

Human Embryo Research in the UK

2006/2007

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introduction

Research on human embryos is important for the continuing development of assisted reproductive technologies (ARTs) and for ensuring the efficacy and safety of existing treatments. Understanding of early human development and genetic disease gained from research on human embryos may ultimately improve the success of fertility and related medical treatments.

The purpose of this report is to provide information on the research carried out under a licence from the Human Fertilisation and Embryology Authority (HFEA) at UK centres between April 2006 and March 2007.

Table 1
**Research purposes
Schedule 2 to the
HF&E Act 1990**

- To promote advances in the treatment of infertility,
- To increase knowledge about the causes of congenital disease,
- To increase knowledge about causes of miscarriages,
- To develop more effective techniques of contraception,
- To develop methods for detecting the presence of gene or chromosome abnormalities in embryos before implantation.

The Human Fertilisation & Embryology Authority

The HFEA was set up in 1991 by the Human Fertilisation and Embryology Act 1990, in order to regulate IVF treatment and human embryo research. The HFEA also regulates the storage of gametes (sperm and eggs) and embryos. The HFEA has a duty to produce a Code of Practice, which gives guidelines to clinics about the proper conduct of licensed activities, publicises its role, and provide advice and information to patients, donors and clinics.

How the Authority licenses research projects

The HFEA's decision making when considering embryo research applications is governed by law. The Authority must determine first whether the research proposal passes the necessity test and the intended purpose test.

Under the Human Fertilisation and Embryology Act 1990 (the HF&E Act) a licence may not be granted unless the Authority is satisfied that any proposed use of embryos is necessary for the purposes of the research; an activity cannot be authorised unless it appears to the Authority to be necessary or desirable for a research purpose accepted by Parliament. (Tables 1 and 2 show the purposes for which embryo research is currently permitted).

Essentially the role of the HFEA is to ensure that the application is lawful; that patients or donors have given properly informed consent and that the use of embryos is justified.

To assist the Authority in making these decisions it takes independent advice by sending out each research application for peer review. The HFEA has a panel of national and international experts in the field of reproductive technologies and infertility. The peer review covers the following specific areas:

- whether the research fulfils the categories for which embryo research is permitted,
- the importance of the research in the field,
- whether the research has been done before,
- whether the use of human embryos is justified.

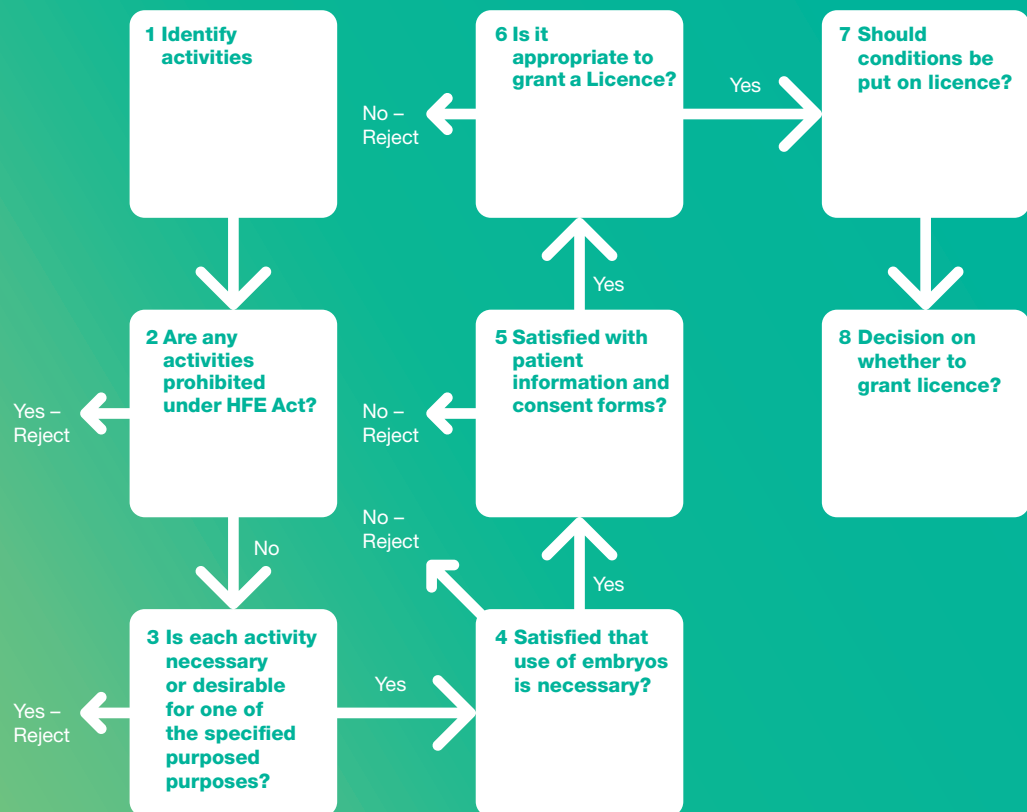
Table 2
**Research Purposes –
 The Human
 Fertilisation and
 Embryology
 (Research Purposes)
 Regulations 2001**

- Increasing knowledge about the development of embryos,
- Increasing knowledge about serious disease, or
- Enabling any such knowledge to be applied in developing treatments for serious disease.

All research applications are considered by a dedicated Research Licence Committee. This Committee is chaired by a lay member of the Authority and the majority of its five members are lay. The Research Licence Committee is guided by a published systematic “decision tree” (see Figure 1). This increases transparency and ensures that applications are dealt with fairly and consistently.

The regulatory system also involves the careful monitoring of the use of embryos in research. Researchers have to report how many embryos they expect to use and provide progress reports documenting exactly how many have been created or used since the last report. This information is audited at the annual inspection.

Figure 1
**Decision Tree for
 Research Applications
 used by HFEA Licence
 Committees**



research activity

New research licence applications 06/07

In 2006–2007 the HFEA received six applications for new research licences. Two of these applications related to the use of embryos created by inserting human nuclei into enucleated animal eggs (hybrid embryos).

The Authority at its meeting in January 2007 directed the Licence Committee not to consider these applications until a wider policy position had been agreed regarding the use of human–animal hybrid embryos in licensed research projects. These applications were therefore not processed during 2006/2007.

Table 3 shows the time taken to process the applications for research licences received during 2006/07. The four applications processed during 2006/07 were considered by the Research Licence Committee within three months of receipt, excluding the time taken for the external peer reviewers to examine the applications. The Research Licence Committee agreed to licence all four projects.

