

Report of how the HFEA made its decision to licence the creation of embryos by cell nuclear replacement

1. As required under the HF&E Act 1990 the HFEA's Licence Committees make all decisions about HFEA licences, where appropriate seeking external advice. Each Committee is made up of five HFEA Members who determine whether a licence should be granted, suspended, varied or revoked. If a licence is granted, centre specific conditions may be attached to that licence.
2. The HFEA received an application from Professor Alison Murdoch, Newcastle Fertility Centre at LIFE, in April 2004 to study the derivation of human embryonic stem cell lines using nuclear transfer and parthenogenetically activated oocytes.
3. This application was considered by the HFEA's Research Licence Committee at its meeting on 16 June 2004. The Research Licence Committee was made up of Authority members with a lay majority and a lay chair. The Committee also had access to additional legal, scientific and clinical expertise to support its decision making.
4. In considering whether to grant a licence, the Committee considered the following documentation:
 - Application form signed by the Person Responsible and the Nominal Licensee
 - *Curricula vitae* of the principal personnel involved in the research
 - Approval of a properly constituted local research Ethics Committee,
 - Report of the HFEA inspection of the research centre that occurred on 27 May 2004.
 - Opinions from 2 peer reviewers selected by the HFEA
 - The Centre's HFEA licensing history
 - Copies of relevant scientific publications authored by the scientists at the Centre
 - Patient Information and Consent Forms submitted by the Centre
5. The Committee also noted correspondence received by the HFEA from Members of the public and various interest groups regarding this application and issues raised in that correspondence.
6. Before granting a licence the Research Licence Committee had to be satisfied that the activities proposed in the licence application were necessary or desirable for one or more of the following purposes:
 - To promote advances in the treatment of infertility
 - To increase knowledge about the causes of congenital diseases

- To increase knowledge about the causes of miscarriage
- To enhance knowledge in the development of more effective contraception
- Detection of genetic or chromosomal abnormalities before implantation
- To increase knowledge about the development of embryos
- To increase knowledge about serious disease
- To enable any such knowledge to be applied in developing treatment for serious disease

[HF&E Act 1990 (Schedule 2 paragraph 3(2)) HF&E (Research Purposes) Regulations 2001 (paragraph 2(2))]

7. In addition, the Research Licence Committee had to be satisfied that the creation and or use of embryos is necessary for the purposes of the research.
8. The Committee also needed to satisfy themselves that the Patient Information and Consent Forms met the criteria set out in Schedule 3 to the HF&E Act 1990 and addressed the following points:

Before patients give consent to donation of their embryos for use in the research project, they must be given oral information supported by relevant written material which confirms:

- i. the specific research project, including any tests which may be performed as part of the licensed research project on embryos or cells derived from the embryos;
- ii. that any stem cells lines created may continue indefinitely and be used in many different research projects;
- iii. that the decision whether to donate will not affect their treatment in any way;
- iv. whether the embryos will be reversibly or irreversibly anonymised, and the implications of this;
- v. whether any information will be fed back to the donors;
- vi. that the donors can vary or withdraw the terms of their consent until the point at which the embryos are used in the project of research;
- vii. that once an embryo has been used in the project of research the donors have no control over any future use of the embryonic cells and any stem cell lines derived;

- viii. that stem cell lines derived in this project will be deposited in the UK Stem Cell Bank and the implications of this including the fact that they may be used for other projects;
 - ix. that stem cell lines must not be generated from donated embryos where the consent from the relevant donors, or one of them, places a constraint on future use;
 - x. that cell lines may be used for commercial purposes, but that the donor will not benefit financially from this;
 - xi. that any cell lines derived, or discoveries made using them, could be patented, but that the donor will not benefit financially from this;
 - xii. how the research is funded, including any benefit which will accrue to researchers and/ or their departments.
9. Finally, the Research Licence Committee had to be satisfied that the character, qualifications and experience of the person responsible are such as are required to supervise the activities, that they will discharge their duties under Section 17 of the HF&E Act 1990 and that the premises where the research is to be carried out are suitable for the activities.
10. The Centre is proposing to use eggs donated from women undergoing *in vitro* fertilisation and women having routine gynaecological procedures e.g. hysterectomy and / or oophorectomy. The adult nuclei to be used for transfer would be obtained from three sources:
- Stem cell lines – nuclei from cells from the Centre’s existing derived ES cell line (activity 1).
 - Women undergoing a gynaecological procedure – a skin biopsy will be taken from a woman undergoing a routine gynaecological operation (activity 2).
 - A patient with Type 1 diabetes – a skin biopsy will be taken from one patient who has Type 1 diabetes (activity 3).
- After nuclear transfer the egg will be activated using different chemical, mechanical, and/or electrical stimuli. To derive parthenotes, the Centre is proposing to artificially activate eggs using different chemical, mechanical, and/or electrical stimuli and then culture the resulting embryos until they reach the blastocyst stage.
11. The Centre had developed information for all the different types of donors and all donors will be asked to sign dedicated consent forms. These forms fulfil the requirements of the UK Stem Cell Bank Steering Committee and the patient information and consent forms have been approved by the Centre’s Research Ethics Committee.

