>4</sup>, and who have no other option of having their own genetic child. As in every area of medicine, moving from research into clinical practice always involves a degree of uncertainty. The panel concluded that evidence available at that time (March 2011) did not suggest that the techniques are unsafe. Nevertheless, these techniques, especially applied to human embryos are novel, and have relatively few data to provide robust evidence on safety. The panel therefore urged that additional research be undertaken to provide further safety information and knowledge about the biology of human mitochondria and the panel proposed a set of experiments that it felt to be critical. Although optimistic about the potential of these techniques, the panel recommended a cautious approach and advised that this research be carried out, and the results taken into account, before the techniques can be considered safe and effective for clinical use.

Following receipt of this report the Secretary of State for Health and the Secretary of State for Business, Innovation and Skills asked the HFEA (together with Sciencewise<sup>5</sup>) to conduct a programme of public dialogue on the social and ethical impact of making these techniques available to patients. The findings of this public dialogue work, together with considerations of the practical implications of allowing these techniques to take place within regulations, will be reported back to the Government in spring 2013.

In anticipation of the outcomes of this public dialogue work the Secretary of State for Health asked the HFEA, in December 2012, to provide an updated view on the science to support the assessment of the efficacy and safety of MST and PNT techniques, including any recently published findings and the extent to which the panel's recommendations have been addressed. This report outlines the panel's updated view. It should be read alongside the panel's 2011 review. The remainder of this executive summary sets out the panel's conclusions regarding the safety and efficacy of MST and PNT (as of March 2013).

The panel's view still stands that MST and PNT have the potential to be used for all patients with mtDNA disorders, which may make them preferential to PGD in the future. In patients with homoplasmy or high levels of heteroplasmy, these are the only techniques that would make it possible for them to have a genetically related unaffected child.

There is currently more published work available to support MST than PNT, but there is still insufficient evidence to recommend one transfer technique over the other. Indeed, once an embryo begins to develop normally, the data accumulating from the two methods would appear to be very complementary.

Although the results with the two techniques are promising, further experiments need to be done before introducing either into clinical practice to provide further

---

<sup>4</sup> Mitochondrial disease can also be due to mutations in nuclear genes that encode products required within mitochondria, for which these methods are not relevant, although PGD can be used in these cases.

<sup>5</sup> The Sciencewise Expert Resource Centre (Sciencewise-ERC) is the UK's national centre for public dialogue in policy making involving science and technology issues.

reassurance with respect to efficiency and safety.

Once assessed as safe to use in clinical practice, the panel strongly recommends that permission is sought from the parents of the children born from MST or PNT to be followed up for an extensive period (then seek permission from the children themselves, when old enough). In the case of females, this ideally should be extended to the next generation. These recommendations should also apply to PGD for mtDNA genetic diseases.

Until knowledge has built up that says otherwise, the panel recommends that any female born following MST or PNT should be advised, when old enough, that she may herself be at risk of having a child with a significant level of mutant mtDNA, putting this child or (if a female) subsequent generations at risk of mitochondrial disease. Thus, we recommend that any female born following MST or PST is advised that, should she wish to have children of her own, that her oocytes or early embryos are analysed by PGD in order to select for embryos free of abnormal mtDNA. This has the potential to eliminate risk in subsequent generations.

The panel recommends the following regarding the minimum set of critical experiments set out in the 2011 report:

- MST using human oocytes that are then fertilised (not activated). This has now been carried out and published, but it is still important for some follow-up experiments to be carried out, notably to improve efficiency if possible, and further corroborative experiments would be valuable.
- Experiments comparing PNT using normally-fertilised human oocytes with normal ICSI fertilised human oocytes appear to be well underway, but their results will need assessing before they can be incorporated into future recommendations.
- The panel no longer feels that PNT in a non-human primate model, with the demonstration that the offspring derived are normal, is critical or mandatory.

The panel now considers the following related set of experiments to also be critical:

- Further studies on mosaicism in human morulae (comparing individual blastomeres) and on human embryonic stem (ES) cells (and their differentiated derivatives) derived from blastocysts, where the embryos have (i) originated from oocytes heteroplasmic for mtDNA and (ii) been created through MST and PNT using oocytes or zygotes with two different variants of mtDNA. Although experiments are already reported on ES cells and their derivatives with MST, further corroborative experiments would be valuable.

The panel makes a number of updated recommendations regarding additional recommended research, which are outlined at 3.9 and 3.10.

# 1. Introduction, scope and objectives

## 1.1 Introduction

- 1.1.1** Mitochondrial malfunction has been recognised as the significant cause of a number of serious multi-organ diseases. The underlying defects can be due to mutations in nuclear DNA affecting gene products required within mitochondria, or to mutations in DNA carried within the mitochondria themselves. The latter encode products required exclusively for the oxidative phosphorylation (OxPhos) process of the electron transfer chain, which generates energy for cells in the form of ATP. Although relatively rare, the seriousness of these diseases and particularly the unusual inheritance pattern of mitochondrial DNA (mtDNA) mutations have made them a focus for research into preimplantation methods to reduce or avoid a disease in offspring.
- 1.1.2** Section 2 of the 2011 report provides an overview of mitochondrial biology and disease including definitions of terms and a list of clinical disorders that are associated with mutations in mitochondrial DNA (mtDNA). Section 3 of the 2011 Report considered and made recommendations on the use of PGD to avoid mitochondrial disease and annex D outlined a glossary. This information has not been repeated within this update.

## 1.2 Scope and objectives of this review

- 1.2.1** The terms of reference for the panel are to “collate and summarise the current state of expert understanding on the safety and efficacy of maternal spindle transfer and pro-nuclear transfer in order to update their report of April 2011.” Accordingly, this review focuses exclusively on the science and the safety and effectiveness of these techniques, and does not consider the ethical and legal issues that are raised by such techniques.
- 1.2.2** The methodology of this review is set out at annex A and the evidence reviewed is listed at annex B.
- 1.2.3** This report is structured as follows: section 2 and 3 consider the effectiveness and safety of MST and PNT, suggests further research and makes recommendations. In addressing its terms of reference, the panel has tried to set out the issues in as clear a manner as possible. However, as the biology of mitochondria is complex, the language used is necessarily technical in parts.