Table 3
**Licence Applications
2006/2007**

Licence	Received	Peer Review Sent	Peer Review Received (final recommendation)	Licence Committee	KPI	Note
The effect of biomass reduction on embryo development (R0175)	18/04/2006	05/05/2006 & 10/05/2006	08/06/2006 & 10/07/2006	26/07/2006	3 months	
Evaluation of cyrostorage using vitrification (R0176)	14/07/2006	20/07/2006	12/09/2006 & 15/10/2006	29/11/2006	3 months	Both peer reviewers raised a number of issues. Total time for the application and centre's response to issues raised to be considered by the peer reviewers was 8
A novel protocol for extracting cells during embryo biopsy (R0177)						Both peer reviewers raised a number of issues. Total time for the application and centre's response to issues raised to be considered by the peer reviewers was 11 weeks
Derivation of Pluripotent Human Embryo Cell Lines (R0178)	02/10/2006	04/10/2006	24/10/2006	29/11/2006	<2 months	

The primary purpose of two of the projects licensed was to develop methods for detecting genetic diseases in preimplantation embryos. The third project licensed will develop methods for freezing embryos and the fourth project licensed will use embryos to derive human embryonic stem cell lines.

During 2006/07 the HFEA renewed 17 research licences. Thirteen (76%) of these licences were renewed for the full three years permitted under the HF&E Act 1990. One licence (6%) was renewed for less than three years at the request of the applicant and three licences (18%) were renewed for one year for the following reasons:

- New Person Responsible (2 licences)
- Lack of progress in research undertaken (1 licence).

All research licences were renewed without the addition of any additional conditions.

Ongoing research

In 2006-2007 a total of 36 projects of research were being conducted under a licence from the HFEA, including the four new licence applications. This research was carried out at 28 centres¹. The projects licensed during 2006-2007 are listed in Appendix 1.

As detailed earlier, the HFEA may only license a research project if it is satisfied that the research being carried out is necessary or desirable for one of the purposes set out in the HF&E Act as amended by the Human Fertilisation and Embryology (Research Purposes) Regulations 2001. Figure 2 shows the purposes under which the 36 projects of research were licensed in 2006/2007 (a research project may be licensed under more than one purpose).

Figure 2 shows that of the projects licensed by the Authority, the majority were concerned with either increasing knowledge about the development of embryos (64%) or promoting advances in the treatment of fertility (53%). Figure 2 also shows that the licences issued by the Authority during 2006/2007, covered all the purposes that Parliament considered important (Tables 1 & 2).

The purposes for which UK scientists are permitted, by law, to carry out research are quite broad. For example, research that helps develop treatments for serious disease may involve creating human embryonic stem cell lines from embryos known to have a genetic disorder or developing new methods that would help patients avoid passing on a genetic disease to their children. Figure 3 shows the broad areas of research carried out under the licences issued by the HFEA during 2006/2007.

¹A licensed centre may have permission (licences) to carry out more than one research project or research may take place at several centres (by law these require separate HFEA research licences).

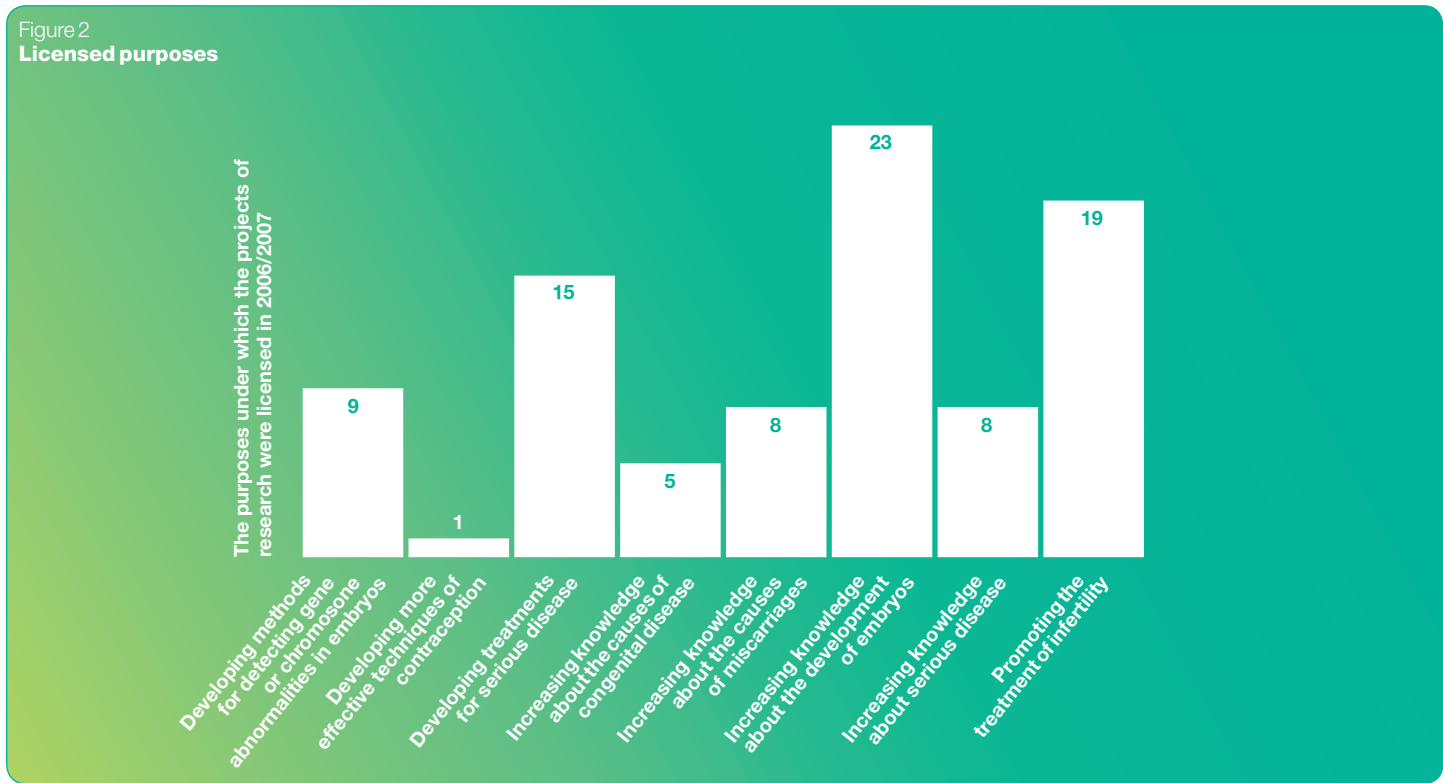


Figure 3 shows that the research authorised by the HFEA covered eight primary areas of research. A research project may involve research in more than one area. For example a project whose primary purpose is to derive human embryonic stem cell lines may also increase knowledge about how embryos develop.

