

HUMAN FERTILISATION AND EMBRYOLOGY AUTHORITY
(“The Authority”)

GUIDE TO LICENSING

The legislative framework

1. One of the Authority’s most important functions is the licensing of UK centres that provide assisted reproduction treatment and storage of gametes (sperm and eggs) and embryos; and of UK research projects involving embryos. The Authority undertakes this licensing process in accordance with the legislative framework established by the Human Fertilisation and Embryology Act 1990 (as amended) (“the Act”).

2. The Act prohibits certain activities absolutely. Other specified activities can only be carried out with a licence issued by the Authority (or in some cases, under a contractual agreement between the person holding the licence from the Authority and a third party-“a third party agreement”).

3. The activities which are absolutely prohibited by the Act include:-
 - a) placing non permitted gametes or embryos in a woman (including human admixed embryos, non human embryos or gametes)(sections 3(2) and 4A(1);
 - b) keeping or using a human embryo or human admixed embryo after the appearance of the primitive streak (sections 3(3)(a) and 4A(3));
 - c) placing a human embryo or human admixed embryo in an animal (sections 3(3)(b) and 4A(4); and
 - d) using female germ cells taken or derived from an embryo or fetus, or using embryos created by using such cells, for the purposes of providing fertility services for a woman (section 3A);

4. Gametes which have not been produced by or extracted from ovaries or testes, or which have had alterations made to their nuclear or mitochondrial DNA are not classed as permitted gametes.

5. Embryos which have not been created by the fertilisation of permitted gametes or which have had alterations made to their nuclear or mitochondrial DNA or to which cells have been added (other than by division of the embryo's own cells) are not classified as permitted embryos.
6. The prohibition on placing non permitted embryos in a woman means that "Human cloning" is a prohibited activity.
7. The activities which can only be carried out with a licence issued by the Authority (or a third party agreement) include:-
 - a) creating human embryos (section 3(1));
 - b) using or keeping human embryos (section 3(1A));
 - c) storing gametes (section 4(1)(a));
 - d) using sperm (other than partner donated sperm which has not been processed or stored) to provide treatment services (section 4(1)(b));
 - e) using the eggs of a woman which have been processed or stored, or the eggs of any other woman, to provide treatment services (section 4(1)(b));
 - f) procuring, testing, processing or distributing gametes intended for human application (section 4(1A));
 - g) creating, keeping or using human admixed embryos(section 4A(2));
and
 - h) mixing human gametes with animal gametes (section 4A (2)).
8. A person who carries out one of the prohibited activities listed above, or who carries out an activity which can only be carried out with a licence issued by the Authority or a third party agreement, without holding such a licence or being party to a third party agreement, commits a criminal offence. If convicted, the penalty for such an offence may be imprisonment for up to ten years, a fine, or both (section 41(1) and (2)).

9. Under section 11 and Schedule 2 of the Act, the Authority can only issue four types of licence:-
 - a. licences for treatment;
 - b. licences for non-medical fertility services (e.g. procuring and distributing sperm);
 - c. licences for storage of gametes, embryos and human admixed embryos; and
 - d. licences authorising activities for the purposes of a project of research
10. A licence can not authorise both treatment and research activities. A separate licence is required for each activity.
11. A licence can not apply to premises in different places; a separate licence is required for each premises at which licensed activities are to be carried out.
12. Every licence issued by the Authority is automatically subject to a number of standard licence conditions. These relate to issues such as record keeping; traceability of gametes and embryos; obtaining of relevant consents in writing; provision of information and counseling to patients and donors; time limits for storage of gametes and embryos; the provision of information and documentation to the Authority; the Authority's right of access to, and inspection of, centres.; and the requirement to use suitable practices in the carrying out of licensed activities.
13. In relation to treatment licences, a key provision requires centres to take account of the welfare of any child to be born as a result of the treatment to be provided (including the need of that child for supportive parenting) and of any other child who may be affected by that birth (section 13(5)). The Authority has issued guidance defining the concept of "supportive parenting" and about how such risk assessments should be conducted.

14. The Act requires the Authority to issue a Code of Practice giving guidance to licensed centres about the conduct of licensed activities. This Code of Practice is updated periodically, and allows new guidance to be produced in relation to new technologies and methods of carrying out licensed activities. The Code of Practice must be approved by the Secretary of State for Health. The 8th Code of Practice will be in force from 1st October 2009 and is available on the Authority's website (www.hfea.gov.uk).
15. A standard condition of all licences issued by the Authority is that centres must not carry out new methods of conducting a licensed activity unless they have first notified the Authority and have been given approval by the Authority to carry out those activities by these new methods (Licence Condition T6).
16. Central to the licensing scheme is the concept of the "Person Responsible." Every application for a licence must nominate a named individual to act as the Person Responsible for that licensed centre (section 16(2)). The Person Responsible does not have to be the holder of the Licence (for example the Licence Holder may be a corporate body such as a Health Trust). The Person Responsible has a number of specific statutory duties under section 17 of the Act. These include:
 - a) ensuring that the conditions of the licence are complied with;
 - b) notifying the Authority and providing it with a report about any serious adverse incidents or serious adverse reactions;
 - c) ensuring that staff at the licensed centre are of good character, and are suitably trained and qualified;
 - d) ensuring that the centre's premises are suitable;
 - e) ensuring that proper equipment and suitable practices are used in the conduct of licensed activities; and
 - f) ensuring proper arrangements are made for the keeping and disposal of gametes and embryos.
17. The Authority requires all individuals wishing to act as Person Responsible to have satisfactorily completed its PR Assessment Programme; to have relevant qualifications; and to have at least two years practical experience

in the relevant field (Guidance note 1 of the 8th edition of the HFEA Code of Practice).