## 2. Review of maternal spindle transfer and pronuclear transfer to avoid mitochondrial disease

### 2.1 Recap summary of the methods

- 2.1.1** In cases where PGD is not appropriate, such as cases where the woman has high levels of mitochondrial heteroplasmy<sup>6</sup> or is homoplasmic<sup>7</sup> for mutant mtDNA, transmission of mtDNA disease can be avoided by using healthy donated oocytes. This method is safe, and has strong supporters<sup>8</sup>. However, whilst this guarantees the disease is not transmitted, it also means that any resultant child will not be genetically related to the mother. The novel methods that the panel reviewed allow the transmission of both parent's nuclear DNA but involve replacing abnormal mitochondria with normal mitochondria: maternal spindle transfer (MST) and pronuclear transfer (PNT).
- 2.1.2** MST uses micromanipulation techniques to transfer the nuclear genetic material (the spindle with maternally-derived chromosomes attached) from one oocyte into another from which its nuclear genetic material has been removed<sup>9</sup>(Figure 1). The reconstituted oocyte is then fertilised to allow embryo development. PNT uses similar micromanipulation techniques to transfer the nuclear genetic material, in this case both the maternal- and paternal-derived pronuclei, from a fertilised oocyte (zygote) into an enucleated donor zygote (Figure 2). MST takes place between mature metaphase II oocytes. PNT takes place between fertilised oocytes, after the stage where the egg has been penetrated by sperm but prior to the first embryonic cell division. Both techniques are therefore carried out prior to the formation of an embryo when the maternal and paternal chromosomes come together within the same nucleus<sup>10</sup>. With either method, any resulting child would inherit nuclear genetic material from both parents, while the mitochondria would be derived largely or perhaps exclusively from the oocyte provided by the donor. These methods could therefore effectively substitute the mitochondria in the oocytes of a woman known to carry mutant mtDNA with mitochondria carrying normal mtDNA from the oocyte donor. If efficient, so that there is little or no transfer of abnormal mtDNA, this method could avoid mitochondrial disease not just in the resulting child, but also in subsequent generations (but see further detail on this below).

---

<sup>6</sup> Where two or more different mtDNA types coexist in a single cell, commonly used (as in this report) where one type is abnormal, and the other normal

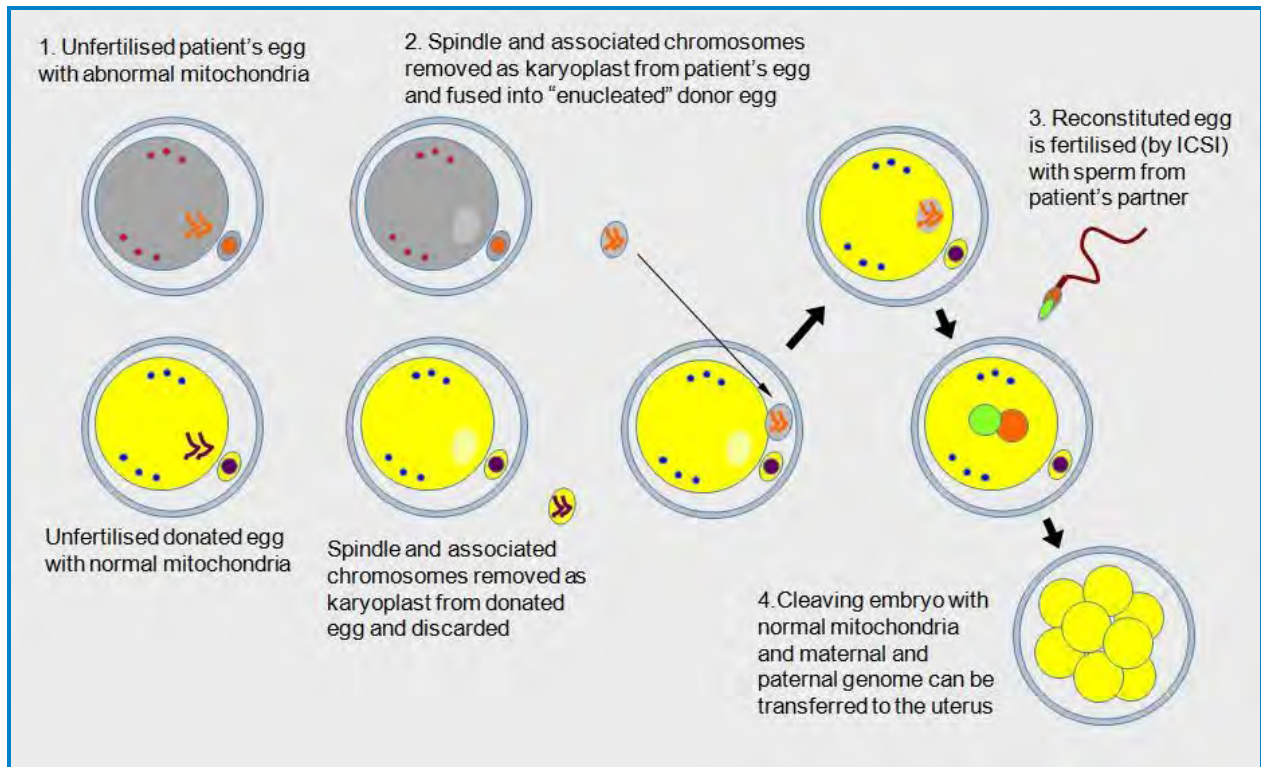
<sup>7</sup> Where all the mitochondria in a cell contain the same mtDNA, which can either be all abnormal or all normal

<sup>8</sup> A statement from Joanna Poulton (Professor and Hon Consultant in Mitochondrial Genetics, University of Oxford), Joerg P Burgstaller (IFA Tulln and University of Veterinary Medicine Vienna) and Iain G. Johnston (Imperial College London)