This section briefly explains the research being carried under licences from the HFEA under each of the eight primary areas of research.

1. Embryo development

The selection of embryos for use in treatment is mainly based on their morphology – how they look when examined under a microscope and on how rapidly they develop. Little is known about how human embryos are formed and what makes some embryos healthier than others.

Six projects (16%) involve the study of early embryo development. The aim of these projects is to carry out a detailed examination of the development of the early human embryo. In this way the researchers hope to learn how to improve culture conditions and devise diagnostic methods that will allow the transfer of single, healthy embryos with a high chance of giving rise to a pregnancy thus minimising the risks of multiple births.

2. PGD

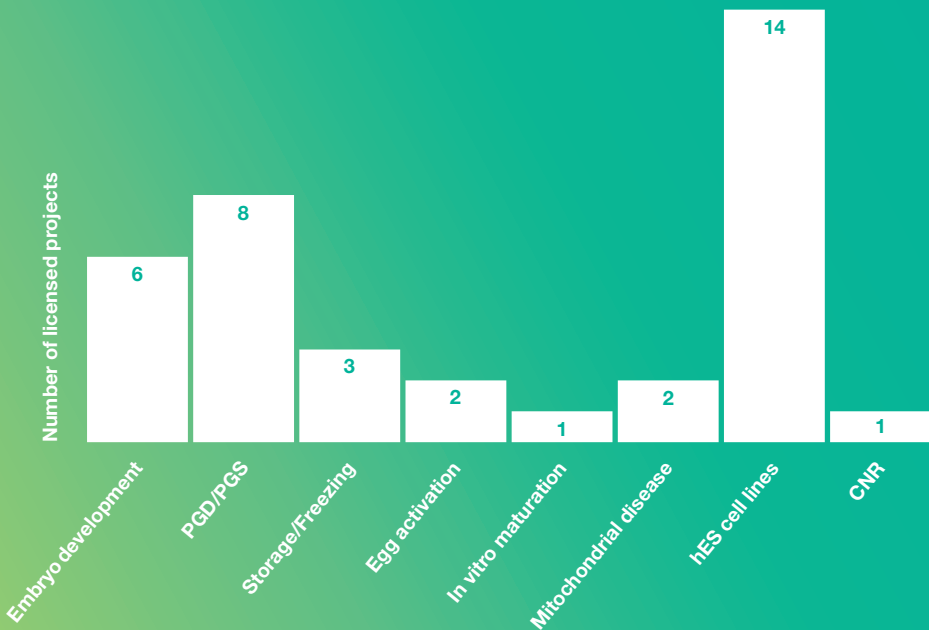
Eight projects (22%) involve the development of techniques to detect serious genetic conditions in embryos.

Pre-implantation genetic diagnosis (PGD) may be suitable for patients who are at risk of passing on an inherited disease to their children. PGD has been used to detect numerical and structural chromosomal abnormalities, the identification of sex for sex-linked diseases and the detection of specific genetic defects that occur in single gene disorders such as cystic fibrosis.

During PGD, one or two cells are removed from an embryo created in vitro and a diagnostic test carried out on the biopsied cell(s). The genetic status of the embryo is determined from the result of the diagnostic test. Unaffected, and in some cases carrier, embryos are replaced in the uterus. For PGD to be feasible, techniques must therefore be available which allow for the diagnosis of a particular gene defect from just one or two cells.

Research licensed by the HFEA aims to extend existing technologies to allow PGD to be applied to a greater range of diseases and develop new technology to improve the process of biopsy and embryo selection, with the ultimate aim of increasing the clinical success of the treatment.

Figure 3
Areas of research carried out under
HFEA Research Licences



A research project may involve research in more than one area.

3. Egg and Embryo Freezing

Three projects (8%) were licensed to carry out research on new methods for freezing eggs and/or embryos. During IVF treatment, about 10 eggs are usually retrieved following ovarian stimulation of which 6 or 7 are successfully fertilised. Usually up to two of these embryos created are used in each fresh treatment cycle. The remaining embryos may be stored (cryopreserved) for transfer at a later date.

However, the chance of having a baby differs depending on whether fresh or frozen embryos are used. In 2004, the national figures for IVF treatment showed that women below 35 years of age had a 28% chance of having a baby if fresh embryos were used in the treatment cycle. This figure dropped to 17% if frozen/thawed embryos were used. One of the reasons for this decrease in success rates is that the process of freezing embryos may damage the embryos, and therefore many do not survive the freeze/thaw process.

UK researchers are working on new methods of freezing embryos that will hopefully decrease the risks of damage with this procedure and thus increase the chance of having a baby following treatment with frozen/thawed embryos.

The ability to freeze and preserve human sperm has been around for decades, but human egg freezing is much more recent. The ability to freeze eggs could be beneficial to women facing medical treatment that may affect their fertility; for example in women undergoing some forms of cancer treatment or in single women concerned about the decline in their fertility as they get older but who are not currently in a position to have a child.

Survival rates for eggs following freezing depend on the quality of the eggs before freezing, but on average only about 70% of the eggs frozen will survive the freezing and thawing process. Of the surviving eggs about 65% of these, in turn, will fertilise in response to ICSI (intra-cytoplasmic sperm injection).

The use of frozen eggs is still a relatively new procedure and it is difficult to provide accurate statistics on pregnancy rates. However, there is no doubt that embryos produced from frozen eggs are less viable than embryos from fresh eggs. Success rates worldwide appear to be about 5% per embryo transferred (rates quoted by individual clinics vary from 5% up to 30%).

Researchers, under a licence from the HFEA, are trying to develop more reliable ways of cryopreserving human eggs. These researchers are using the technique known as vitrification (a form of snap-freezing) to freeze the eggs. The vitrified eggs are then thawed, activated parthenogenetically and allowed to develop to discover whether this method works. The embryos obtained are then compared with embryos from eggs that were not frozen, to determine whether their genes are still working normally.

