Hybrids and Chimeras

A consultation on the ethical and social implications of creating human/animal embryos in research

April 2007

HUMAN FERTILISATION & EMBRYOLOGY AUTHORITY

Contents

How to respond

This consultation is open for any organisation or member of the public to share their views. The consultation period will run from 26 April to 20 July 2007.

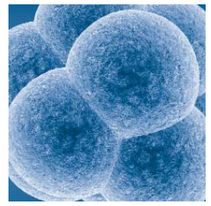
To respond to the consultation please fill in your views online at **www.hfea.gov.uk/hybrids**

If you are unable to access the internet then please submit your response in writing to:
Hybrids and Chimeras
Human Fertilisation and Embryology Authority
21 Bloomsbury Street
London
WC1B 3HF

If you have any questions about the Hybrids and Chimeras consultation please contact Helen Coath, Policy Manager, on hybrids@hfea.gov.uk

Public meeting

We are holding a public meeting in June to discuss the issues raised in this paper. To register your interest in attending please email hybrids@opinionleader.co.uk



Chair's foreword

We don't want to hold research up unnecessarily. On the contrary, we want research to prosper. But it can only do so in an environment of public support and trust, something which has a long tradition in the UK.

Stem cell research and cell nuclear replacement are not new areas of research. Research teams around the world are now using stem cells derived from human embryos to develop their understanding of a number of different diseases. In addition, many scientists now believe that embryonic stem cells may lead to new therapies for debilitating diseases.

Difficulties surrounding the supply of human eggs have led scientists to propose using animals as the source of the significant quantities of egg needed for this kind of research. They want to create cytoplasmic hybrid embryos from which stem cell lines can be produced. Creating this kind of embryo would be a new research activity in the UK. For those of you who, like me, are not scientists, this science is explained in the document.

Mixing human and animal DNA raises a number of ethical and social questions. Should we ever allow the creation of embryos which contain genetic information from different species? If this is to be allowed, where should the limits be and what should be the controls? We think it's only fair that people have a chance to give their views on these issues. That is why the Authority decided in January 2007 that there needs to be a full and proper public debate and consultation as to whether, in principle, this kind of research should be allowed.

We don't want to hold research up unnecessarily. On the contrary, we want research to prosper. But it can only do so in an environment of public support and trust, something which has a long tradition in the UK. Scientists tell me that this is one of the reasons that they choose to undertake their research here.

Through this consultation, we want to hear the views of members of the public as well as those with special interests in this research and its potential outcomes. You can respond by answering the questions, listed on page 18, via our online questionnaire. However, it is important to remember that this is not a referendum. We will not be counting 'votes' for or against any particular type of hybrid or chimera embryo research. Instead, we want to understand why people feel worried or enthusiastic about this research in order to help us make a judgement about the best way to proceed.

Thank you for taking time to consider these issues.

Shirley Harrison
Chair

1 Introduction

Research teams around the world are now using stem cells from human embryos in research to develop their understanding of a number of different diseases.

1.1 Stem cell research has become a high-profile area of science over the past few years. When the first mammalian clone (Dolly the sheep) was created in 1997 and, the following year, researchers in the United States first derived stem cells from human embryos in the laboratory, the scientific community started to see this as a promising area of research. Nearly ten years down the line, many research teams around the world are now using stem cells from human embryos in research to develop their understanding of a number of different diseases. Many scientists now believe that embryonic stem cells may also, in future, lead to new therapies (See Section 2 for a full explanation of this research).

1.2 In the UK, where such research is permitted under licence from the Human Fertilisation and Embryology Authority (HFEA), a number of teams are carrying out research on stem cells - some derived from donated embryos and some from embryos created through cloning.

Box 1: **About the HFEA**

The Human Fertilisation and Embryology Authority (HFEA) is a body set up by an Act of Parliament, the Human Fertilisation and Embryology (HFE) Act 1990, to oversee IVF treatment and research using human embryos in the UK.

Anyone wishing to carry out research using human embryos must apply to the HFEA for a licence which should, in turn, decide whether the proposed research meets the requirements of the Act. If the licence is granted, the HFEA must carry out regular inspections of the laboratory in order to monitor the progress of the research.

Besides licensing, the HFEA also has a policy function. The HFEA's Code of Practice, which is revised every few years, gives guidance on the standards and procedures by which clinics and laboratories are expected to operate. In addition to the Code, the HFEA develops policy on new issues which emerge from clinical practice or from research. Besides guiding clinical and laboratory practice, these policies also guide the HFEA committees which make decisions about licence applications.

1.3 In November 2006, the HFEA received applications from two different research teams for a licence to derive stem cells from human embryos. However, in order to overcome the shortage of egg donors, the researchers proposed using animal eggs instead of human eggs to create the embryos. These embryos would be a kind of hybrid, known as a cytoplasmic hybrid embryo, containing a small amount of animal DNA from the egg.

1.4 If this research is permitted, it will be the first time that scientists in the UK have created embryos in a research project which contain both human and animal DNA. Because of this and the fact that the issue raises significant social and ethical implications, the HFEA has decided to postpone consideration of the research licence applications until a consultation, seeking the views of the public, interest groups and the scientific community, has been carried out. However, the purpose of the consultation is not to seek views on the particular licence applications already submitted to the HFEA. Instead, it aims to consider this kind of research in the broad context of embryonic stem cell research, other possible kinds of hybrid research and chimera research.

1.5 This consultation document gives you the opportunity to give your views on this issue. Other methods for measuring public opinion, such as a public meeting, deliberative groups and a public opinion poll will also be used during the consultation period, which runs from 26 April to 20 July 2007. At the end of the process, we will consider the views we have gathered (alongside other information) and decide whether this kind of research should go ahead. In the light of that decision, the HFEA, through its normal licensing system, will consider whether the specific applications already received should be approved.