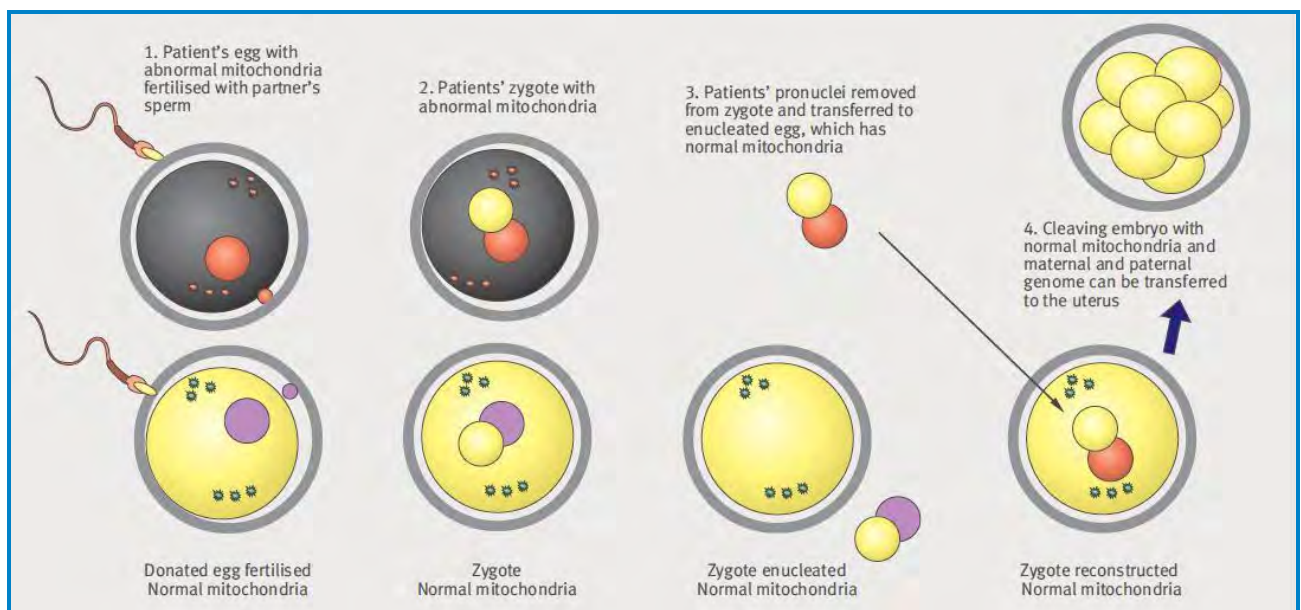
<sup>9</sup> This is equivalent to the oocyte being enucleated, and this term is used by some, although the chromosomes are not contained within a nuclear membrane at this stage.

<sup>10</sup> MST occurs pre-fertilisation and PNT occurs post-fertilisation but prior to the breakdown of the pronuclear membranes (syngamy)





**Figure 1. Maternal spindle transfer technique**



**Figure 2. Pronuclear transfer technique<sup>11</sup>**

<sup>11</sup> Bredenoord, A and P. Braude (2010) "Ethics of mitochondrial gene replacement: from bench to bedside" BMJ 341. Image reproduced with permission of Author

**2.1.3** Although similar methodology is employed, it is important to stress that neither MST nor PNT is equivalent to reproductive cloning (somatic cell nuclear transfer, or SCNT). Any children resulting from MST or PNT would have arisen from fertilisation and be genetically unique. They would be the genetic child of the woman receiving treatment and her partner. MST and PNT do not involve reprogramming cells or nuclei as SCNT does, which is a relatively inefficient process and associated with significant risks of abnormal development<sup>11</sup>.

## **2.2 Effectiveness of MST and PNT**

**2.2.1** A review of the effectiveness of MST and PNT, based on studies published up to March 2011, is outlined in section 4.2 of the original report.

**2.2.2** Since 2011, several significant proof-of-principle studies with respect to the possible use of MST and PNT methods for treating mitochondrial disease have been carried out using human oocytes and zygotes and also with Macaque oocytes:

**2.2.3** MST has been carried out on 65 human oocytes donated for research (a further 33 served as controls). Although some oocytes displayed clear evidence of abnormal fertilisation (53% - determined by an irregular number of pronuclei), remaining embryos were capable of developing to blastocysts and producing embryonic stem cell lines at rates similar to controls. All five of the embryonic stem cell lines derived from zygotes predicted to have undergone normal fertilisation after MST had normal euploid karyotypes and contained exclusively donor mtDNA<sup>12</sup> (Tachibana et al, 2013).

**2.2.4** A second study has also demonstrated the use of MST with human oocytes, although these were parthenogenetically activated rather than fertilised. The primary purpose of the study was to assess the degree of mitochondrial DNA carryover rather than establishing a technique for creating embryos for clinical use. MST was shown not to reduce developmental efficiency to the blastocyst stage, and genome integrity was maintained, provided that spontaneous oocyte activation was avoided through the transfer of spindle–chromosome

---

<sup>11</sup> The panel examined substantial evidence about SCNT as part of the 2011 review, including studies on heteroplasmy where mitochondria in the somatic cell persisted, sometimes at high levels, in the cloned embryo and offspring. This was usually associated with fusion of the somatic cell with an enucleated oocyte. This can introduce significant numbers of mitochondria that are in an active and replicating state, together with associated mitochondrial replication factors made by the somatic cell nucleus. In contrast, these factors are probably absent in mitochondria in mature oocytes or zygotes, as these mitochondria do not replicate until later. MST and PNT do not involve somatic cells.

<sup>12</sup> An ES cell line was also established from a zygote that had 3 pronuclei and one polar body (3PN/1PB) instead of the normal 2PN/2PB. This had a triploid karyotype consistent with a failure to extrude the second polar body and retention of its genetic material.

complexes that were incompletely assembled or partially disassembled (depolymerised). The authors claim to be able to achieve the latter by cooling the oocyte. Mitochondrial DNA transferred with the nuclear genome was initially detected at levels below 1%, decreasing in blastocysts and embryonic stem-cell lines to undetectable levels, and remained undetectable after passaging for more than one year, clonal expansion, differentiation into neurons, cardiomyocytes or pancreatic beta-cells, and after cellular reprogramming to derive iPS cells. Stem cells and differentiated cells had mitochondrial respiratory chain enzyme activities and oxygen consumption rates indistinguishable from controls. These cells were homozygous for all alleles (as they have become diploidised from an originally haploid state) and so would only give information about maternal imprinting. (Paull et al, 2013)

**2.2.5** The panel was informed of unpublished findings regarding PNT and MST from the “Newcastle Group”. Initial experiments using normally fertilised human zygotes for PNT have revealed the importance of timing of the various procedures and of matching developmental stage of the two zygotes. With optimisation, they have begun to obtain a significant proportion of manipulated embryos developing to blastocyst stages. Some zygotes resulting from PNT have been successfully vitrified and further work is being carried out to improve the quality and rate of development to blastocysts and to minimise mtDNA carryover at the blastocyst stage.

**2.2.6** The panel noted that this information, together with comments from both the other groups interviewed, suggests that issues of timing may be relevant to any intended use of MST or PNT clinically since the cycles of the two egg donors will need to be synchronised. Egg retrievals will need to be carefully timed in order to be near coincident, the eggs need to be fertilised as soon as possible after collection, and for PNT the procedure needs to be carried out as soon as possible after normal fertilisation is confirmed. If there is a prolonged period of time between the two egg collections then one set of eggs may be over-mature, potentially leading to reduced development and an increase in abnormality rates. As this synchrony may not always be possible in a clinical setting, vitrification of eggs has been suggested as a solution. This is probably not an issue of safety, but one of efficiency, because the abnormalities are likely to be obvious and/or lead to early embryo lethality.