4. Egg Activation

Two projects are licensed by the Authority to examine the activation of eggs. As a human sperm approaches the egg it undergoes an event called the acrosome reaction (AR), which is thought to be necessary for successful fertilisation. In the female reproductive tract or in the laboratory this reaction is thought to be induced by interaction between the sperm and the zona pellucida (ZP), a sticky coat surrounding the egg. Despite the crucial role of the acrosome reaction in fertilisation very little is known about what happens as a sperm moves through the outer egg coat.

One of the licensed projects is employing advanced fluorescent imaging (microscopy) techniques to examine in detail the events occurring as human sperm and egg interact. The second project is investigating how sperm stimulate eggs to begin cell division and development. These researchers have identified a protein that when injected into eggs, stimulates them to begin development.

The results of these research projects will give new insight into the very early events occurring in fertilisation, which may lead to the development of new diagnostic and treatment regimes.

5. In vitro maturation of eggs

In each menstrual cycle, natural hormones trigger egg containing follicles within the ovaries, to develop. Usually only one of these follicles ripens and releases a single mature egg. The remaining follicles, containing immature eggs disappear.

Conventional IVF treatment involves the use of hormone drugs to stimulate the ovaries to produce a number of mature eggs, which can be collected and fertilised in the laboratory.

An alternative procedure is to collect eggs from ovaries that have been given only modest hormonal stimulation and to mature these eggs in the laboratory. This is known as in vitro maturation, or IVM.

The difference between IVM and conventional IVF is that the eggs are immature when they are collected and need to be matured in vitro.

However, the great advantage of IVM is that the woman does not need to take as many drugs as in normal IVF – something which is of particular benefit to women who are more susceptible to ovarian hyper-stimulation syndrome (OHSS), such as those with a polycystic ovarian syndrome (PCOS). IVM is a relatively new technique, and so far only about 300 children have been born worldwide via this route.

A group of researchers, licensed to study IVM, have shown it is possible to collect eggs from young healthy women following only very mild hormone stimulation and mature these eggs in the laboratory. Approximately half of the eggs matured in the laboratory were successfully fertilised when injected with donor sperm, and the majority of the fertilised eggs developed into embryos.

As IVM is still relatively new, it is important that tests are carried out to determine whether embryos created from in vitro matured eggs are healthy and develop normally. The research groups studying IVM are consequently comparing eggs matured in the laboratory with in vivo matured eggs. Encouragingly, they have shown that maturing eggs in the laboratory does not appear to have any adverse effect on the development of these eggs (and subsequent embryos created using them), when compared with in vivo matured eggs.

6. Mitochondrial Disease

Mitochondria are small complex structures, which exist in virtually every cell of the body (except red blood cells). These mitochondria produce most of the energy which all our cells need to live and grow. Mitochondrial diseases are chronic, genetic disorders that occur when mitochondria fail to produce enough energy. They affect about 1 in 10,000 people in the UK. Examples include Leigh disease, myoclonic epilepsy and mitochondrial encephalopathy. Mitochondria are uniquely programmed not by nuclear DNA but by special DNA contained in the mitochondria known as mitochondrial DNA (mtDNA).



The inheritance of mtDNA is via mitochondria contained in the egg. Thus mitochondrial genes are inherited only through the mother. Some women are carriers of defective mitochondrial genes; they carry both normal and damaged mitochondrial genes and can pass potentially devastating diseases on to their children. It is particularly difficult to advise such women about the extent of their individual risk, because the way that mitochondrial genes are transmitted is not well understood.

Two projects are licensed to carry out research into mitochondrial disease. The first one aims to establish techniques for identifying defects in mitochondrial DNA in human embryos created by IVF. This will allow the selection of non-affected embryos using pre-implantation genetic diagnosis (PGD) prior to transfer into the woman.

The aim of the second project is to see if it is possible to prevent the transmission of mitochondrial disease by moving the pronuclei from an egg containing defective mitochondria to another egg which contains only normal mitochondria. Pronuclei are the structures that ultimately develop into an embryo's nucleus containing the embryo's 'nuclear' DNA.

7. Human embryonic stem cell lines

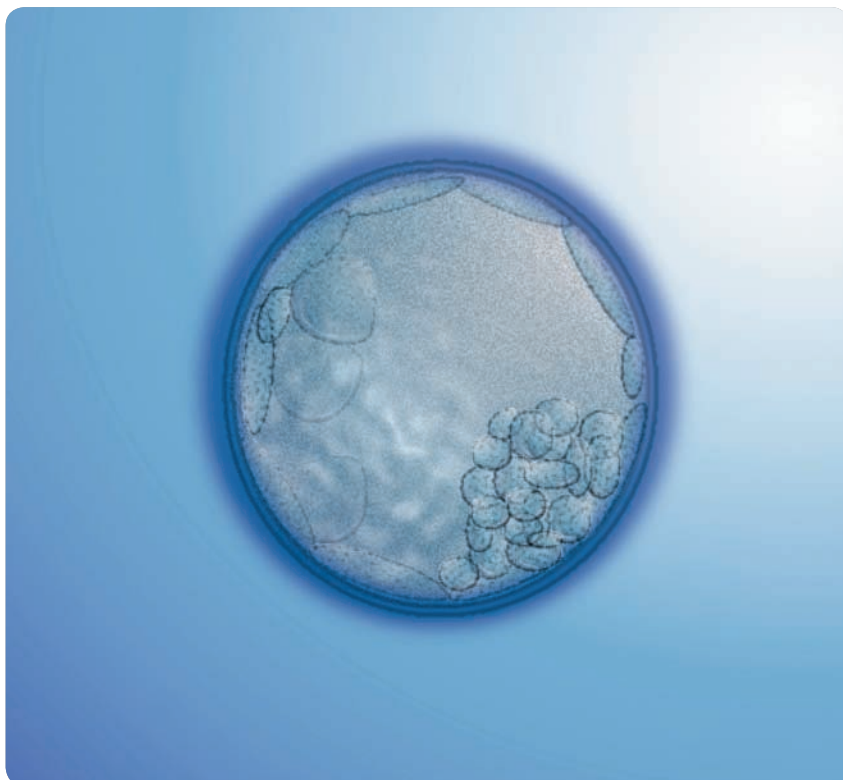
Stem cell science is becoming a very active area of research. Figure 3 shows that 14 (39%) of research projects licensed by the HFEA during 2006–2007 involved the derivation of human embryonic stem cell lines. Human embryonic stem cells are useful for studying a wide range of diseases in the laboratory. These stem cells could, in the future, be used to develop new therapies for serious diseases such as diabetes, Alzheimer's or Parkinson's disease. These cells could also be used for drug screening and toxicity testing or as vehicles for drug delivery.