2 Scientific background

2.1 Since the late 1990s, when the first cloned mammal was created and the first human embryonic stem cells were derived, stem cell science has become an active area of research. Human embryonic stem cells (unspecialised cells which can develop into any of the body's 200 different cell types) are useful for studying a wide range of diseases in the laboratory. These cells could also, in the future, form the basis of new therapies for currently untreatable conditions such as Alzheimers or Parkinson's disease.

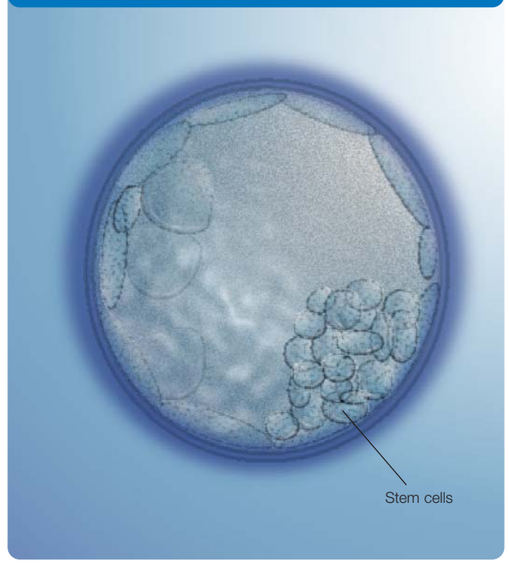
2.2 To derive stem cells, researchers allow an embryo to grow in the laboratory for five to six days after fertilisation (See Box 2). They then isolate the stem cells, thereby destroying the embryo, and place them in a mixture of nutrients which keep the cells in their unspecialised state.

2.3 One way of studying a particular disease is to create stem cells which contain the same features as a person suffering from the disease. To do this, researchers take a cell (such as a skin cell) from an adult with the disease in question and extract the genetic information (the nucleus) from the cell. They then transfer that genetic information into an egg from which the genetic information has been removed, activating the egg so that it starts to divide. This process is called cell nuclear replacement (CNR), though it is often referred to as cloning (See Box 3 on page 8).

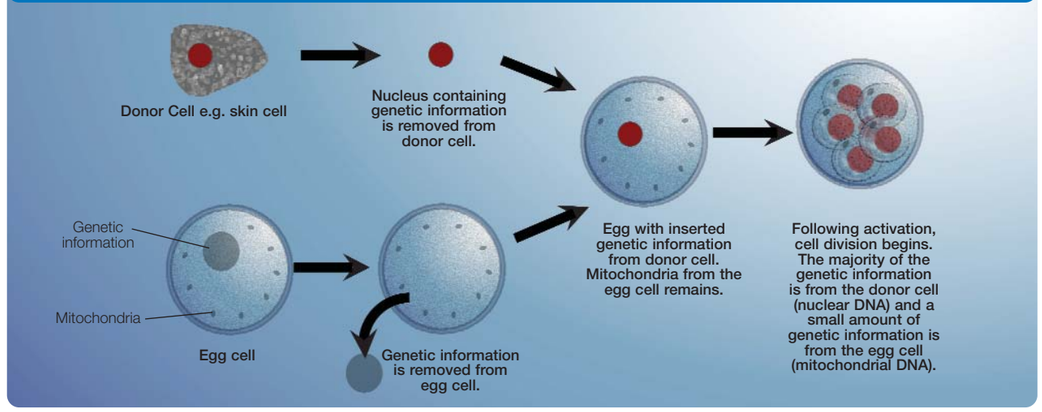
2.4 The resulting embryo, which is a clone of the adult, is grown in the laboratory for a few days, after which stem cells are isolated. Once in a stable state in the laboratory, the stem cells could be encouraged to specialise into particular cell types, such as brain or pancreatic cells. These cells could provide a model for the disease in question.

2.5 Another purpose of research in which cloned embryos are created, is to understand what happens to the DNA in an adult cell when it is put into an egg during CNR and transformed into an embryonic state. If this process were understood, it could become possible to take a cell from an adult and to change it into an unspecialised cell which could be used in therapies without first having to make an embryo.

Box 2: **Embryo at Day 6**



Box 3: How cell nuclear replacement works



Egg donation and CNR research

2.6 Where do the eggs used in cell nuclear replacement come from? Some IVF patients donate eggs that they are unable to use in their own treatment (usually because the eggs have failed to fertilise properly). However, scientists seeking to derive stem cells say that they need to use viable eggs in order to create stable stem cell lines. As a result, some UK research programmes are seeking to use viable eggs either from IVF patients or from women who are not patients.

2.7 The main practical difficulty with using donated eggs in CNR research is that it is very difficult to recruit egg donors, largely because donation is a physically demanding process which can, in rare cases, harm the donor's health. As a result, there are long waiting lists for people seeking donor eggs for IVF treatment and research programmes struggle to obtain enough eggs for their work.

Cytoplasmic hybrid embryos

2.8 One way around this shortage is to use animal, rather than human, eggs in research. Where animal eggs are used in cell nuclear replacement, the resulting embryo is not only a clone, but is also a kind of hybrid. Known as a cytoplasmic hybrid embryo, it contains a small amount of genetic information (DNA) from the animal which is left behind when the majority of the genetic information is removed (see Box 4). However, the amount of animal DNA in the cytoplasmic hybrid embryo would be minimal - less than one percent.

Box 4: Mitochondrial and nuclear DNA

Although almost all (more than 99%) of the DNA in any cell in the body is found within the nucleus, a small amount is present in structures, called mitochondria, found outside the nucleus. The DNA in mitochondria is involved in the production of chemical energy used in the cell. The mitochondria found in the embryo, which originated from the egg, produce the energy required by the embryo during development.

