

## Version for Piloting

### For Information

#### Donating Oocytes for Stem Cell Research

##### **An invitation to contribute to stem cell research**

During routine IVF treatment, it is common to have some oocytes (eggs) that are not fertilised. As the evidence indicates that they are not suitable for further use in an IVF treatment cycle they are usually discarded. **We are approaching you to give you information about how you can help medical research by donating any such oocytes that are not fertilised during your IVF treatment. Your decision to donate oocytes will not make any difference to the way your embryologist conducts or decides which embryos to use for your IVF treatment and you will always get the best embryos for use in your treatment.**

This leaflet explains the reasons for this research (which promises benefit for other people who have infertility problems or serious diseases), what it involves, how it is regulated, and your rights if you participate. Please take time to read and consider this information carefully before deciding whether or not you want to contribute. Please ask us about anything that is not clear, or if you would like further information.

**You do not have to take part in this research and if you choose not to participate you do not have to say why. Your treatment and subsequent medical care will not be affected in any way, whether or not you decide to participate. If you do agree to take part, you can still change your mind and withdraw your consent to the use of your oocytes at any time until the oocytes are being cultured / grown for use in research. If researchers generate stem cells or stem cell lines from the oocyte(s), you cannot withdraw your consent to the use of these stem cells or stem cell lines; so it is important to make your decision before the oocytes leave the clinic.**

##### **What are stem cells?**

After fertilisation embryos keep on dividing to generate the many different cell types that comprise the human body. After five days a hollow ball of cells called the blastocyst forms. The outer blastocyst layer forms the placenta while an inner group of around 50 stem cells (inner cell mass) will form the developing embryo's tissues. If isolated and cultured under the right conditions these stem cells can form any cell type of the human body, and may in future be used for transplantation (see diagram).