**2.2.7** Data obtained from Macaques in the Tachibana et al (2013) study showed that cytoplasm is more sensitive to vitrification-induced damage than the spindle, which might suggest that the affected mother’s oocytes should be frozen and thawed when a fresh donor oocyte become available. However, Macaque oocytes seem to be more sensitive than human oocytes to this freezing method. Paull et al (2013) also examined this, and found that they could freeze isolated “karyoplasts” from human oocytes (the spindle plus chromosomes, surrounded by oocyte membrane, but with little cytoplasm), and use these in MST after thawing.

**2.2.8** Current research using PNT in Macaques has yet to be shown to be successful. From unpublished data<sup>13</sup> it appears that Macaque zygotes do not survive the PNT process well and published evidence suggests that there may be important differences between human and Macaque oocytes and early embryos; for example, different sensitivities to cryopreservation, and Macaque oocytes being less prone to abnormal activation/fertilisation following MST than human oocytes (as seen in Tachibana et al (2009) versus Tachibana et al (2013)). The panel now believes that the Macaque may not be a sufficiently good model for the human. Although this review is focused on the science, it is an ethical concern to carry out experiments on animals, especially non-human primates, if these are likely to not be informative. Therefore, given that the most critical species in which to obtain results is the human, and because there are differences in the very early embryology between mammalian species, the panel also concludes that if any additional experiments on PNT and MST in other animal models reveals differences with the human, it would be not just reassuring, but important if such experiments revealed the underlying reasons, and did not merely state the problem.

## **2.3 Safety of MST and PNT**

**2.3.1** A review of the safety of MST and PNT, based on studies published up to March 2011 is outlined in section 4.3 of the original report. Based on the new evidence submitted the panel re-examined and commented on the following safety issues of the MST and PNT techniques: the carryover of mtDNA from the affected oocyte or zygote; the methods to prevent premature activation of oocytes or detect abnormally fertilised oocytes, the nuclear-mitochondrial interactions involved and the potential for long-lasting nuclear epigenetic modifications resulting from manipulation or altered mitochondrial states associated with mitochondrial disease. The panel did not specifically revisit previous discussions regarding the safety of reagents used to carry out the micromanipulation techniques. However, it was noted that the study by Paull et al (2013) relied on the use of several such reagents, the combination of which might have been expected to be deleterious, yet development of the (parthenogenetically activated) embryos, and ES cell lines derived from them, was apparently normal. It was felt by the panel, and by those it interviewed, that the number of reagents and their concentration should be kept to a minimum.

**2.3.2 mtDNA carryover:** Carryover of mtDNA from the affected oocyte or zygote might be expected with both techniques because the spindle or the pronuclei are enclosed in a karyoplast during the manipulation technique, which contains a small amount of surrounding cytoplasm enclosed in cell membrane in addition to the nuclear DNA. In theory, carryover of abnormal

---

<sup>13</sup>Reported at a media briefing in October 2012 and reflected in a number of articles e.g. [http://www.sciencenews.org/view/generic/id/346024/description/Cloning-like\\_method\\_targets\\_mitochondrial\\_diseases](http://www.sciencenews.org/view/generic/id/346024/description/Cloning-like_method_targets_mitochondrial_diseases)



mtDNA may be an issue if abnormal mtDNA is preferentially replicated and if there is a marked difference in segregation across tissues. However evidence presented to the panel continues to be reassuring that neither occur, at least in somatic cell lineages (see 2.3.5 and 2.3.10 below for germ cells, where the situation is more complex).

**2.3.3** It is relevant to note that a threshold of mitochondrial function is required for normal development, and despite developmental plasticity of the embryo, impaired mitochondrial function in the embryo affects subsequent fetal and placental growth (Wakefield et al, 2011).

**2.3.4** One study suggested that (experimental) admixture of two normal but different mouse mtDNAs can be genetically unstable and can produce adverse physiological effects (Sharpley et al, 2012). These results could indicate that the differences between mtDNAs within a mammalian species may not be neutral and are suggested to explain the advantage of uniparental inheritance of mtDNA. This could be a concern for MST and PNT. However, the study used approximately equal amounts of mtDNA from two very different mouse strains, which could be considered distant subspecies. Also, another study, exploring mtDNA segregation during early embryogenesis in Macaques, produced distinctly different results - no such problems were observed with mixtures of mtDNA from two Macaque subspecies. However, the oocytes created to be heteroplasmic (50/50) for these two types of Macaque mtDNA variants resulted in embryos exhibiting significant partitioning of the mtDNA between different blastomeres and to some extent between trophectoderm and ICM. This partitioning seems to have resulted in some of the fetuses, or ES cell lines derived from such embryos, also showing a skewed ratio (in one case about 94% of one of the mtDNA variants was present). There was no evidence of preferential selection for 'resident' versus 'alien' mtDNA, suggesting that both variants work equally well with the resident nuclear DNA, even though the mtDNA sequence of the two sub-species of Macaque are as different from each other as they are from other primate species (Lee et al, 2012). The degree of heteroplasmy was so substantial that it could lead to homoplasmy. This could be an issue if one of the mtDNA variants is defective, with, by chance, either a beneficial or poor outcome for the individual born. However, the starting point in these experiments was about 50-50, whereas MST (or PNT) should give very low levels of carryover of mutant mtDNA, making homoplasmy for the normal mtDNA even more likely.

**2.3.5** The authors also carried out MST between oocytes of the two Macaque subspecies to explore whether this preimplantation segregation of mtDNA variants could be a problem. They first determined that isolated karyoplasts carry "bound" mtDNA (there is no evidence that it is physically bound, just closely associated) at an average level of about 0.6% of the numbers within the cytoplasm. After MST, about 68% of fertilised oocytes developed to blastocysts, confirming earlier published data from the same group

(Tachibana et al, 2009)<sup>14</sup>. They then selected female blastocysts for embryo transfer, recovering two fetuses in which to survey levels of heteroplasmy. The mtDNA variant from the spindle donor oocytes was very low or undetectable in somatic tissues, suggesting a tendency towards homoplasmy. However, two out of 24 oocytes isolated from the fetal ovaries showed around 15% heteroplasmy. This difference between somatic and germ line was also evident in their earlier experiments, with segregation in oocytes appearing to be largely independent of that occurring in other tissues.

**2.3.6** These findings largely support what is known about mtDNA levels and founding cell numbers of somatic tissues and the germ line during early postimplantation development and bottleneck theories as outlined in the panel's 2011 report. However, the observation of much earlier segregation of mtDNA, in cleavage stage embryos, is novel and contradicts evidence obtained from human embryos where blastomeres within an embryo tend to have very similar levels of heteroplasmy (as also demonstrated by Sallevelt et al, 2013 and Treff et al, 2012 - although with a few outliers). This could suggest that there is relatively little mixing of cytoplasm after spindle (or cytoplasm) transfer, such that cleavage divisions are responsible for the segregation, whereas with heteroplasmy already existing in a growing oocyte, the mtDNA variants are likely to be distributed at random.