When CNR is carried out, the nucleus from the donor egg is removed and is replaced with the nucleus from another cell. Because the mitochondria from the donor egg are still present, the resulting embryo contains nuclear DNA from the other cell and mitochondrial DNA from the egg. This means that when animal eggs are used, the CNR embryo contains mostly human DNA from the nucleus, but also a small amount of animal DNA from the mitochondria present in the animal egg (less than 1%).

However, because of the way that CNR is performed, it is likely that human mitochondria from the donor cell will also be present. This means that in any resulting embryo there is likely to be a mix of human and animal mitochondria alongside the human nuclear material.

2.9 So far only two research teams, based in China and the United States, have created cytoplasmic hybrid embryos and published their findings[1]. One team used rabbit eggs to create the embryos and were able to derive stem cells from them. The rabbits were given drugs to produce large numbers of eggs after which time they were killed and their ovaries removed. The other team used cow eggs, taken from the animal's ovaries which were obtained from an abattoir.

2.10 Two research teams in the UK now want to carry out cell nuclear replacement using eggs from rabbits or cows. The reason for wanting to use animal eggs is, in this instance, to sidestep the shortage of human eggs available for research. As with the CNR research already licensed in the UK, the purpose of carrying out the research is to understand more about particular serious diseases.

'True' hybrids and hybrid embryos

2.11 When most people think of hybrids or chimeras, they don't think of cytoplasmic hybrid embryos created in stem cell research. Instead, they imagine the kind of half-human, half-animal monsters, like the Minotaur, that are associated with myths and legends. In real life, the hybrid creatures that we are most familiar with are mules (male donkeys crossed with female horses) and hinneys (female donkeys crossed with male horses). These are the only two species which are genetically similar enough to produce live, though usually infertile, offspring when they mate. Any attempt to create a living hybrid from two closely-related species would be extremely unlikely to even produce a viable pregnancy.

2.12 In the laboratory, it might be possible to create hybrid embryos for research by mixing the eggs and sperm (known collectively as gametes) of different species. These embryos would be different from cytoplasmic hybrid embryos in that they would have an equal amount of DNA from the two species from which eggs and sperm are obtained.

2.13 Following discussions with scientists, we understand that such embryos would be very unlikely to develop beyond fertilisation, unless they were from two closely related species, such as humans and non-human primates. None of the scientists that we consulted could see a purpose for carrying out such research using human gametes, which is banned under the current legislation.

2.14 Another type of hybrid embryo could be created by inserting animal genes into an early embryo. This kind of hybrid embryo, called a transgenic human embryo, would be different from a cytoplasmic hybrid embryo because the animal DNA could contain genes which have a function in the embryo. Transgenic animals are already created by inserting human genes into animal embryos. This is usually done so that the resulting animal will produce human products (such as proteins which cause blood to clot) for use in medicines. However, no animal genes have ever been inserted into human embryos.

Chimeras and chimera embryos

2.15 A chimera is an animal or human which contains cells from a different animal or human. In normal conception, the genetic information from the father and the mother combine to create an individual with a new and unique genome. Every cell in that individual's body is made up of the same genetic information. By contrast, a chimera contains some cells which have different genetic information. Strictly speaking, anyone who has undergone any kind of transplant or a blood transfusion is a chimera because their body contains cells from a donor.

2.16 These kinds of chimeras are created during adulthood, whenever the transplant occurs. The other kind of chimera is created at the embryonic stage, when one or more cells from a different animal or human are introduced into the early embryo. Unlike a hybrid embryo, which is created by mixing the genes of another species, a chimera embryo contains cells from another species. As a result, a chimera has two different kinds of cells: some which derive from one species and some which derive from another (known as a mosaic). By contrast, a hybrid embryo contains cells which are all the same but which are a genetic combination of two different species.

2.17 There are two kinds of chimera embryos which could be created for research. The first is an animal chimera embryo, created by inserting human cells into an animal embryo. This kind of research, because it is carried out on animal embryos, is licensed by the Home Office[2] and is therefore not within the HFEA's remit.

[1] Embryonic stem cells generated by nuclear transfer of human somatic nuclei into rabbit oocytes' Chen Y et al Cell Research (2003) 13(4) 251-263 and 'Evaluation of the embryonic preimplantation potential of human adult somatic cells via an embryo interspecies bioassay using bovine oocytes' Illmensee K et al *Fertility and Sterility* (85) Supplement 1, April 2006

[2] Animals Act 1986

2.18 Another purpose of research using animal chimera embryos, which would also need to be licensed by the Home Office, might be to test the pluripotency (the capacity to develop into different cell types) of human embryonic stem cells. Scientists may wish to insert human embryonic stem cells into a mouse embryo which is then transferred to a female mouse. When the mouse pup - a chimera - is born, it could be tested for the presence of functioning human cells. However, the stem cell research community has agreed that, because there are other ways of carrying out this test, none of them wish to create this kind of chimera.

2.19 The other kind of chimera that might be used in research is a human chimera embryo, created by inserting animal cells into a human embryo. This kind of work would be within the HFEA's remit and is not currently banned in the legislation. This means that the HFEA could, if it wished, issue a licence for it. However, none of the scientists that we consulted could see a purpose for carrying out such research.

How will research develop in the future?

2.20 It is always difficult to predict how scientific research might develop in the future, largely because unexpected discoveries often emerge during the course of research. As a consequence, areas of study not previously anticipated or thought possible can sometimes open up, making new demands upon regulation. When UK legislation covering embryo research was passed in 1990, for example, CNR research was not thought to be a viable area of study. Nearly 20 years on, however, the scientific picture is dramatically different.

