HUMAN FERTILISATION AND EMBRYOLOGY AUTHORITY

REGULATION OF RESEARCH ON HUMAN EMBRYOS

Role of the HFEA

1. The Human Fertilisation and Embryology Authority (HFEA) is a statutory body reporting to the Secretary of State for Health. Established by the Human Fertilisation and Embryology Act 1990, it has been operational since 1 August 1991. The HFEA's principal tasks are to license and monitor those clinics that carry out *in vitro* fertilisation (IVF), donor insemination (DI) and human embryo research. The HFEA also regulates the storage of gametes (sperm and eggs) and embryos.

2. The HFEA's other statutory functions are:

   - to produce a Code of Practice which gives guidelines to clinics about the proper conduct of licensed activities;
   - to keep a formal register of information about donors, treatments and children born from those treatments;
   - to publicise its role and provide relevant advice and information to patients, donors and clinics; and
   - to keep under review information about human embryos and any subsequent development of such embryos, and the provision of treatment services and activities governed by the 1990 Act and advise the Secretary of State, if asked, about those matters

Membership of the HFEA

3. The HFEA has 18 Members appointed by UK health ministers in accordance with Nolan guidelines. The Members determine HFEA policies and scrutinise treatment and research license applications. The 1990 Act requires that the Chairman, Deputy Chairman and at least half of the Membership are or have not been involved in human embryo research or providing infertility treatment.

The Legal Framework

Prohibitions under the 1990 Act on Human Embryo Research

4. Parliament also decided that the following should be prohibited by law:

   - keeping or using an embryo after the appearance of the primitive streak, or after 14 days whichever is the earlier
   - placing an embryo in a non human animal
   - placing non human gametes or embryos in a woman
   - replacing a nucleus of a cell of an embryo with a nucleus taken from the cell of another person, another embryo, or a subsequent development of an embryo

- altering the genetic structure of any cell while it forms part of an embryo

Human Embryo Research under the 1990 Act

5. In passing the 1990 Act Parliament decided that human embryo research may be permitted for the following purposes:

   - 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

6. Since the Act was passed there have been a number of important developments in this very fast moving area of science. The issues arising from these developments were looked at in 1998 jointly by the HFEA and the Human Genetics Advisory Commission (HGAC), which undertook a public consultation on human cloning. In September 1999, following this report, the Government set up an expert group, under the chairmanship of the Chief Medical Officer, Professor Sir Liam Donaldson, to undertake an assessment of the benefits of new areas of research using human embryos. In light of the expert group's report, the Government brought forward draft regulations extending the purposes for which research on human embryos could be lawfully undertaken. In January 2001, following large majorities in both Houses of Parliament by free votes, the Human Fertilisation and Embryology (Research Purposes) Regulations were passed which added three new purposes for which research on human embryos are permitted:

   - 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.

7. In response to the 2001 Research Purposes Regulations being passed, the ProLife Alliance applied for a judicial review of the legislation, seeking a declaration that an embryo created by cell nuclear replacement does not fall within the definition of embryo in the 1990 Act. On 15 November 2001, the High Court agreed with the ProLife argument.

8. The Government immediately introduced legislation to cover cell nuclear replacement and similar techniques. The legislation outlawed any attempts at reproductive cloning. The Human Reproductive Cloning Act was passed on 4 December 2001.

9. In an appeal against the earlier ruling, the Government was successful with the effect that embryos created by cell nuclear replacement are

within the scope of the 1990 Act. The Court of Appeal ruled, in January 2002, that an embryo is an embryo, whether created by fertilising an egg with sperm, or by cloning. Furthermore, in allowing the Government's appeal, Lord Phillips, the senior civil judge in England, said: *"I hold that an organism produced by CNR falls within the definitionin the Act."*

10. ProLife Alliance petitioned the House of Lords and was granted leave to appeal. The case went to the House of Lords and judgement was given against the ProLife Alliance in April 2003.