**2.3.7** Modelling the inheritance of mtDNA has led to the conclusion that for a disease with a clinical threshold of say 60% mutant mtDNA (which is fairly typical) reducing the mutant mtDNA load to <5% with MST or PNT should dramatically reduce the chance of disease recurrence not just in the child, but in subsequent generations (Samuels et al, 2013). However, >5% carryover was associated with a significant chance of recurrence. Mutations with a lower clinical threshold were also likely to have a higher risk of recurrence, but reducing the amount of carryover would counteract this. If the threshold is very low, and the panel noted that there has been one report of heteroplasmy levels of less than 10% causing disease for a dominant mitochondria mutation initially detected in muscle<sup>15</sup>, then the modeling may not be adequate. Moreover, it does not take account of the possibility of preferential replication or selection of mtDNA carrying specific mutations, however, there is little evidence of this occurring.

**2.3.8** Publications and discussions with researchers indicate that PNT currently shows higher level of carryover than MST (up to 2% versus 0.3%) (Tachibana et al, 2013; Paull et al, 2013; Craven et al; 2010<sup>16</sup>). This may be due to

---

<sup>14</sup> Tachibana M et al. (2009) Mitochondrial gene replacement in primate offspring and embryonic stem cells. *Nature*. 17;461(7262):367-72.

<sup>15</sup> Alston CL et al. (2010). "A novel mitochondrial tRNAGlu (MTTE) gene mutation causing chronic progressive external ophthalmoplegia at low levels of heteroplasmy in muscle." *J Neurol Sci*. 15;298(1-2):140-4.

<sup>16</sup> Craven L., H. A. Tuppen, et al. (2010). "Pronuclear transfer in human embryos to prevent transmission of mitochondrial DNA disease." *Nature* 465(7294):82-5

differences in the geometry and volume of the transferred structures, since two pronuclei are transferred in PNT rather than one spindle associated chromosome set in MST.

**2.3.9** During the discussions, the panel was also minded to draw attention to parallels with PGD for mtDNA mutations in terms of acceptable levels of heteroplasmy in offspring. Although the intention of such therapy is to select embryos for transfer with as low a level of mutant mtDNA as possible to avoid the birth of a child who would manifest the disease in their lifetime, issues to do with variable segregation of mutant mitochondria in their tissues and especially their gametes also apply here. Hence clear rules for acceptable levels of mtDNA heteroplasmy allowing transfer or not of an embryo should be developed for each disease by the specialist clinical team in conjunction with their patients, and follow up of such children and their offspring is strongly recommended, as the panel have recommended for offspring arising for MST and PNT – see 2.3.21.

**2.3.10** In conclusion, any early segregation of a very low level of mutant mtDNA is unlikely to be a problem for children born as a result of MST (or PNT). Nevertheless, it would be reassuring to verify this with human preimplantation embryos generated as a result of MST and PNT for research purposes, and in ES cells and their differentiated derivative cell types obtained from such embryos. There is a potential concern, however, for subsequent generations if a female child born after the use of these techniques has a proportion of oocytes with a significant level of heteroplasmy. This could be researched by, for example, following differentiation protocols reported to generate primordial germ cells from human ES cell in vitro. Alternatively, it may be sufficient to explore these ‘bottleneck’ issues by looking at ES cell sub-lines derived from single cells (‘clonal analysis’). If it turns out that there is a significant risk that a proportion of oocytes and therefore any resulting embryos from a woman born after MST or PNT could be heteroplasmic, then a recommendation might be for her to make use of PGD to select for embryos homoplasmic for the normal mtDNA variant.<sup>17</sup> From the data on macaques derived by MST, if the child is female, then it is possible that some of her oocytes may have a significant proportion of mutant mtDNA, considerably higher than her somatic tissues. The levels may still not be sufficient to cause her children to have a problem, but subsequent generations could be affected. Although diagnostic technology may well have advanced by then, by carrying out PGD (on embryos created from oocytes of female offspring resulting from MST or PNT, who might be carriers of the mutation in some of their oocytes) it ought to be possible to select embryos for implantation that have no abnormal mitochondria. This would guarantee that subsequent generations would be free from disease.

---

<sup>17</sup> There is an accepted precedent for a method of ART having a known consequence for reproduction in the next generation. This is when ICSI is used for male infertility when the cause is known to be due to a Y chromosomal defect. Any son born as a result will carry the same defect and ICSI will be required for him to have a child – and so on.

- 2.3.11 Methods to prevent premature activation of oocytes or detect abnormally fertilised oocytes:** The proof of principle studies, outlined in section 2.2, have demonstrated that nuclear genome transfer carried out in the process of MST can lead to premature oocyte activation and abnormal fertilisation. The panel explored the measures that could be put in place to address these risks.
- 2.3.12** The panel was reassured to hear that the abnormally fertilised eggs created followed MST can easily be identified using a standard stereo-microscope by looking for normal number of pronuclei and polar bodies which have failed to extrude at the PNT stage. As part of the tests to look for normality of development, array comparative genome hybridization (CGH) was used on trophectoderm biopsies from MST derived human blastocysts. Analysis did not detect abnormalities in uniformly triploid embryos suggesting some shortcomings of CGH approaches<sup>18</sup>. Some of the abnormalities associated with MST can be detected only after sperm fertilisation and some are likely to have been due to problems with oocyte ageing (Tachibana et al, 2013).
- 2.3.13** Paull et al (2013) reported that premature oocyte activation could be prevented by partial depolymerization of the spindle–chromosome complex through cryopreservation or cooling to room temperature, allowing normal polar body extrusion (Paull et al, 2013). The authors confirmed that they were satisfied that implementing a spindle chilling stage did not damage the spindle since they had not seen dispersion of the spindle, as had been suggested in a previous research paper (Pickering et al, 1990)<sup>19</sup>. The spindle came back to normal size on warming and the oocyte extruded a polar body.
- 2.3.14 Nuclear-mitochondrial interactions:** A concern has been raised that there might be a failure of correct nuclear-mitochondrial interaction following MST or PNT because the donor mtDNA may be of a haplogroup different from that with which the maternal nuclear genome had been functioning. Mitochondria from separate human lineages can be classified according to similarities or differences in their DNA sequence into many different haplogroups. The more evolutionary distant the separation of two maternal lineages, the greater the differences between mitochondrial haplogroups. This is typified by comparisons between European and African mtDNA. However, the panel maintains the view that there is no evidence for any mismatch between the nucleus and any mtDNA haplogroup, at least within a species (with the possible exception of the study by Sharpley et al (2012) mentioned in 2.3.4). Fifty per cent of nuclear genes are paternally inherited

---

<sup>18</sup> Details relating to the shortcomings of CGH testing were provided by Mitalipov et al in supplementary information, to the core panel, and are not included in the Tachibana et al 2013 published article. The Panel was informed that CGH analysis of biopsied trophectoderm in blastocysts did not detect uniform triploidy. Therefore uniform triploidy was confirmed by deriving ESCs from the same blastocyst using conventional G-banding.