Box 5: **Different types of human/animal embryos**

To summarise, the five types of embryos which contain human and animal DNA are:

Cytoplasmic hybrid embryos: embryos which are created through cell nuclear replacement using animal eggs;

Hybrid embryos: embryos which are created by mixing human sperm and animal eggs or human eggs and animal sperm;

Human chimera embryos: human embryos which have animal cells added to them during early development;

Animal chimera embryos: animal embryos which have human cells added to them during early development; and

Transgenic human embryos: human embryos which have animal genes inserted into them during early development.

2.21 Following this pattern, it is possible that the scientific picture on human/animal embryos will change. Scientists may, in the future, see a use in creating hybrid embryos (by mixing gametes) or human chimera embryos for research and, if in the UK, they may seek an HFEA licence to do such research. One of the HFEA's functions is to monitor developments in science in order to anticipate, as much as is possible, new types of research which will fall within its remit.

3 Legal background

3.1 In the UK, a number of different types of embryo research are permitted. However, the research may only go ahead if it is licensed by the HFEA and the embryos created are never transferred to a woman and are destroyed before 14 days of development. But what does the law in the UK have to say about creating the different types of hybrid and chimera embryos? And how have other countries tackled this issue and what can we learn from their approach?

Is this research legal in the UK?

3.2 The UK was one of the first countries to introduce legislation covering IVF and human embryo research. The Human Fertilisation and Embryology (HFE) Act, passed in 1990, permits scientists to use human embryos in research, whether those embryos are donated by IVF patients or are created, by fertilisation or cloning, for research purposes. However, researchers must be licensed by the HFEA to carry out this research and must be subject to regular inspections by HFEA staff.

3.3 Despite this permissive approach, some activities are strictly prohibited under the legislation. For example, the mixing of human and animal gametes (i.e. creating true hybrid embryos) for any purpose except the testing of sperm during IVF treatment, is prohibited[3]. However, the Act does not mention the creation of chimera embryos or of cytoplasmic hybrid embryos.

[3] This test, rarely used now, involves the mixing of human sperm and a hamster egg to observe the capacity of the sperm to penetrate the egg's outer shell. Unlike all other embryos created for research under the Act, these embryos must be destroyed at the two-cell stage (about one day after fertilisation).

3.4 As a result of a legal decision, the HFEA believes that it probably has the power to licence the creation of cytoplasmic hybrid embryos, although the HFEA's jurisdiction over such embryos could be tested in the courts[4]. It is a criminal offence to create any embryo which falls within the HFEA's jurisdiction unless the person creating it has an HFEA licence to do so.

If this kind of research goes ahead, will any scientist be able to do it?

3.5 The HFEA has a dedicated research licence committee which decides, on the basis of the legislation, whether applications for licences should be accepted or rejected. If the HFEA already has a policy to permit a particular area of research or clinical practice, this guidance will be taken into account by the licence committee on the basis that the practice is ethically acceptable.

The HFEA has a dedicated research licence committee which decides, on the basis of the legislation, whether applications for licences should be accepted or rejected.

[4] In section 1(1)(a), the Human Fertilisation and Embryology Act defines an embryo under the HFEA's jurisdiction as 'a live human embryo'. When this definition was used in the legal case of R (Quintavalle) v Secretary of State for Health [2003] UKHL 13, it was described as 'a live human organism containing within its cell or cells a full set of 46 chromosomes with the normal potential to develop'.

Box 6: **Prohibitions and research purposes under the HFE Act**

The following activities are prohibited under the Human Fertilisation and Embryology Act 1990:

- keeping or using an embryo beyond 14 days of development
- placing an embryo in any animal
- keeping or using an embryo in any circumstances in which regulations prohibit its keeping or use
- replacing a nucleus of a cell of any embryo with a nucleus taken from a cell of any person, embryo or subsequent development of any embryo
- altering the genetic structure of any cell while it forms part of an embryo.

No research using human embryos can proceed unless it fulfils one of the following purposes identified in the Act:

- promoting advances in the treatment of infertility
- increasing knowledge about the causes of congenital disease
- increasing knowledge about the causes of miscarriage
- developing more effective techniques of contraception
- developing methods for detecting the presence of gene or chromosome abnormalities in embryos before implantation
- increasing knowledge about serious disease
- enabling any such knowledge to be applied in developing treatments for serious disease.

3.6 However, even if a particular type of research is considered to be acceptable, this does not necessarily mean that an individual licence application will be granted. Before granting a licence, the research licence committee must satisfy itself that:

- the proposed research activity is not prohibited under the HFE Act (see Box 6);
- the purpose of the research fits with those identified in the Act (see Box 6); and
- the creation and/or use of human embryos is necessary (i.e. animal embryos could not be used to the same effectiveness or, in the case of CNR research, that normally fertilised embryos could not be used).

Could a hybrid or chimera embryo ever become a baby?

3.7 No scientist or clinician has ever expressed a desire to create a hybrid or chimera baby. However, even if anyone did wish to do so, they would be committing a criminal offence if they transferred either a hybrid embryo (created by mixing human and animal gametes) or a cytoplasmic hybrid embryo (created through CNR using animal eggs) to a woman.

Will the law stay the same in the future?

3.8 The UK Government is in the process of reviewing the Human Fertilisation and Embryology Act and, in December 2006, published a white paper containing proposals for revised legislation[5]. In the white paper, the Government proposed a ban in the new legislation on the creation of all types of hybrid and chimera embryos in research. However, the proposal also includes a regulation-making power, which would enable Parliament to permit the HFEA to licence particular types of hybrid or chimera embryo research. A draft bill will be put before Parliament for consideration this summer. However, because the new Act is not likely to come into force until 2009, the current legislation, and any HFEA policy on hybrid and chimera research, will stand until then.

3.9 The HFEA had already expressed a view about the creation of hybrids in research. In its response to the Government's consultation on the review of the Human Fertilisation and Embryology Act[6], the HFEA recommended that the current law, which permits the creation of hybrids only for very limited purposes, should be extended so that hybrid embryos can be created for the same research purposes as other embryos[7]. However, these comments were made in response to questions about how the law should look in the future and formed part of a wide range of recommendations about all aspects of the current legislation.