To date, over 30 human embryonic stem cell lines have been derived in the UK. Eight of these lines have been banked in the UK Stem Cell Bank and four lines are available for release. The other four lines have completed the banking process and are currently undergoing quality control testing prior to being released. Eleven further human embryonic stem cell lines, derived under licence from the HFEA, have been approved for banking (by the Steering Committee for the UK Stem Cell Bank and the Use of Stem Cell Lines) but have yet to be deposited in the Stem Cell Bank.

8. Cell nuclear replacement

Cell nuclear replacement (CNR) involves placing the nucleus of an adult cell, e.g. a skin cell, in an egg which has had its own nucleus removed. The egg-cell combination is then stimulated to develop into a blastocyst, from which embryonic stem cells can be extracted after about five days of growth. Obtaining stem cells for potential therapies in this way is known as therapeutic cloning. It is recognised that human embryonic stem cells offer great potential for therapies for many diseases such as diabetes.

However, if stem cell treatments are to reach their full potential, scientists believe that they need to derive stem cell lines which are genetically similar to the recipient, so as to prevent rejection. This may require the application of techniques such as cell nuclear transfer. The research currently being undertaken is mainly aimed at understanding the science underlying this technology. The research team has successfully derived a human blastocyst following nuclear replacement.



material for research

donating gametes and embryos for use in research

The HF&E Act requires that, prior to donating embryos to research, patients must give their consent to the use of any embryo created using their gametes. It is imperative that embryos (or gametes donated to produce embryos) for research are freely given and that people donating them have made an informed choice. For this reason, licensed centres must have safeguards in place to ensure that if a patient decides to donate gametes and/or embryos for use in research, this donation must not affect their treatment in any way. Centres must ensure that a designated individual who is not involved in the research project is available to discuss the implications of donation with the prospective donor.

Table 4
The UK Stem Cell Bank

The UK Stem Cell Bank was established in 2002 to provide a repository for human stem cell lines of all types. The Bank will ensure that there is a single national independent institute responsible for supplying ethically approved, quality controlled stem cell lines both for basic research and for the development of clinical applications.

The Bank operates in accordance with strict principles of governance laid down by a high level committee, chaired by Lord Patel, known as The Steering Committee for the UK Stem Cell Bank and the Use of Stem Cell Lines (the Steering Committee). This Committee regulates the use of human embryonic stem cell lines and has developed codes of practice for the stem cell bank and for the use of stem cell lines.

The HFEA has introduced additional requirements for centres using embryos to derive human embryonic stem cell lines. Patients donating sperm, eggs or embryos to these research projects must be given information so that they understand fully the implications of this type of research, including the immortal nature of stem cell lines.

The national network of stem cell co-ordinators (hESCCO) have developed national patient information and consent forms which are used in centres where patients are asked to consider donating embryos for use in the derivation of stem cell lines. These forms have been approved by several Local Research Ethics Committees as well as the HFEA Research Licence Committee. It is a condition of all research licences which authorise the use of embryos to derive embryonic stem cell lines to deposit a sample of these lines in the UK Stem Cell Bank (see Table 4).

Use of embryos in research

The majority of embryos used in research projects are obtained from patients undergoing fertility treatment. These embryos are either unsuitable for use in treatment or the patients may decide they do not wish to cryopreserve their spare embryos. In addition, patients who have embryos cryopreserved for future use sometimes decide that they no longer wish to use these embryos in treatment services (for example, IVF may have been successful for them), and consent to the embryos being used instead in a research project.

As part of an in vitro fertilisation (IVF) treatment cycle, a number of eggs are collected from the female patient. If the eggs are mature then they will be mixed with sperm in order to create embryos. Not all these eggs will be fertilised successfully. These “failed to fertilise” eggs may also be used in research, provided the patient has given their consent.

A number of projects require the creation of embryos in order to determine whether the research has been successful. For example, in order to ascertain whether eggs can be matured in the laboratory (a process known as in vitro maturation), the eggs need to be fertilised to discover if the procedure is effective. Also, in order to derive embryonic stem cells from cloned embryos, it is thought that fresh, good quality eggs are required.

The eggs used in these projects may be obtained from fertile women who are undergoing sterilisation or from those undergoing fertility treatment who consent to donate some of their eggs for research; these may be mature or immature eggs. Recently, the Authority agreed to allow researchers to use eggs obtained from either non-patient donors or from women undergoing IVF who consent to donate a proportion of the eggs collected as part of the treatment cycle.

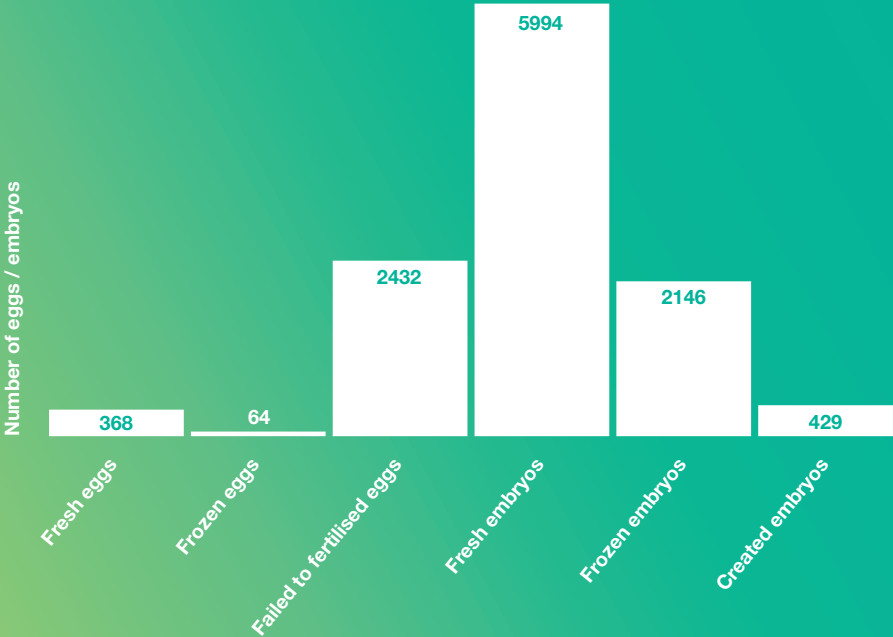
The majority of sperm used in research is either obtained from patients undergoing fertility treatment who donate sperm which is then not required to fertilise their partner's eggs, or from donors who have reached the limit of 10 live birth events (10 families).