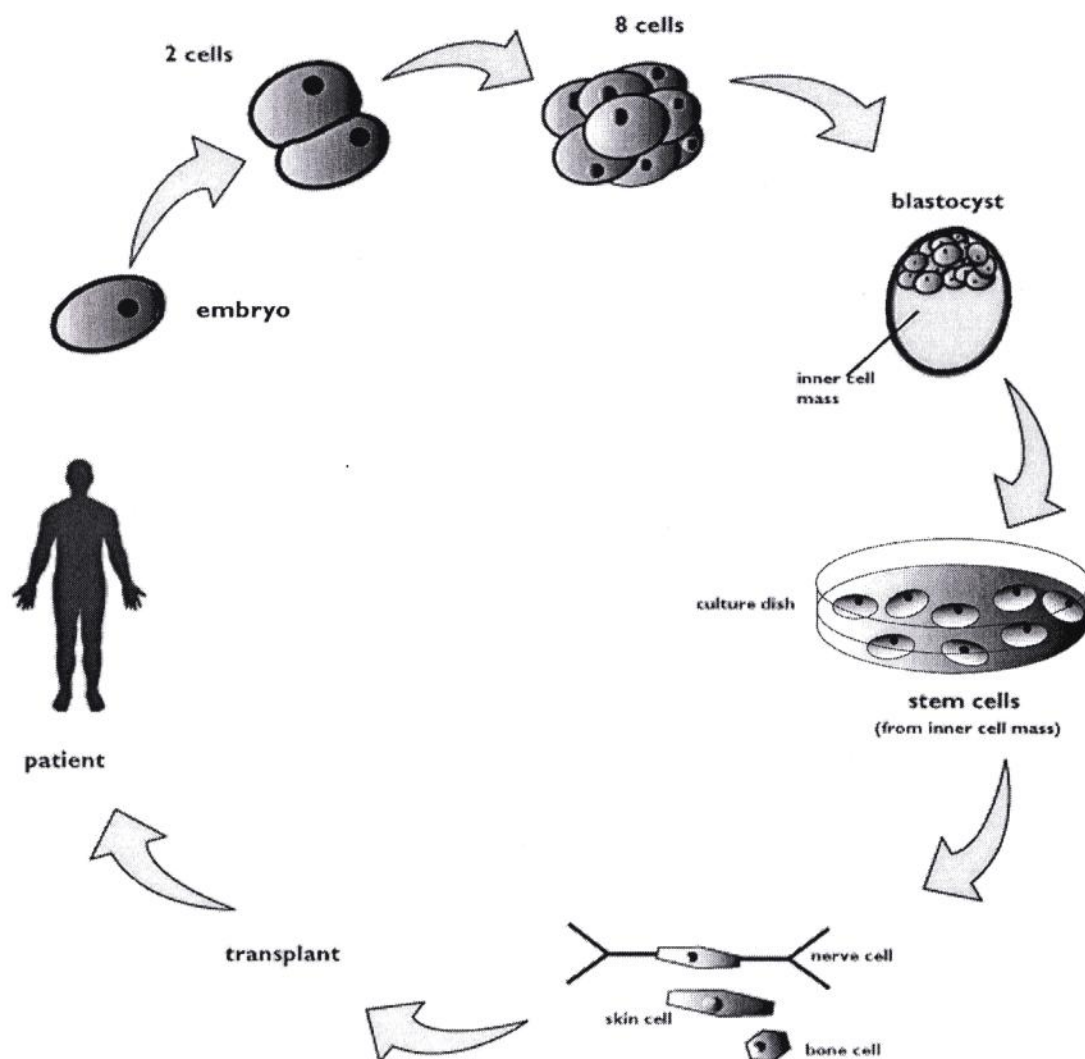
##### **What are stem cell lines?**

Stem cell lines come from stem cells, which have been grown in culture. They continue to multiply and under appropriate culture conditions they can survive indefinitely.

##### **Why are stem cells important for medical research?**

Stem cell research offers new and exciting opportunities; to learn more about the early processes of embryo development, to discover how stem cells, or cells derived from them, can be used to repair or replace damaged tissues in serious conditions such as heart disease, Parkinson's disease or diabetes, and to test the beneficial or toxic effects of drugs, diagnostics and environmental agents. The UK recently became the first country in the world to pass laws that permit appropriately conducted research with the aim of deriving human embryonic stem cells. Below are some of the ways your participation could help advance this important research though other uses may develop.

- **IVF treatment programmes** – identifying the conditions that stem cells need to grow well in the laboratory will help to work out the ideal way to look after human embryos in culture and so provide IVF patients with the best possible embryos for implantation.
- **Cell replacement therapy** – Successful treatment for certain diseases can already be achieved through transplant surgery, but there are not enough organ donors to treat all patients. In the future, embryonic stem cell-lines could be collected, grown and stored to provide a plentiful supply of healthy replacement cells for transplantation using less invasive surgery than conventional whole organ transplants. Bone marrow transplants used to treat leukaemia patients provide an example of stem cell therapy that is already in use.
- **Cancer research** – Studying the behaviour of stem cells could provide valuable insights into factors, which regulate or fail to regulate the growth of cancers.
- **Drugs and diagnostics** – such studies could lead to fewer, less costly and better designed human clinical trials, leading to more specific diagnostic procedures and more effective therapies. They could also reduce the use of animal testing.
- **Environmental agents** - It is possible to use stem cells to investigate the effects of environmental toxins on the developing embryo and fetus.





### **How are stem cells collected?**

After egg collection and fertilisation, embryos are normally grown in the laboratory for two to three days and checked to see which are suitable for transfer to the womb. At this early stage the embryo consists of a microscopic ball of around 4-10 non-specialised cells and has not yet formed any tissues or organs.

### **Embryo formation by cell nuclear replacement**

Two cells are required for the formation of embryos by cell nuclear replacement. These are an unfertilised oocyte obtained at the time when fertilisation normally occurs and a cell from another tissue, usually of another person. The genetic information of the oocytes is removed before it is replaced by the genetic information from the other cell. Almost all of the characteristics of the resulting embryo will be determined by the genetic information from the donor cell. The embryo produced in this way must then be stimulated to begin development in ways that mimic an effect of the spermatozoa during fertilisation. Oocytes that were not fertilised during your IVF treatment may be used in cell nuclear replacement to produce embryos from which embryo stem cell lines would be derived.

### **The value of stem cells obtained by cell nuclear replacement**

Opportunities that are not available in any other way will be provided by the derivation of embryo stem cells by cell nuclear replacement. These stem cells would have the genetic characteristics of the person who provided the cell that provided the genetic information. In the case of a research proposal to study a genetic disease this means that they would have the characteristics of a person who would have developed that disease. Research workers would be able for the first time to study the factors that cause the development of the disease. They would be able to assess in the laboratory possible methods for treatment or prevention of the disease before subsequent use with patients. Motor Neuron disease is one of many inherited diseases that are not understood that could benefit from such research. Others cause psychiatric disease or affect heart function and may lead to sudden death.