What have other countries done about this issue?

3.10 Some countries, including a number in Europe, have decided to prohibit all kinds of embryo research or, at least, the creation of embryos for research purposes. Those countries have not, therefore, seen a need to revise their legislation in the light of the research on cytoplasmic hybrid embryos published by Chinese and American scientists. However, some countries in which embryo research is permitted have considered whether cytoplasmic hybrid embryo research should also be permitted.

3.11 In Australia, legislation banned the creation of cloned embryos in research. However, in December 2005, a government-appointed commission, called the Lockhart Review[8], published a list of recommendations for new legislation on embryonic stem cell research and cloning. One recommendation was that the creation of cytoplasmic hybrid embryos for research should be permitted under licence. When the issue came before the Australian Parliament in late 2006, most of the Lockhart Review's recommendations were adopted. However, research involving the creation of all kinds of hybrid and chimera embryos, including cytoplasmic hybrid embryos, was banned following the tabling of a last-minute amendment during the parliamentary debates.

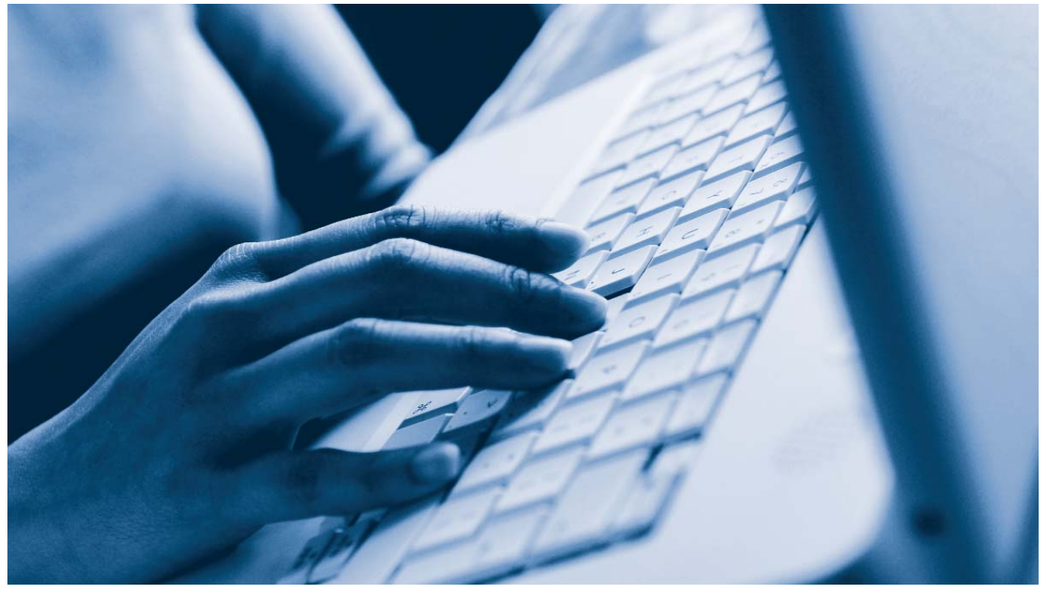
3.12 Before 2004, researchers in Canada were not subject to any legislation regarding human embryo research. However, when the Assisted Human Reproduction Act 2004 came into force, it introduced a regulatory system for embryo research which permits research for a limited number of purposes. The Act prohibits the creation of human chimera embryos for research, but permits the creation of true hybrid embryos or cytoplasmic hybrid embryos for research. The transfer of any human/animal embryo to a woman is banned.

[5] Review of the Human Fertilisation and Embryology Act: proposals for revised legislation Department of Health, December 2006

[6] Review of the Human Fertilisation and Embryology Act: consultation Department of Health, August 2005

[7] Response by the HFEA to the Department of Health's consultation on the Review of the HFE Act HFEA, November 2005

[8] Reports on the Prohibition of Human Cloning Act 2002 and the Research Involving Human Embryos Act 2002, December 2005



4 Ethical and social issues

4.1 It is difficult to consider the ethical and social implications of creating hybrid or chimera embryos in research without considering the wider issue of embryo research. However, the issue of whether human embryos should be used and destroyed in research has been extensively debated for the past 30 years and although many people's views remain unchanged, a compromise has been reached through the law.

4.2 As discussed in the previous section, the law in the UK permits the creation and use of human embryos in research, including research which creates embryos through cell nuclear replacement (CNR). However, it does not allow any embryo used in research to be transferred to a woman or kept beyond 14 days of development.

4.3 In order to explore the ethical and social issues arising from the creation of human/animal embryos, it may help to think of the different types of embryos used in research in the following order:

Spare embryos: embryos donated by IVF patients

Research embryos: embryos created through normal fertilisation using donated eggs and sperm

CNR embryos: embryos created through CNR using human eggs

Cytoplasmic hybrid embryos: embryos created through CNR using animal eggs

True hybrid embryos: embryos created by mixing human and animal gametes

Human chimera embryos: human embryos created through normal fertilisation which are subsequently injected with animal cells

4.4 Some people believe that any of these embryos should be able to be used in research, whilst some believe that no human embryo should be used in research. Others may draw the line somewhere in between.

Arguments against the creation of human/animal embryos

Moral repugnance

4.5 People often feel an instinctive moral repugnance towards the prospect of creating hybrid or chimera embryos. However, precisely because this sentiment is based upon an instinctive reaction to something, it is very difficult to characterise or, more importantly, to engage with in discussion. Nonetheless, some philosophers argue that revulsion can be morally important and should not be ignored.