Licensing Research Applications

11. Approval by a properly constituted external Research Ethics Committee is a prerequisite for the HFEA to consider an application for a research licence. In addition, all applications must contain a range of information on the proposed project including its objectives, protocols to be used and why the use of embryos is necessary. In response to the new Regulations the HFEA made a number of enhancements to its licensing process. In particular:

    - Applicants will be required to justify why embryonic stem cells are to be used, rather than adult stem cells,
    - Applicants will be required to provide detailed information on the fate of the stem cells throughout the process, and
    - Applicants will be required to place a sample of all cell lines in the UK Stem Cell Bank

12. When an application for a research licence is received, it is sent out for peer review. The HFEA has a panel of reviewers who are recognised national and international experts in the field of reproductive biology and infertility. Before considering a research application the HFEA obtains at least two peer review reports on the project's merits covering:

    - Whether the research fulfils at least one of the categories for which embryo research is permitted
    - The importance of the research in the field
    - Whether research has been done before
    - Whether the research requires human embryos to fulfil its aims and objectives
    - Whether the research requires the numbers and types of embryos outlined in the application
    - The suitability of the methods
    - The length of the study
    - The applicant's qualifications
    - Meets the requirements of the HFEA Code of Practice including ethical approval and patient information

    All peer reviewers must declare any conflict of interest in an application that they have been asked to review. Furthermore peer reviewers have an obligation to protect the ideas and plans of the applicants. The

identity of the reviewers of individual research applications is confidential to the HFEA. This confidentiality allows the free exchange of views amongst reviewers and is in line with the policies of the UK funding bodies and scientific and medical journals. A list of peer reviewers, current as of 31 August 2003, is published in the HFEA Annual Report 2002/3 and an updated list will be published on the HFEA website and the next annual report.

13. In response to the new regulations the HFEA has made number of enhancements to existing systems:

- Applicants will be required to justify why embryonic stem cells are to be used, rather than adult stem cells or animal stem cells.
- Applicants will be required to provide detailed information on the fate of the stem cells throughout the project, keeping them within the licensed project
- Six monthly progress reports to be made
- Additional guidance provided to peer reviewers
- Additional peer reviewers with expertise in the field have been recruited

14. The HFEA inspects centres prior to the granting of a research licence and all research centres are inspected on an annual basis. Furthermore, the HFEA requires all research centres to submit progress reports on licensed research projects.

15. The Human Fertilisation and Embryology Act requires that prior to donating gametes or embryos to research patients must give their effective consent to the use of their gametes or any embryos created using their embryos. Therefore 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, it is not permitted for donation to affect treatment in any way. Centres must ensure that a designated individual who is not directly involved in the patient's treatment is available to discuss the research and the possibility of donating material with patients. In order to ensure that the implications of donation are understood, including the immortal nature of stem cell lines, the HFEA also requires patients to be informed that:

i. any stem cells lines created may continue indefinitely and be used in many different research projects;

ii. 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;

iii. that cell lines may be used for commercial purposes, but that the donor will not benefit financially from this; and

iv. that any cell lines derived, or discoveries made using them, could be patented, but that the donor will not benefit financially from this.

16. It is a condition of licences that a sample of all embryonic stem cell lines be placed in the UK Stem Cell Bank. The Bank will ensure that there is a single national independent institute responsible for managing and supplying ethically approved, quality controlled stem cell 'lines' for research.

18. The UK Stem Cell Bank operates under the control of a high level Steering Committee with medical and scientific members sitting along side ethicists and consumer representatives. The Chair of the Authority and a member of the Executive serve as observers on this Committee. This Committee regulates the use of embryonic stem cell lines and has developed codes of practice for the stem cell bank, and for the use of stem cell lines. The existence of the bank will also ensure that the minimum numbers of embryos are used in research.

19. As of May 2004, the title and lay summary of all new applications for a research licence will be published on the HFEA's website (www.hfea.gov.uk). Once a licence has been granted the information on the website will be updated to include the title and the lay summary of the licensed research project.

20. The HFEA had previously granted three licences under the 1990 Act for research that aimed to produce embryonic stem cells. In 2002 the Authority issued the first two licences for stem cell research made under the 2001 Research Purposes Regulations.

Research Licence Committee

21. The HFEA has set up a dedicated Research Licence Committee that will meet on a bi-monthly basis.

22. In considering whether to grant or renew a licence, the Committee will have access to 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 inspection of the research centre
- Comments from 2 peer reviewers
- The centre's licensing history
- Copies of relevant publications
- Patient Information and Consent Forms

23. Before considering whether it is appropriate to grant or renew a licence the Research Licence Committee has to be satisfied that activities proposed in the licence application are necessary or desirable for one or

more of the purposes set out in Schedule 2 to the HF&E Act 1990 (as amended by the Research Purposes Regulations 2001). In addition, the Research Licence Committee has to be satisfied that any proposed use of embryos is necessary for the purposes of the research.

25. In addition the Research Licence Committee has to be satisfied that the character, qualifications and experience of the Person Responsible are such as are required to supervise the activities that s/he 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.

26. If the Licence Committee decides to grant or renew a licence, the Licence Committee will consider whether any conditions should be specified in the licence.