In the longer term cells obtained by cell nuclear replacement may also be used for treatment of other diseases, such as spinal cord injury, Parkinson's disease, diabetes, heart attack and damage to the liver. These diseases all arise from death or damage in cells that are not repaired or replaced. Treatment of these diseases using stem cells derived from donated embryos would almost certainly require treatment of patients with immunosuppressive drugs for the rest of their life to prevent rejection of cells since they would almost certainly be immunologically different from the patient who would receive them. Immunosuppression has the disadvantage that it makes the patient more vulnerable to infection. As an alternative approach, cells that were immunologically matched to the patient could be obtained by cell nuclear replacement using a donor cell from the patient.

### **What will happen to donated oocytes?**

The oocytes will be examined in the laboratory and if necessary cultured for a few hours to allow them to reach the required stage of development. They may then be frozen and stored. As oocyte storage is not yet a routine procedure in IVF treatment experiments will be carried out to establish the most effective procedure. This knowledge may be useful in the future in allowing storage of oocytes for later use in IVF treatment, for example if a young woman has cancer. Treatment of the cancer may render her infertile, but oocytes recovered and stored before treatment could be used later in IVF to give her the chance of having a child.

After being thawed and cultured briefly to allow them to recover from freezing and thawing the genetic information would be removed from the oocytes. Genetic information from a patient who has the genetic disease under study would be introduced into the oocytes. The resulting embryo would then be stimulated to begin development and grown in the laboratory for about a week. Legally, researchers can only grow embryos in the laboratory up to a maximum of 14 days.



**What will happen to the embryos?**

At the time embryos form a hollow ball of cells called the blastocyst, they will contain around 50 'stem cells', each of which has the unique potential to develop into any cell type in the body. Stem cells will be removed from the blastocysts for further culture, effectively ending embryo development. These will not be able to develop into a fetus; however, the stem cells can carry on multiplying in culture and will be studied to discover more about their unique properties. For example, researchers would like to know how stem cells can grow into different cell types, such as nerve or muscle cells, and how their genes regulate this process. Some stem cells may die naturally during these studies, but others may be maintained as 'cell lines'.

**What will happen to stem cell lines?**

The stem cell lines will be created and used in the research project that is described in the attached consent form. Stem cell lines will also be preserved in a stem cell bank, which the UK Medical Research Council has established together with the Biotechnology and Biological Sciences Research Council as a resource to help doctors and scientists to develop new treatments for disease. Keeping cell lines in a stem cell bank that can be accessed by many scientists will help to reduce the number of embryos that are needed for research. The stem cell lines will be characterised, standardised, frozen and stored for future use in approved research projects, perhaps many years later. Such research projects may help us to understand and develop treatments for serious diseases or injuries, or they could have other health related goals, e.g. development of drugs and diagnostics. All scientists who want to use banked stem cell lines derived from embryos will have to seek approval from a high level Stem Cell Steering Committee that reports to the Medical Research Council; approval will only be given if i) the research is necessary and of high quality, ii) the scientists are following UK legal and ethical guidelines, and iii) the scientists provide evidence that they have secured all essential licences or accreditations from relevant UK ethical and regulatory authorities. International scientists will be permitted to access cell lines stored in the bank, but only where they are able to demonstrate that their projects meet all the conditions (i) – (iii) which apply to UK scientists.

**Your consent to donate will therefore cover both the research project in which stem cell lines are created and any future research on those stem cell lines. If you decide to donate oocytes for stem cell research you cannot restrict the use of cell lines derived from your embryos to specific research projects or diseases. This policy was recommended in the House of Lords report (2001) and is aimed at reducing the total number of embryos required for stem cell research. It is also consistent with existing guidelines for donating human tissues for research.**

**Are there personal or financial benefits?**

**You will receive no financial reward from future commercial application of such research. Similarly, since this is long term research it is unlikely to be of immediate medical benefit to you.**

In the future, stem cell lines derived from donated oocytes might be used to develop new treatments, including cell replacement therapy. It will not be possible to turn this research into new treatments that will provide widespread health benefits without involving commercial companies.

Cell lines and developments arising from stem cell research might be patented by academic researchers or commercial companies. However, the research and development process involves many stages and the contribution of your individual embryo(s) to any future profits will be impossible to quantify.



### **Additional tests**

It is routine practice for couples undergoing IVF treatment to be given a blood test for HIV 1 and 2, and for Hepatitis B and C. It may also be necessary to test your blood sample for HTLV (Human T-Cell Lymphotropic Virus) and other conditions. The implications will be fully explained during counselling.