<sup>19</sup> Pickering SJ, et al (1990) "Transient cooling to room temperature can cause irreversible disruption of the meiotic spindle in the human oocyte." *Fertility and Sterility* 54(1):102-108



and are consequently 'alien' to the mtDNA; backcrossing can replace the nuclear DNA entirely in a few generations. Furthermore, mitochondrial disease has not been noted to be more frequent amongst mixed-race children. Tachibana et al (2013) also conducted a 3-year follow-up study on MST-derived macaque offspring born in 2009. The two species of Macaques used in these MST experiments have distinct mitochondrial haplotypes, yet neither the mixing of mitochondria nor swapping the haplotype with respect to their nuclear genome with which it normally resides, appears to result in any adverse effects in offspring. All four (males) were healthy and had normal mitochondrial function. Moreover, there were no significant changes with age in the degree of heteroplasmy in blood and skin cell samples, which remained less than 1% from the spindle donor. However, if further concerns were raised, it would be possible to match mtDNA haplogroups from the egg donor and the mother.

**2.3.15 Long lasting nuclear epigenetic modifications:** Concerns have been expressed relating to the potential for long lasting damaging effects on development or the health of offspring resulting from nuclear epigenetic perturbations resulting either from MST or PNT manipulations or associated with mitochondrial disease and manifest prior to manipulations. While the panel cannot rule out the possibility of epigenetic alterations in either instance, there is no evidence at present that such alterations have a significant or far reaching effect on development or health. One of the more recent studies reporting on MST in humans includes 3 year follow up health data on non-human primates created by this procedure which failed to reveal any adverse effects (Tachibana et al, 2013). It remains unknown whether there are aberrations in maternally epigenetically imprinted genes in oocytes linked to mitochondrial disease. If so, one would anticipate that this would perturb development of normally fertilised embryos and to the panel's knowledge there is no evidence that this is the case. For example, pathologies associated with typical imprinting defects, such as Angelman or Beckwith Wiedemann syndromes, have not been noted to occur in children with mitochondrial disease. Moreover, the mitochondria in growing oocytes are in a form that suggests that they are mostly inactive; therefore, on theoretical grounds the presence of mutant mtDNA in a growing and maturing oocyte is likely to be of little or even no consequence to the nuclear DNA.

**2.3.16 The panel's view still stands that MST and PNT have the potential to be used for all patients with mtDNA disorders, which may make them preferential to PGD in the future. In patients with homoplasmy or high levels of heteroplasmy, these are the only techniques that would make it possible for them to have a genetically related unaffected child.** Even where a proportion of embryos have levels of mutant mtDNA below the threshold known to lead to clinical disease, the evidence the panel has reviewed here, and in the original report, suggests that this does not always reflect the levels seen in offspring (due to bottleneck effects). Moreover, subsequent generations (if the embryos implanted after PGD are female), will continue to be at risk, even if the levels of heteroplasmy for the mutant

mtDNA are low. It might be hoped that improvement to MST or PNT might eventually lead to no or such minimal levels of carryover that the mtDNA disease has effectively been eliminated from the germline.

**2.3.17** There is currently more published work available to support MST than PNT, but there is still insufficient evidence to recommend one transfer technique over the other. Indeed, once an embryo begins to develop normally, the data accumulating from the two methods would appear to be very complementary.

**2.3.18** Although the results with the two techniques are promising, further experiments need to be done before introducing either into clinical practice to provide further reassurance with respect to efficiency and safety.

**2.3.19** The frequency of premature activation/abnormal fertilisation noted by Tachibana et al (2013) is of concern, because when combined with what are probably methodological failures and the normal attrition of early human embryos, the number of normal blastocysts obtained is rather low and it might require more than one cycle to obtain a suitable embryo for transfer let alone to become a successful implantation. The cooling method used by Paull et al (2013) may assist, but this has not been tested with fertilisation. The data on PNT with normal fertilised zygotes are yet to be published, and the panel would be reassured if this included ES cell data of a comparable type to that in Tachibana et al (2013) and Paull et al (2013). More work needs to be done to ask whether mtDNA carryover associated with the spindle in MST or with the pronuclei in PNT becomes segregated in preimplantation development in a manner that is different with naturally occurring heteroplasmy. The panel is reassured both by the actual data on carryover of variant mtDNA, and by the modeling data showing that if carryover of mutant mtDNA is <2% then it is unlikely that any resulting child will show signs of mitochondrial disease. Nevertheless, there is still a concern about segregation and bottleneck issues leading to an unacceptably high level of abnormal mitochondria in the germ line of any female offspring, putting her children at risk. This can be explored with ES cell lines produced from MST and PNT embryos, preferably by deriving germ cells from them or by clonal analysis, as discussed above (2.3.2).

**2.3.20** Once assessed as safe to use in clinical practice, the panel strongly recommends that permission is sought from the parents of the children born from MST or PNT to be followed up for an extensive period (then seek permission from the children themselves, when old enough). In the case of females, this ideally should be extended to the next generation. These recommendations should also apply to PGD for mtDNA genetic diseases.

**2.3.21** Until knowledge has built up that says otherwise, the panel recommends that any female born following MST or PNT should be advised, when old enough, that she may herself be at risk of having a child with a

significant level of mutant mtDNA, putting this child or (if a female) subsequent generations at risk of mitochondrial disease. Thus, we recommend that any female born following MST or PST is advised that, should she wish to have children of her own, that her oocytes or early embryos are analysed by PGD in order to select for embryos free of abnormal mtDNA. This has the potential to eliminate risk in subsequent generations.