Respect for the human embryo

4.6 Another argument against the creation of human embryos which contain some animal DNA is that it shows too little respect for the human embryo. Some people are opposed to all human embryo research because they believe that embryos have a similar moral status to that of children or adults. However, others feel that human embryo research is acceptable, but that research which creates hybrid or chimera embryos is a step too far.

4.7 Many people feel that human embryos have a special status which should make us very careful about what we allow scientists to do to them. This idea was discussed in the Warnock Report, a set of recommendations for legislation on IVF and embryo research drawn up in 1984[9]. Although the status of embryos is not spelled out in the Act, human embryos are clearly given more legal protection than animal embryos, even though this protection falls well short of that afforded to human children or adults. Some people believe that in order to respect the human embryo's special status, scientists should be prevented from creating any kind of human/animal embryo.

Human dignity

4.8 Another argument against the creation of hybrid or chimera embryos is that such research violates human dignity. Although it is difficult to gain a consensus on the definition of human dignity, humanness is clearly central to the idea. Some people feel that creating embryos which contain even a very small amount of animal DNA undermines the humanness of the embryo and, as a result, diminishes its dignity. For them, creating embryos which contain animal DNA blurs a very important distinction between humans and animals.

Slippery slopes

4.9 One concern that people often raise about new advances in science is that it will lead to undesirable activities in the future. An objection to the creation of cloned embryos in research, for instance, was that it would put us on a slippery slope leading to the creation of cloned babies. In the context of cytoplasmic hybrid embryos, some have expressed a concern that these embryos too might be transferred to a woman to create babies with some animal DNA in them. Another concern is that saying yes to using animal eggs in CNR research commits us to accepting the creation of any kind of human/animal embryo.

4.10 These concerns point to two different types of slippery slopes. The first is practical - is one activity likely to lead to another, less desirable, activity? Will scientists, having created a hybrid embryo, want to go one step further and transfer it to a woman? No scientist has ever expressed an interest in transferring such embryos in the hope that a baby, if that were medically possible, would develop. Even if they did, it would be a criminal offence to do so.

4.11 One response to the practical slippery slope argument is to use legislation to stop any slippage. A concern, for example, that the creation of cytoplasmic hybrid embryos in research will lead to such embryos being transferred to a woman in the hope that it will become a baby can be addressed by pointing to the legislative ban on such an activity. Similarly, a concern that research creating cytoplasmic hybrid embryos might lead to research creating human chimera embryos could be addressed by banning the creation of human chimeras in the legislation.

4.12 However, there is a second kind of slippery slope which is more logical than practical. If one area of research is permitted, does that logically make the case for other kinds of research? For example, if the creation of cytoplasmic hybrid embryos is considered to be acceptable, does that commit the HFEA to accepting a request to create human chimera embryos or true hybrid embryos? Some argue that accepting the creation of any human embryo which contains even a tiny amount of animal DNA will commit the HFEA to accepting the creation of human embryos with much more animal DNA.

The use of animals in research

4.13 The fact that animals are or would be used in hybrid or chimera embryo research may make some people feel unable to support it. However, because the use of animals in research is licensed by the Home Office, this issue is beyond the scope of the HFEA and is not therefore part of this consultation. We are, however, aware that this is a significant issue for some people.

[9] Report of the Committee of Inquiry into Human Fertilisation and Embryology HMSO Cmnd. 9314, July 1984

Arguments against the creation of cytoplasmic hybrid embryos

4.14 Some people are opposed to research mixing human and animal DNA in any way. Others, however, may have particular objections to the creation of cytoplasmic hybrid embryos. As discussed above, some people are concerned that permitting one type of hybrid research will commit the HFEA to accepting any kind of research which mixes human and animal DNA. Furthermore, if CNR hybrids are permitted in order to overcome the shortage of human eggs for research, will other more controversial areas of research be permitted for the same reasons?

4.15 Other concerns raised about the creation of cytoplasmic hybrid embryos in particular relate more to scientific issues than ethical ones. Some commentators argue that this work is unjustified because it is unlikely to be effective; because the efficiency of the process would be too low to warrant such a controversial technique; or because the differences between human and animal eggs are such that anything that results would not be biologically informative. Others argue that the potential benefits of this research have been overestimated and that studies on animal or adult stem cells (taken directly from a patient) should be prioritised.

Arguments for the creation of cytoplasmic hybrid embryos

A more ethical source of eggs?

4.16 Scientists working in the field have often been the first to admit that the creation of cloned embryos is an inefficient process - large numbers of eggs are needed to make a small number of cloned embryos. Some have argued that it is precisely this inefficiency that makes CNR research using animal eggs a justifiable activity. They argue that using animal eggs in research that would need many attempts to succeed is more justifiable than using human eggs, which are in very short supply. For them, human eggs would be used most productively in treatment or in research which does not need to use so many in order to be successful.

4.17 Others argue that regardless of the efficiencies of the research or the shortage of human eggs, obtaining eggs from animals is ethically more acceptable than obtaining them from humans because of the risks, though small, of egg donation to the women who undergo it.

All CNR embryos are essentially the same

4.18 Another argument for the use of animal eggs in CNR research is that there is no qualitative difference between cytoplasmic hybrid embryos and cloned embryos created using human eggs. Those who hold this view argue that the genetic contribution of the animal to the resulting embryo is so tiny, that it is essentially a human embryo. As such, cytoplasmic hybrid embryos should be treated in exactly the same way as CNR embryos created with human eggs.

4.19 Proponents of this view might be more inclined to draw an ethical distinction between cytoplasmic hybrid embryos and true hybrid embryos, than they would between cytoplasmic hybrid embryos and CNR embryos created with human eggs. Creating a cytoplasmic hybrid embryo might be acceptable because the embryo is still essentially human, whereas the creation of a true hybrid embryo may be more problematic because the proportion of animal DNA would be much greater.