Figure 4 shows the number of eggs and embryos used in research². This figure shows that the majority of embryos (70%) used in licensed research were fresh embryos. The majority of eggs (85%) used in research projects had failed to fertilise after mixing with sperm as part of an assisted conception treatment cycle.

This figure also shows that 25% of the embryos used in research had been frozen for potential future use in treatment services, but had then been donated for use in a research project. 5% of the embryos used in research were created specifically for that purpose.

²This information has been obtained from the information submitted to the HFEA as part of the inspection process. This data covers a period from 2005 until early 2007. The number of embryos reported as having been used in research may include embryos that have been reported as being used in more than one research project. For example, embryos may be used in a licensed research project that involves non-invasive tests at one centre, and then these embryos may be transferred to another centre for use in another research project that involves the derivation of embryonic stem cells. The embryos created for use in research will have been created from either some of the failed to fertilised eggs (embryos), or fresh eggs.

Figure 4
Use of Eggs/Embryos in Licensed Research
Projects (2005 – 2007)



information

publishing information

One of the primary roles of the HFEA is to provide information for the public and patients about fertility treatment and research. The Authority considers it important to involve the public in its decision making process when it receives an application for an initial research licence. A summary of every proposed research project, in lay language, is published on the HFEA website (www.hfea.gov.uk). The estimated date that the Research Licence Committee will consider these applications is also given so that the public has the opportunity to submit their views on the proposed research. These views are considered by the Licence Committee when deciding whether or not a licence should be granted.

A list of all research projects licensed by the HFEA, together with a summary explaining the research in lay language, is published on the HFEA website (www.hfea.gov.uk). The published reports of the inspection of all research centres also contain a summary of the research that has taken place during the previous year and, in addition, reports the number of embryos that have been used in the project.



inspection

inspecting research centres

The HFEA inspects research laboratories prior to the granting of a research licence, and all research centres are inspected on an annual basis.

Research inspections are all led by one of the HFEA's scientific inspectors, supported by a clinical or generalist inspector. Usually the team members are all HFEA-employed inspectors but occasionally external advisers are included, when necessary. The primary purpose of the inspection is to ensure that the research and associated activities are being carried out in accordance with the HF&E Act 1990 (as amended by the HF&E (Research Purposes) Regulations 2001) and the HFEA's Code of Practice.

During the inspection the inspection team assesses the effectiveness of the centre against five criteria:

- How well the centre is organised
- Standards of premises and equipment
- Procedures for donation of gametes and embryos for use in licensed research
- Patient information and consents
- Standards of scientific practice

Each area is evaluated and categorised, and an overall judgment is given:

- No improvements required – given to centres where there are no code of practice or legal requirements, and no recommendations or conditions that need to be imposed.
- Some improvements required – given to centres that are generally satisfactory but have areas that need attention. Recommendations will usually be made to help Persons Responsible to improve the service.
- Significant improvements required – given to centres that have considerable scope for improvement and have unacceptable outcomes in at least one area. An immediate action plan will be imposed, and/or conditions could be put on the licence.

Following each inspection a report is written. These reports are presented to the Research Licence Committee to help it make evidence-based decisions. Reports are then published on the HFEA website (www.hfea.gov.uk) to provide information to the public and other interested stakeholders on the research being carried out at licensed research centres.

Inspection findings

A review of the reports of the inspections carried out during 2006/07 showed that, in general, the inspectorate was satisfied that the research centres were well-organised and managed and that the centres had complied with the requirements of the HF&E Act 1990 and the HFEA Code of Practice.

The inspectorate did identify that the following breaches of the HF&E Act had occurred:

- The storage of embryos beyond the consented storage period
- The use of embryos in research without evidence that consent had been obtained from the gamete providers
- Failure to report adverse incidents to the HFEA.

The Research Licence Committee noted the seriousness of these breaches and asked that those centres that had breached the HF&E Act 1990 should put in place safeguards to ensure that such breaches could not happen again. The Committee also asked that these safeguards should be the focus of the next inspection.

The inspectorate identified a number of issues during the inspection of research centres and recommended that centres make improvements in the following areas:

- Patient information and consent forms
- The timing of provision of information to patients regarding the donation of gametes and/or embryos to research
- The timing of obtaining consent from patients to the donation of gametes and/or embryos for use in research
- Separation of clinical and research roles
- Access to research laboratories/security of storage dewars and laboratories
- Notification of staff changes to the HFEA
- Recording the use of gametes and/or embryos in licensed research
- Auditing the storage of embryos

- Recording the date that embryos stored for use in research are due to reach the end of their statutory storage period to ensure that embryos are not used beyond this period
- Documenting the training undertaken by staff
- Formulating procedures for actions to be taken if a patient withdraws their consent to the use of embryos created using their gametes in licensed research
- Formulating a written adverse incident handling policy.

The majority of research centres had put procedures in place to implement these recommendations prior to the reports being considered by the Research Licence Committee. In all cases the Research Licence Committee asked that the implementation of these recommendations be followed up at the next inspection of the research centres.

The Research Licence Committee also noted that some of the research centres licensed to use human embryos to derive embryonic stem cell lines were using methods that involve allowing the inner cell mass of embryos to outgrow in a culture dish, rather than separating it from the outer cells either mechanically or by immunosurgery. In this technique, the embryo is allowed to attach to the surface of a culture dish, the embryo flattens and cells from the two cell lineages (the trophectoderm and the inner cell mass) spread out over the surface of the dish.

The Committee noted that the HF&E Act 1990 provides that a licence cannot authorise keeping or using an embryo after the appearance of the primitive streak, where the primitive streak is to be taken to have appeared in an embryo not later than the end of the period of 14 days beginning with the day when the gametes are mixed, not counting any time during which the embryo is stored [Sections 3 (3a) and 3(4)].

Centres were advised that where whole embryos are cultured to form outgrowths, the centre should consider how it can be demonstrated that they have complied with the Act to terminate culture after 14 days. Furthermore the Research Licence Committee asked that this issue be referred to the Authority's advisory committees for consideration.

In considering the renewal of one research licence the Research Licence Committee noted that, even though the peer reviewer had recommended the renewal of licence, the reviewer had raised concerns of the number of embryonic stem cell lines derived compared to the number of embryos that had been used in the project of research.