### 3. Further research

- 3.1** From the evidence received, the panel stands by the conclusions reached in 2011 and has not identified any new evidence that indicates that the MST and PNT methods are fundamentally unsafe. Nevertheless, these techniques are novel, especially as applied to human embryos, and with relatively few data. The panel therefore continues to recommend that additional studies be undertaken both on basic research to improve the knowledge about the biology of human mitochondria especially in development, and on research aimed specifically at providing further safety information on MST and PNT. However, complete reassurance will never come from experiments conducted in animal models and with human material *in vitro*. Therefore, it should be accepted that there will always be a risk associated with the use of MST or PNT in humans until it is tried in practice.
- 3.2** Basic research is needed into how the mitochondrial bottleneck functions and the critical parameters involved in the segregation of normal and any specific abnormal mitochondria amongst cell types in humans, because this is generally not well understood. For example, in the long term it may eventually be possible to influence or control replication of abnormal mtDNA in the early embryo to affect its segregation or inheritance in subsequent development. This research may aid decisions about threshold levels when carrying out PGD, although it may be less relevant when considering the use of MST and PNT.
- 3.3** The panel discussed the usefulness of the development of embryonic stem cell lines to help understand the distribution of mitochondrial heteroplasmy after PNT, since it would be critical to know whether the anticipated low level of mutant mitochondria carryover following PNT (or MST) did not change adversely during development, nor that there was preferential amplification in different tissues. This could be established by examining individual blastomeres at the morula stage and potentially by examining various tissues (such as striated muscle, myocardium, neural tissue, etc; i.e. those tissues especially sensitive to mitochondrial defects), which are easily generated from embryonic stem cells cultured from blastocysts. These experiments are required to ask if heteroplasmy that occurred as a result of MST or PNT techniques (even if it is <2%) leads to more segregation than naturally occurring heteroplasmy, as discussed above in section 2.3.2 – 2.3.10, Although more difficult practically, analysis of single cell (clonally)-derived embryonic stem cell sublines or, preferably, of primordial germ cells derived from such embryonic stem cells in order to examine levels of heteroplasmy in these cells might give an indication of next generation heteroplasmy.
- 3.4** The panel noted an interesting development in disease modeling. Three strains of “mito-mice”, carrying mitochondria with mutations in mtDNA known to be pathogenic in humans appear to be good models for use in a range of studies relevant to mitochondrial biology and disease. The authors focus the discussion on their use in trialing drugs for potential treatment rather than MST or PNT. The work is at a very early stage, but they propose some

interesting strategies that require generation of additional animal models and further trials (Nayada and Hayashi, 2011).

- 3.5** The panel reviewed its 2011 recommendations and the experiments that it considers are critical to assessing the effectiveness and safety of MST and PNT techniques as well as and experiments that will provide useful information on MST and PNT or mitochondria and disease. This research may also inform which of the two techniques is likely to be the most appropriate for clinical use. Many of the latter experiments, whilst of potential importance for basic research and for exploring alternative methods whereby abnormal mtDNA can be selected against, will not necessarily inform the decision as to whether it is safe to proceed to clinical application of MST and PNT methods.
- 3.6** The 2011 report recommended the following (minimum) set of experiments to be undertaken and the results taken into account before MST and PNT techniques can be assessed as safe to use clinically:
- MST using human oocytes that are then fertilised (not activated)
  - PNT using normally-fertilised human oocytes and development compared to normal ICSI-fertilised human oocytes
  - PNT in a non-human primate model, with the demonstration that the offspring derived are normal.
- 3.7** Experiments on the first of these have now been carried out and published. It is still important for some follow-up experiments to be carried out, notably to improve efficiency if possible, and confirmatory experiments would be valuable. Experiments on the second appear to be well underway, but it will be necessary to see full details (preferably published) before any assessment is possible. Due to the various issues outlined above, the panel no longer feels that their third recommendation is critical or mandatory. While it is of course possible that further experiments using non-human primates could provide some additional useful biological information, many of the important issues around heteroplasmy with variant mtDNAs have already been addressed or at least highlighted in Macaques, rodents and human studies. Others relating to the behaviour of mutant mtDNA may be better carried out in emerging mouse models or directly using human oocytes and zygotes and assays in preimplantation embryos and ES cells derived from them. But in terms of assessing both safety and efficacy of MST and PNT the panel is concerned that the differences between Macaque and human oocytes/early zygotes will be unhelpful. Indeed, if there are critical periods of development where the human is unique, such experiments may even be misleading if carried out in animals<sup>20</sup>.
- 3.8** In light of evidence and concerns about carryover of mutant

---

<sup>20</sup> Conducting experiments on non-human primates where they are not fully justified raises ethical issues.

mitochondria the panel considers it important to demonstrate the degree of heteroplasmic mosaicism in morulae<sup>21</sup>, and to provide data to address whether there was any amplification of mtDNA carried over. Therefore the following is now considered to also be a critical experiment:

- Studies on mosaicism in human morulae (comparing individual blastomeres) and on human embryonic stem (ES) cells (and their differentiated derivatives) derived from blastocysts, where the embryos have (i) originated from oocytes heteroplasmic for mtDNA and (ii) been created through MST and PNT using oocytes or zygotes with two different variants of mtDNA<sup>22</sup>. Although experiments are already reported on ES cells and their derivatives with MST, further corroborative experiments would be valuable.

**3.9** Given new published data and the panel's recent discussions with researchers, the following recommendation is no longer considered a critical experiment:

- PNT in a non-human primate model, with the demonstration that the offspring derived are normal.

**3.10** In the initial Report, the panel had also recommended the following additional research to provide useful information on mitochondrial disease and the MST and PNT techniques. The italicised text after each point outlines the panel's revised position:

- Removing the spindle or pronuclei and replacing them back into the same oocyte/zygote to better identify the impact of the manipulation technique: *Given the successful development to blastocyst stages after both MST and PNT with human oocytes and zygotes, the panel now considers this to be unnecessary.*
- Karyotype analysis and comparative genomic hybridisation/copy number variation arrays of embryos derived from MST or PNT: *this has been carried out for MST (further studies on mtDNA carryover have now been conducted in the Macaque model, as outlined above), but remain to be done after PNT, which the panel continues to recommend.*

---

<sup>21</sup> The stage of an embryo just prior to blastocyst formation, where it is a mass of blastomeres

<sup>22</sup> ES cells have a low number of mitochondria that do not need to function. Differentiated cells derived from the ES cells, such as muscle, can have high numbers of mitochondria. These can be put in conditions requiring oxidative phosphorylation. It may also be possible to derive primordial germ cells in vitro to explore aspects of the mitochondrial bottleneck and whether certain abnormal mtDNA have a replication advantage.