Arguments for the creation of human/animal embryos

4.20 People often take different views about how much respect should be given to the human embryo. Amongst supporters of research, some believe that there should be no limits to what research can be carried out on human embryos because the idea of having respect for something that will be used and destroyed in research is nonsensical. Meanwhile, many feel that human embryos deserve some protection, but that the level of protection should be balanced against the benefits which might arise from the research in question.

4.21 However, if someone believes that embryos deserve a degree of respect, this does not necessarily commit them to opposing the creation of hybrid or chimera embryos. Some people feel that any research can be carried out on a human embryo as long as the embryo is never transferred to a woman.

4.22 For them, the test for the acceptability of a particular type of research is not what kind of embryo it would create, but the purpose for carrying out the research in the first place. If the goal of the research is to understand more about human diseases or to find new treatments for them, the presumption should be in favour of the research, unless it can be shown that the research will cause people harm. Those taking this view believe that the status of the human embryo is simply not high enough to justify preventing research which could bring benefits to human health.

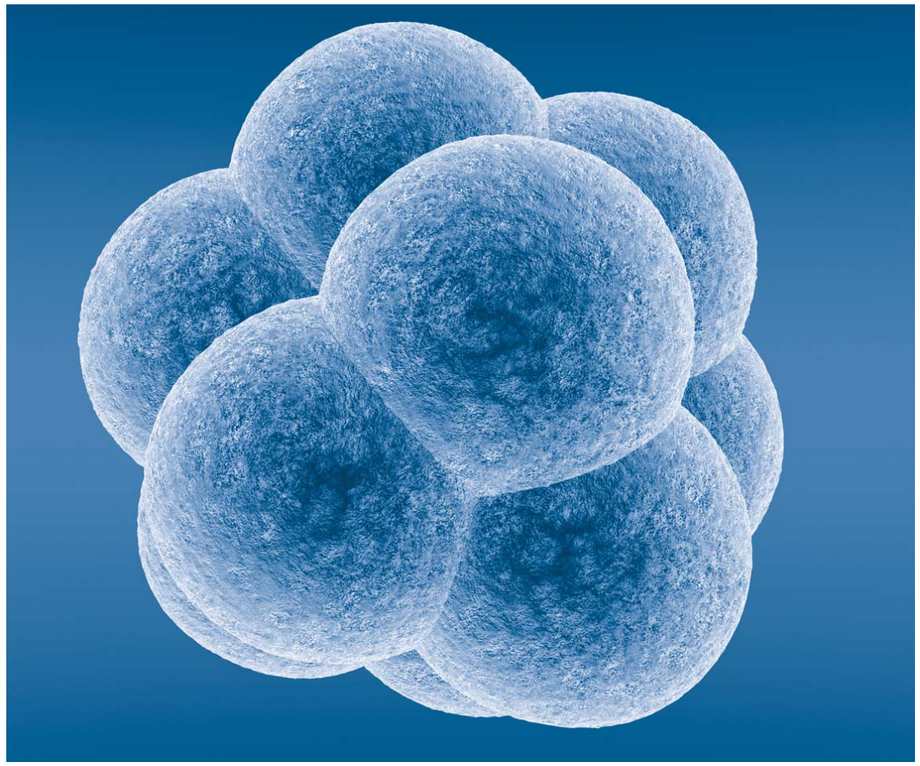
Box 7: **Summary of arguments against and for human/animal embryo research**

Arguments against:

- The creation of human/animal embryos is instinctively repugnant
- Adding animal DNA/cells to a human embryo fails to respect its special status
- Adding animal DNA/cells to a human embryo undermines human dignity
- Cytoplasmic hybrid embryo research may lead to research using true hybrid embryos or human chimera embryos
- The creation of any kind of human/animal embryo in research may lead to the transfer of these embryos to a woman

Arguments for:

- Human eggs should not be used in CNR research because it is inefficient
- There is no moral difference between cytoplasmic hybrid embryos and normal CNR embryos (made with human eggs)
- The creation of any human/animal embryo is acceptable as long as the embryo is never transferred to a woman
- The potential research benefits outweigh any ethical concerns



Your views

We would like to know your views about the creation of the different types of hybrid and chimera embryos in research. Below is a list of questions to which you can respond via an online questionnaire at www.hfea.gov.uk/hybrids

The closing date for responses is 20 July.

Questions

1. The following types of embryo research are already legally permitted and licensed in the UK. Which of them, in your view, are acceptable?
   - Research using human embryos donated by IVF patients
   - Research using human embryos created specifically for research from donated eggs and sperm
   - Research using cloned human embryos created specifically for research through cell nuclear replacement (CNR)
   - No research using human embryos is acceptable
   - Not sure/undecided
2. Do you think that the HFEA should issue licences to allow research using cytoplasmic hybrid embryos?
3. Do you think that the law should in future permit the creation of true hybrid embryos for licensed research purposes?
4. Do you think that the HFEA should in future issue licences to allow research using human chimera embryos?
5. If you have answered yes to questions 2 to 4, what limits do you think should be placed upon human embryo research?

Further reading

Report of the Committee of Inquiry into Human Fertilisation and Embryology HMSO Cmnd. 9314, July 1984
The report only considered true hybrid embryos, recommending that their creation should be permitted only for alleviating infertility and only if the embryo is destroyed at the two-cell stage. This recommendation became law in the HFE Act 1990.

Stem cell research: medical progress with responsibility Department of Health, June 2000
http://www.dh.gov.uk/assetRoot/04/06/50/85/04065085.pdf
This report, written by an expert group set up by the Chief Medical Officer, recommended that the creation of cytoplasmic hybrid embryos should be prohibited. In its response, the Government agreed with the recommendation and called on funding bodies not to fund this research.