12. The Committee decided on 16 June 2004 that it did not have sufficient information to grant a new licence and therefore agreed to adjourn and reconsider the application upon receipt of further expert opinion on the genetics of diabetes and whether the use of hES cell lines derived from embryos created by cell nuclear replacement using the nuclei taken from a cell of a patient with Type 1 diabetes would satisfy the criteria under the Act for granting a research licence (see above).
13. Even though the Centre's Patient Information and Consent Forms had been approved by the local ethics committee the Committee thought they needed to be amended in order to ensure the patients donating gametes and genetic material to this project were fully informed and therefore capable of giving their informed consent.
14. The Committee discussed the role of the Person Responsible and agreed, in keeping with HFEA preferred practice, that it was not appropriate for the same person to be in charge of both the treatment and research activities at any one centre. Therefore, to avoid any actual or perceived conflict of interest the Committee agreed that the Centre should have the opportunity to submit a revised application nominating a different individual as Person Responsible.
15. Following feedback from the Licence Committee held on 16 June 2004, Professor Murdoch asked that the application for a research licence to create embryos using nuclei of a skin cell taken from a patient with Type 1 diabetes (activity 3) be withdrawn. In addition Professor Murdoch informed the HFEA that she wished to apply to be the Person Responsible for the research licence but that another person from the Centre, Dr Jane Stewart would take on the duties of the Person Responsible for the Centre's treatment licence, subject to the approval of the Licence Committee. The Centre also submitted revised Patient Information and Consent Forms.
16. The Research Licence Committee reconvened on 3 August 2004 to discuss the revised application from Professor Murdoch.
17. The Committee noted that Professor Murdoch had withdrawn her application for a research licence to create embryos using nuclei of a skin cell taken from a patient with Type 1 diabetes (activity 3). Therefore, this aspect of the application was not discussed.
18. The Committee was satisfied that the activities of the project i.e. to derive human embryonic stem (hES) cell lines from human embryos created by the transfer of nuclei taken from (1) the Centre's existing stem cell line (activity 1) and (2) skin biopsies taken from women undergoing gynaecological procedures into enucleated oocytes (activity 2), are necessary or desirable for "*increasing knowledge about the development of*

embryos” and, in the case of the second activity also for “*enabling any such knowledge to be applied in developing treatments for serious disease*” [in accordance with the purposes set out in paragraph 3(2) of Schedule 2 to the HF&E Act 1990 (as amended by the HF&E (Research Purposes) Regulations 2001)].

19. The Committee also agreed that the creation of embryos by CNR was necessary for the purpose of research as this is the only way to enable the hES cell lines to be derived which will be antigenetically matched to the recipient. In addition the Committee noted that this research will enable the researchers to gain knowledge about cell reprogramming and non-controlled differentiation of human stem cells which, again could not be achieved by using another model. The Committee was satisfied that there was a demonstrable and exceptional need to create embryos through CNR as the aims of the research could not be achieved by any other means.
20. The Committee was satisfied with the revised Patient Information and Consent Forms.
21. The Committee was satisfied that Professor Alison Murdoch was of suitable character, qualifications and experience to discharge the duties of Person Responsible. The Committee was also that the premises where the research is to be carried out are suitable.
22. The Research Licence Committee agreed to grant a licence to study the derivation of human embryonic stem cell lines using nuclear transfer and parthenogenetically activated oocytes for a period of 12 months, with the standard licence conditions for projects involving the derivation of embryonic stem cell lines.