### **Legal and ethical safeguards**

The Human Fertilisation and Embryology Authority (HFEA) is authorised to approve and license research on embryos no more than 14 days old and for strictly limited purposes. For a research license to be granted the HFEA must be satisfied that the goal of the research cannot be achieved in any other way (including research on adult stem cells) and that there are no existing stem cell lines in the bank that would be suitable for the proposed research. Furthermore, the researchers must demonstrate that ethical approval has been obtained, and that the use of human embryos is 'necessary or desirable' for at least one of the following purposes:

- Advancing infertility treatment, or improving contraception techniques
- Increasing knowledge about embryo development, and the causes of miscarriages and birth defects
- Developing methods to detect abnormalities in embryos before implantation
- Increasing knowledge about serious disease, and using this knowledge to develop treatments

The law does **not** allow research that involves using human embryos for any purposes not covered by an HFEA license. The research described on the attached consent form has already been approved by the HFEA and by the lead researcher's Local Research Ethics Committee. The HFEA patient information sheet relating to embryo research accompanies this leaflet. The requirements of research (e.g. the conditions used to culture embryos) will not affect your treatment in any way.

### **Protecting your confidentiality**

The HFE Act imposes strict requirements about patient confidentiality. Personal information will be coded to ensure anonymity and confidential records will be maintained securely in a restricted area;

The following personnel will have access to your consent and medical history forms:

- Staff at the clinic where you receive your IVF treatment
- The principal investigator licensed by the HFEA to conduct the research
- The HFEA which is required by law to hold information on all IVF treatments on its national database
- The Secretary to the Stem Cell Steering Committee; this is because the consent form must be carefully checked by the Secretariat as part of the researcher's application to the Steering Committee to deposit stem cell lines derived from embryos in the UK Stem Cell Bank.

The following personnel will never have access to your consent and medical history forms without your permission:

- Researchers other than the HFEA licence holder
- Members of the Stem Cell Steering Committee
- Staff of the UK Stem Cell Bank

Your GP, with your permission, will be notified by the clinic that you have decided to contribute to the research

### **Will researchers discover new information about your health?**

It is important that you appreciate that any cell lines derived from cell nuclear replacement embryos will only carry genes from the cell that served as a nuclear donor, and not the oocyte that was donated.

### **Information about the outcome of the research project**

Information about the UK stem cell initiative, including the results of research using embryonic stem cells and stem cell lines will be published on the web page of the UK stem cell bank ([www.ukstemcellbank.org.uk](http://www.ukstemcellbank.org.uk)). Copies of this information will also be available at IVF clinics and the HFEA.

It will not be possible for any research results publicised in this way to be linked back to the original donors of the embryos.

### **How to give consent**

To allow research using surplus oocytes from your IVF treatment, you will both need to sign the consent form that accompanies this leaflet, having read the details of the specific research project in which the stem cell lines are created. The signed consent form will be retained by the clinic; however, if a stem cell line has been derived a copy will also be lodged with the Secretary to the Stem Cell Steering Committee; you will receive a copy of the completed form for your own records. It is important that you understand that your consent also covers research using banked stem cell lines created from your embryo(s).

Once the oocyte has been used in the project described on the consent form you will have no control over any future use of the embryonic cells, or of the stem cell lines created from your embryos. Your consent also covers any genetic information derived from the stem cell lines.

### **Withdrawing your consent**

You can decide not to take part in this research, and may withdraw from participating even after you have already agreed to, without it affecting your IVF treatment in any way. If you change your mind your consent can be withdrawn at any time until the oocytes have been used for the purpose of any project of research. An oocyte will be regarded as so used after it is under the control of the researchers at Roslin Institute and it is being cultured/grown for use in research. If you wish to withdraw your consent before the oocytes have left the IVF Clinic you should discuss with your clinician the options available to you. You do not have to give a reason for changing your mind.

**To withdraw your consent you must write to [address of IVF clinic]:**

**Name:**.....

**Address:**.....

.....

**Tel no.:**..... **Email:**.....

**Signature (member of IVF clinic staff):**.....

If you have any questions or concerns about this research, we will be happy to discuss them with you.

**THANK YOU FOR TAKING THE TIME TO READ THIS LEAFLET\***

Further information: [www.mrc.ac.uk](http://www.mrc.ac.uk), [www.hfea.gov.uk](http://www.hfea.gov.uk), [www.royalsoc.ac.uk](http://www.royalsoc.ac.uk), House of Lords report ([www.parliament.the-stationery-office.co.uk/pa/ld200102/ldselect/ldstem/83/8301.htm](http://www.parliament.the-stationery-office.co.uk/pa/ld200102/ldselect/ldstem/83/8301.htm)), Chief Medical Officer's Expert Advisory Group on Therapeutic Cloning (<http://www.doh.gov.uk/cegc/stemcellreport.htm>)

HFEA Application Wilmot. MRC Draft Donor Info Consent Form for CNR research v5.doc