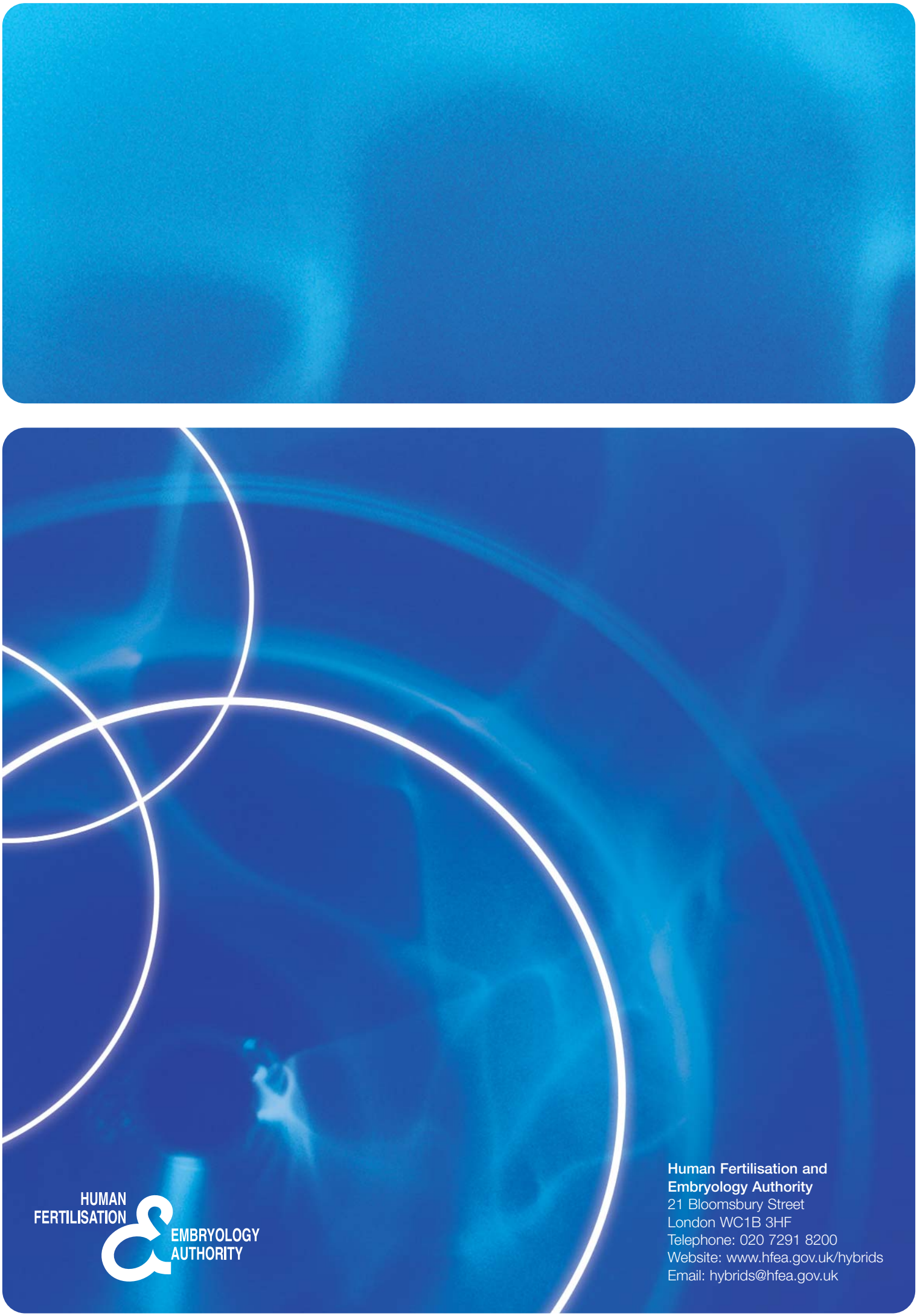
Stem cell research House of Lords Stem Cell Research Committee, House of Lords, February 2002
http://www.parliament.the-stationery-office.co.uk/pa/ld/ldstem.htm
The House of Lords committee briefly considered cytoplasmic hybrid embryos, although it did not come to a view about the issue. However, the report noted that the view had been expressed that it may be ethically more acceptable to use animal eggs than human eggs in CNR research.

Human reproductive technologies and the law House of Commons Science and Technology Select Committee, House of Commons, March 2005
http://www.publications.parliament.uk/pa/cm200405/cmselect/cmsctech/7/702.htm
This committee recommended that the creation of all types of hybrid and chimera embryos should be permitted for research, but that their transfer to a woman should be prohibited. In its response to this report, the Government promised to seek wider public views on whether there is a compelling case to allow the creation of hybrids and chimeras for research purposes.

Review of the Human Fertilisation and Embryology Act consultation Department of Health, August 2005
http://www.dh.gov.uk/assetRoot/04/11/78/72/04117872.pdf
In this consultation document, the Government indicated its intention to continue the current prohibition on the creation of true hybrids. The document invited views on the creation of cytoplasmic hybrid embryos and chimera embryos for research.

Response to the Review of the HFE Act consultation HFEA, November 2005
http://www.hfea.gov.uk/cps/rde/xbcr/hfea/ ReviewoftheActresponse.pdf
In its response to the Government's consultation, the HFEA recommended that the creation of hybrids and chimeras should be permitted for research purposes.

Review of the Human Fertilisation and Embryology Act proposals for revised legislation Department of Health, December 2006
http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_073098
In this white paper, the Government set out its plan to prohibit the creation of hybrid or chimera embryos. However, regulation-making powers to permit some research will be in the new Act.



HUMAN FERTILISATION & EMBRYOLOGY AUTHORITY

Human Fertilisation and Embryology Authority
21 Bloomsbury Street
London WC1B 3HF
Telephone: 020 7291 8200
Website: www.hfea.gov.uk/hybrids
Email: hybrids@hfea.gov.uk