Members of the Committee noted that the HFEA had never specified an expected success rate in the derivation of stem cell lines and that the number of lines derived did not deviate significantly from the reviewer's expectations. However, in renewing the licence the Committee asked that the use of embryos in this research project should be closely monitored.



appendix 1

Research Centres/Projects licensed by the HFEA between 1 April 2006 and 31 March 2007

Aberdeen Fertility Centre (Centre 0019)

- A Study of Morphology and Metabolism in Pre-implantation Human Embryos Leading to the Generation of Embryonic Stem Cell Lines (R0157)
- Development of methods for oocyte freezing and vitrification and provision of cryopreserved oocytes for cell nuclear replacement and stem cell production (R0159)
- Development of methods for the vitrification of human embryos in sealed Containers (R0164)

Assisted Conception Service, Glasgow Royal Infirmary (Centre 0037)

- The effect of biomass reduction on embryo development after biopsy of either one or two blastomeres (R0175)

Birmingham Women's Hospital (Centre 0119) /Institute of Biomedical Research (Centre 0209)

- Chromatin and epigenetic associated with the development and generation of embryonic stem cells (R0151)
- Human Gamete Interaction and Signalling (R0172/ R0173)

Bourn Hall, Cambridge (Centre 0100)

- The Disaggregation of Embryos for the Purpose of Deriving Stem Cells from Human Surplus Embryos (R0167)

Cardiff Assisted Reproduction Unit (Centre 0049)

- Investigation into the Role of Sperm PLC-Zeta in Human Oocyte Activation (R0161)

CARE, Nottingham (Centre 0101)

- Evaluation of blastocoele collapse v expanded blastocysts for successful cryostorage using vitrification (R0176)
- A novel protocol for extracting cells during embryo biopsy without the use of acid Tyrodes (R0177)

Centre for Assisted Reproduction, Coventry (Centre 0013)

- Indicators of Oocyte and Embryo Development (R0155)

Centre for LIFE, Newcastle-upon-Tyne (Centre 0017)

- Epigenetic Studies of Preimplantation Embryos and Derived Stem Cells (R0145)
- Derivation of Human Embryonic Stem Cell Lines using Nuclear Transfer and Parthenogenically Activated Oocytes (R0152)
- Mitochondrial DNA Disorders: Is there a way to prevent transmission? (R0153)

Centre for Stem Cell Biology, University of Sheffield (Centre 0191)

- Optimisation of human embryonic stem cell derivation and the development of treatments for degenerative diseases (R0115)

Chelsea & Westminster Hospital (Centre 0158)

- Isolation of human embryonic stem cells and in vitro derivation of specific cell types (R0150)

Clarendon Wing, Leeds General Infirmary (Centre 0052)

- Maturation of fertilisation of human eggs in vitro (R0104)

Guy's Hospital, London (Centre 0102)

- Improving methods for biopsy and pre-implantation diagnosis of inherited genetic disease of human pre-implantation embryos (R0075)
- Correlation of embryo morphology with ability to generate embryonic stem cell lines and subsequent growth differentiative characteristics (R0133)

Human Genetics and Embryology Laboratories, University College Hospital, London (Centre 0245)

- The development of novel pre-implantation genetic diagnosis (PGD) procedures and the study of early human development (R0113)

Institute for Stem Cell Research, Edinburgh (Centre 0166)

- Derivation of pluripotent human embryo cell lines (R0132)

Note: On 1 December 2006 the research licence at Centre 0166 was revoked and the research transferred to the Wellcome Trust Centre for Stem Cell Research University of Cambridge (Centre 0252)

- Derivation of Pluripotent Human Embryo Cell Lines (R0178)

Institute of Reproductive and Developmental

Biology, Imperial College London (Centre 0249)

- Comparative studies on human embryonic stem cells and stem cells derived from male germ cells (R0174)

Lister Hospital, London (Centre 0006)

- Analysis of the Impact of Human Embryo Mosaicism on the Reliability of Pre-implantation Genetics Screening (PGS) (R0163)

London Fertility Centre (Centre 0088)

- Analysis of chromosomes in human pre-implantation embryos using FISH and CGH (R0169)

Ninewells Hospital, Dundee (Centre 0004)

- Studies of Embryo Development and Metabolism (R0154)

NURTURE, Nottingham (Centre 0076)

- Evaluation of cardio myocytes derived from embryonic stem cells as a means to characterise receptor/channel expression in human tissue (R0141)

Oxford Fertility Unit (Centre 0035)

- Development of a model to study implantation in the human (R0111)
- To derive human embryonic stem cells and trophoblast cell lines (R0143)
- To Develop Pre-implantation Genetic Diagnosis (PGD) for Mitochondrial DNA Disease (R0149)

Princess Anne Hospital, Southampton (Centre 0251)

- Environmental Sensitivity of the Human Pre-Implantation Embryo (R0142)

Reproductive Genetics Institute, London (Centre 0206)

- Investigation of Major Histocompatibility Complex Products and Soluble Protein Expression in human Embryos at the Pre-implantation Stage (R0165)

Roslin Institute, Edinburgh (Centre 0202)

- Platform technologies underpinning human embryonic stem cell derivation (R0136)

St Mary's Hospital, Manchester (Centre 0067) / Manchester Fertility Services (Centre 0033) / University of Manchester (Centre 0175)

- In vitro development and implantation of normal human pre-implantation embryos and comparison with uni- or poly- pronucleate pre-embryos (R0026)
- Derivation of Human Embryonic Stem Cell Lines from Embryos created from Clinically Unused Oocytes or Abnormally Fertilised Embryos (R0170/R0171)

University of Cambridge (Centre 0246)

- Derivation of human Stem Cells from Human Surplus Embryos: The Development of hES Cultures, Characterisation of Factors Necessary for Maintaining Pluripotency and Specific Differentiation towards Transplantable Tissues (R0162)

University of York (Centre 0062)

- Biochemistry of early human embryos (R0067)

glossary

Assisted Reproductive Technologies (ARTs):

Collective name for all artificial techniques used to assist women to conceive children, including IVF and ICSI.

Blastocyst: An embryo that has developed for five to six days after fertilisation.

Blastomere: A cell taken (by biopsy) from a blastocyst.

Cell: The basic unit of all living organisms. Complex organisms such as humans are composed of somatic (body) cells and germ line (reproductive) cells.

Cell Nuclear Replacement (CNR): The transfer of the nucleus from an adult somatic cell (any cell forming the body of an organism) into an egg from which the nucleus has been removed.

Chromosome: Threadlike structure of DNA with associated proteins located in the cell nucleus, containing genes which carry genetic information.