- Detailed analysis of epigenetic modifications and gene expression, with a range of markers for blastocyst cell types or embryos derived from MST or PNT: *this has been carried out for MST (further studies on mtDNA carryover have now been conducted in the Macaque model, as outlined above), but remain to be done after PNT, which the panel continues to recommend.*
- MST on unfertilised human oocytes that have abnormal mtDNA and PNT on fertilised oocytes that have abnormal mtDNA : *the panel considers that this might be useful to perform, especially if any evidence arises to suggest a specific mtDNA mutation may have a replicative advantage, but the panel now recognises that it may be very impractical to obtain sufficient numbers of oocytes or zygotes with mutant mtDNA for research.*
- Similar experiments using induced pluripotent stem (iPS) cells derived from patients carrying different mtDNA mutations<sup>23</sup>: *the panel continues to recommend this is carried out.*
- Further studies on the mtDNA carryover in a non-human primate model into the possible heteroplasmy of tissues in the fetus. The possibility of carryover of even a small percentage of abnormal mtDNA, means that any females born from MST or PNT should be considered at risk of transmitting the disease to their offspring: *Some relevant experiments have now been published on this, notably by Lee et al, (2012) in the Macaque. On the basis of these, the panel recommends that further experiments are carried out to address this issue with human material, along the lines suggested below in 3.10.*
- Further studies on vitrifying zygotes created through PNT: *the panel continues to recommend this is carried out.*

**3.11** The following additional research is also now recommended to provide useful information on mitochondrial disease and the MST and PNT techniques:

- Tests for heteroplasmy should be carried out on primordial germ cells obtained from human ES cells derived from blastocysts created through MST and PNT where the oocytes had variant or abnormal mtDNA. If primordial germ cell derivation is not possible or limitations in the model undermine its utility, clonal analysis of single cell-derived human ES cells could be used. Comparisons beginning with blastocysts known to be heteroplasmic for variant or abnormal mtDNA would be informative.

---

<sup>23</sup> It is not possible for iPS cells to provide information on mitochondrial behaviour in the early embryo.



## Annex A: Methodology of review

1. The Human Fertilisation and Embryology Authority (HFEA) agreed to a request from the Secretary of State for Health, in December 2012, to provide an updated view on the science to support the assessment of the efficacy and safety of pro-nuclear transfer and maternal spindle transfer techniques.
2. In order to carry out this review, the HFEA convened a small panel to collate and summarise the current state of expert understanding on the efficacy and safety of pro-nuclear transfer and maternal spindle transfer techniques. Panel members, the majority of whom sat on the panel which produced the 2011 review, were selected for their broad-ranging scientific and clinical expertise, and for having no direct interests in the outcome of the review.
3. Membership of the panel:
  - Professor Neva Haites (chair), University of Aberdeen
  - Professor Peter Braude, King's College London
  - Dr Paul De Sousa, University of Edinburgh
  - Professor Robin Lovell-Badge, Medical Research Council National Institute for Medical Research
  - Professor Anneke Lucassen, University of Southampton and formerly Human Genetics Commission
4. The panel put out a call for evidence on 4 January 2013. It asked for scientific evidence from experts in any relevant field on the safety or efficacy of pro-nuclear transfer and maternal spindle transfer techniques to avoid the transmission of mitochondrial disease, including published studies (published since March 2011), unpublished research or statements from individuals or organisations, to be submitted by 18 January 2013.
5. The call for evidence was sent directly to more than 30 experts in the field and to 25 professional bodies; the majority of whom had been sent the call for evidence for the original review. Recipients were invited to circulate the call to colleagues.
6. The Core Panel then reviewed the submitted evidence and spoke to the following researchers for additional information and clarification, via teleconferences on 30 January and 12 February:
  - Dr Mary Herbert, Professor Alison Murdoch and Professor Douglas Turnbull, Newcastle University
  - Dr Shoukhrat Mitalipov, Oregon Health and Science University



- Dr Dieter Egli and Dr Daniel Paull, The New York Stem Cell Foundation Laboratory
- Professor Michio Hirano, Columbia University

7. Annex B lists the written evidence reviewed by the panel.

## **Annex B: Evidence reviewed**

### **1. Statements**

- A statement from Dr David King, Director of Human Genetics Alert
- A statement from The Wellcome Trust
- A statement from Joanna Poulton (Professor and Hon Consultant in Mitochondrial Genetics, University of Oxford), Joerg P Burgstaller (IFA Tulln and University of Veterinary Medicine Vienna) and Iain G. Johnston (Imperial College London)
- A confidential statement regarding 'Progress towards experiments requested in the HFEA Core Panel Scientific Review' from Alison Murdoch, Mary Herbert and Doug Turnbull, Newcastle University

### **2. Published articles and reports (submitted)**

- Paull, D, et al (2013) "Nuclear genome transfer in human oocytes eliminates mitochondrial DNA variants." *Nature* 31;493(7434):632-7.
- Treff, N. R. et al (2012) "Blastocyst preimplantation genetic diagnosis (PGD) of a mitochondrial DNA disorder." *Fertil Steril.* 98(5):1236-40.

### **3. Published articles and reports (identified by panel members)**

- Amarnath, D. et al. (2011) "Nuclear–cytoplasmic incompatibility and inefficient development of pig–mouse cytoplasmic hybrid embryos." *Reproduction* 142 295–307.
- Jiang, Y. et al. (2011) "Interspecies Somatic Cell Nuclear Transfer Is Dependent on Compatible Mitochondrial DNA and Reprogramming Factors." *PLoS ONE* 6(4): e14805.
- Kemp, J.P. et al. (2011) "Nuclear factors involved in mitochondrial translation cause a subgroup of combined respiratory chain deficiency." *Brain* 134; 183 195.
- Lee, H-S. et al. (2012) "Rapid mitochondrial DNA segregation in primate preimplantation embryos precedes somatic and germline bottleneck." *Cell Rep.* 1(5): 506–515.

- McCormick, E. et al. (2012) "Molecular Genetic Testing for Mitochondrial Disease: From One Generation to the Next." *Neurotherapeutics*. DOI 10.1007/s13311-012-0174-1.
- Nakada, K. and Hayashi, J-I. (2011) "Transmitochondrial Mice as Models for Mitochondrial DNA-Based Diseases." *Exp. Anim.* 60(5):421-431.
- Payne, B.A.I. et al. (2013) "Universal heteroplasmy of human mitochondrial DNA." *Human Molecular Genetics* 22, 2: 384–390.
- Samuels, D.C. et al. (2013) "Preventing the transmission of pathogenic mitochondrial DNA mutations: can we achieve long-term benefits from germ line gene transfer?" *Human reproduction* 28(3):554-9.
- Saneto, R.P. and Sedensky, M.M.(2012) "Mitochondrial Disease in Childhood: mtDNA Encoded." *Neurotherapeutics* DOI 10.1007/s13311-012-0167-0.
- Sharpley, M.S. et al. (2012) "Heteroplasmy of Mouse mtDNA is Genetically Unstable and Results in Altered Behavior and Cognition." *Cell* 151: 333–343.
- Tachibana, M. et al. (2013) "Towards germline gene therapy of inherited mitochondrial diseases." *Nature* 493(7434):627-31.
- Wakefield, S.L. et al. (2011) "Impaired Mitochondrial Function in the Preimplantation Embryo Perturbs Fetal and Placental Development in the Mouse." *Biology of Reproduction* 84, 572-580.