Cleavage: The division of the zygote (cell formed by fertilisation) to produce a blastocyst.

Congenital malformations: Any malformation seen at birth, either resulting from genetic (inherited) or environmental causes.

Cryopreservation: The storage of gametes or embryos by freezing at low temperatures.

DeoxyriboNucleicAcid (DNA): The major constituent of chromosomes, and the hereditary material of all living organisms.

Derivation of stem cells: The process of obtaining stem cells from a source such as embryos, bone marrow, or cord blood.

Egg or oocyte: The gamete produced by a woman during her monthly cycle.

Egg collection or egg retrieval: Collection of eggs from a woman's ovary using an ultrasound guided needle, or a laparoscope (a fiberoptic telescope used for looking into the abdomen) and needle.

Embryo: A fertilised egg that has the potential to develop into a foetus.

Embryo biopsy: The removal and culture of one or two cells from an embryo in vitro prior to genetic screening.

Embryo division: Splitting of an embryo grown in vitro, at a very early stage, into two or more sections. Each section can be grown separately producing multiple clones (fission cloning) of the single original embryo.

Embryo freezing and embryo storage: Spare embryos can be frozen (cryopreservation) and stored for future use.

Embryo transfer: The replacement of embryos back into the female patient.

Embryonic stem cells: Cells taken from an early stage embryo that have the potential to form a wide range of other cell types.

Embryonic stem cell lines: Cells from an embryo that can continuously divide to produce identical cells and can also produce cells that have formed (differentiated) into other cell types.

Fertilisation: The penetration of an egg by a sperm resulting in the formation of an embryo. Naturally fertilisation occurs in the woman's body (in vivo), but it can also occur in the laboratory (in vitro).

Follicle(s): A small sac in the ovary in which the egg develops.

Follicle-stimulating Hormone (FSH): A pituitary hormone which stimulates the follicle production by the ovary. Often administered in assisted conception to stimulate production of several follicles (ovulation induction).

Gamete: The male sperm or female egg which fuse together to form a zygote.

Gene: Units of hereditary information that are made up of DNA and determine specific characteristics in offspring. Genes are carried on chromosomes.

Genome: The basic set of genes in the chromosomes in any cell, organism or species.

Gonadotrophin Releasing Hormone (GnRH): Hormone released by the hypothalamus which stimulates the pituitary to produce Luteinising Hormone (LH) and Follicle-stimulating Hormone (FSH).

Gonadotrophins: Drugs used to stimulate the ovaries similar to GnRH.

Gradient sperm sorting methods: Way of sorting X and Y chromosomes containing sperm, for sex selection.

Human Chorionic Gonadotrophin (HCG): A protein hormone usually secreted by the chorionic villi of the placenta. Its presence in the maternal blood or urine indicates pregnancy.

HF&E Act: The Human Fertilisation and Embryology Act 1990.

HFEA: Human Fertilisation and Embryology Authority.

Implantation: Where an embryo embeds itself in the uterus lining, after passage through the Fallopian tubes.

Inner cell mass: A clump of cells growing within and to one side of the blastocyst from which the embryo develops.

Intra-cytoplasmic Sperm Injection (ICSI): Where a single sperm is directly injected into the egg.

In Vitro Fertilisation (IVF): Human eggs and sperm mixed together in a laboratory to achieve fertilisation outside the body. The embryos produced may then be transferred into a female patient.

In vitro: Performed outside the body (i.e. in the laboratory).

In vivo: Performed in the body.

Licence: A legal document stipulating terms and conditions for which a centre may carry out a licensable fertility treatment at a specified premise.

Mitochondria: Structures in the cytoplasm of the cell that make the energy for the cell and contain a small amount of genetic material (DNA).

Mitochondrial diseases: A group of disorders relating to the mitochondria in a cell.

Mitochondrial genome: The genetic material contained within mitochondria.

Morula: The ball of cells forming about 3 - 4 days after the cleavage of the fertilised ovum.

Multiple birth: When a multiple pregnancy actually results in the birth of two or more babies.

Multiple birth rate: The percentage of all births in which more than one baby was born.

Multiple pregnancy: A pregnancy where two or more fetuses develop at one time in the uterus (womb).

Nucleus: The part of a cell which contains the genetic material, DNA.

Oocyte: The female gamete (egg).

Ovary: The female reproductive organ producing oocytes from hormone-stimulated germ cells.

Ovarian Hyperstimulation Syndrome (OHSS):

A serious complication following stimulation of the ovaries with gonadotrophin drugs.

Ovulation: The release of an egg from a follicle in the ovary.

Ovum: The female gamete (egg).

Parthenogenesis ("Virgin birth"): An embryo develops directly from an oocyte without sperm fertilisation (triggered through electric or chemical stimulation, but can also sometimes happen naturally).

Pluripotent: The ability of cells (e.g. embryonic stem cells) to develop into a wide range of cells and tissues including all three embryonic tissue layers.

Polycystic Ovarian Syndrome: Condition where many small cysts form on the ovary, resulting in hormonal imbalances which can cause infertility. Treatment involves drugs or surgery.

Pregnancy rate: The number of pregnancies achieved from every 100 treatment cycles commenced.

Preimplantation Genetic Diagnosis (PGD):

The removal of one or two cells from an embryo to test for specific genetic disorders/characteristics prior to embryo transfer.

Preimplantation Genetic Screening for Aneuploidy

(PGS): The removal of one or two cells from an embryo, for testing to ensure the chromosome number is correct (euploidy) and not more or less than usual (aneuploidy).

Primitive streak: Thickening in surface of embryos which results in the first clearly recognisable stage in embryonic development.

Sperm: Male gametes (or mature male germ cells). Of the millions of sperm present in the ejaculate roughly half carry X chromosomes, and half Y chromosomes. A single sperm is called a spermatozoon.

Stem cells: Cells that can continuously divide to produce identical cells and also have the ability to produce cells that have different, more specialised properties.

Stimulated cycle: A treatment cycle in which stimulation drugs are used to produce more eggs than usual in the woman's monthly cycle.

Stimulation drugs: Stimulate a woman's ovaries to produce more eggs than usual in a monthly cycle. Also known as superovulatory drugs.

Therapeutic cloning: The process of creating embryos through SCNT (above) to produce embryonic stem cells that are genetically matched to a particular person, for the treatment of disease.

Treatment cycle: One complete licensed treatment. Commences with drug administration or first insemination.

Zygote: The cell formed as a result of fertilisation.