18. From October 2009, the Authority's general functions will include a duty to:

“(ca) maintain a statement of the general principles which it considers should be followed-

(i) in the carrying-on of activities governed by this Act, and

(ii) in the carrying-out of its functions in relation to such activities,

(cb) promote, in relation to activities governed by this Act, compliance with-

(i) requirements imposed by or under this Act, and

(ii) the code of practice under section 25 of this Act...”

19. The 8th edition of the Code of Practice sets out 13 regulatory principles, and the Authority expects Persons Responsible to ensure that their licensed centres demonstrates adherence to these principles.

The Authority's licensing procedures

20. The Authority's licensing process is governed by the provisions of sections 16 to 21 of that Act.

21. The Authority has issued a Direction (D.0008) which sets out the information and documents which applicants for licences are required to provide. An application must be made using the appropriate form, and submitting the additional documents referred to in the Direction. The appropriate fee must also be paid. Failure to provide all required information and documents will result in the consideration of an application being delayed; under section 16(4), the Authority may not consider an application until the applicant has provided all information requested by the Authority...

22. Licences for treatment, non medical fertility services, and storage may be granted for a period of up to 5 years (schedule 2, paragraphs 1(5), 1A (3), and 2(3)). Licences for research may be granted for a period of up to 3 years (schedule 2, paragraph 3(8)). The Authority has issued guidance on the criteria it will take into account when deciding what period a licence should be issued for.
23. From October 2009, routine decisions on licensing (other than research licence applications) will be taken by a panel of 3 members of the Authority's staff ("the Executive Licensing Panel"). Before taking a decision, the Executive Licensing Panel can seek legal advice. Complex matters, or applications which raise novel or controversial issues will be referred to a Licence Committee composed of members of the Authority, for consideration. The Licence Committee sits with a legal adviser, and may sit with clinical or specialist advisers if the Chair considers it appropriate to do so.
24. The Executive Licence Panel and the Licence Committees are established under the Authority's Standing Orders. The Standing Orders set out the scope of delegation to the Panel and the Committee and set out provisions relating to their membership.
25. More detailed procedures relating to the Executive Licensing Panel and the Licence Committee are set out in additional protocols.
26. If the Executive Licensing Panel is minded to refuse an application for a new or renewal licence, or considers that an existing licence should be varied or revoked, it will issue a written notice of proposal. The applicant or licence holder will then have the opportunity, under section 19 of the Act, to make written or oral representations to the Licence Committee.
27. When considering representations under Section 19 of the Act, the Licence Committee will not use the Protocol. Instead it will act in accordance with Regulations made by the Authority. These Regulations are made under section 19(6) of the Act and specifically relate to **consideration of representations** against a proposal to refuse a licence application, or to vary, suspend and revoke an existing licence.

28. Where an applicant or licence holder is dissatisfied with a decision made by the Executive Licensing Panel or by a Licence Committee, he can request that the decision is reconsidered by the Appeal Committee.
29. The members of the Appeal Committee are not members or staff of the Authority and the procedures of the Committee will be governed by a set of Appeal Committee Regulations made by the Secretary of State under sections 20A and 20B of the Act. The Appeal Committee may sit with such clinical or specialist adviser as the Chair considers appropriate.
30. The applicant or licence holder may also appeal to the High Court (Court of Session in Scotland) on a point of law.
31. The Chair of the Licence Committee will be required to prepare a regular Licence Committee Report to the Authority. The report will be published on the Authority's website and will identify relevant trends, learning and feedback points to the fertility sector.
32. The aim is to process new licence applications within 4 months of receipt. In the period 1st April 2007 to 31st March 2008, the HFEA processed 43 new licence applications and 49 licence renewals

Research Licences

33. Applications for new or initial licences for research will be considered by the Authority's Research Licence Committee. The Research Licence Committee will act in accordance with the Protocol and Regulations mentioned above, and the Chair of the Committee will also produce an annual report to the Authority.
34. In 2008, the Research Licence Committee considered a total of 7 initial applications for projects of research. The projects of research which are granted are published on the HFEA website and also published as an annex to the HFEA's Annual Report and Accounts.
35. Licences are usually granted for three years. However, for novel projects, licences may be granted for 12 months so that the Licence Committee is able to monitor the progress of the research. The Authority has issued guidance on the criteria by which it will determine the length of any licence issued.

36. Under the Act, no research can be carried out on an embryo after the appearance of the primitive streak, which is deemed to have appeared no later than 14 days after the embryo was created (section 3(3) and (4)).
37. The use of embryos is governed by strict legal criteria-the “necessary and desirable” tests, which are explained below.
38. Before women donate eggs for research, either altruistically or as part of an egg sharing scheme (by which they receive cheaper IVF treatment in return for donation), they must be provided with proper information and the opportunity to receive counseling (schedule 3(3)).
39. Where eggs are donated as part of an egg sharing scheme, the HFEA guidance requires that the eggs should be shared by someone independent of the research.
40. Direct payment for donation of eggs for research is prohibited, but women can be compensated for expenses and loss of earnings (Direction 0001)
41. No eggs can be used in research unless the donor has provided a specific consent in writing (schedule 3 (1) and 2(c)).

Types of Research licence granted

42. Research licensed by the HFEA fall into 8 primary categories:

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. Some projects aim 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 to devise diagnostic methods that will allow the transfer of singly healthy embryos with a high chance of giving rise to a pregnancy thus minimizing the risk of multiple births.

2. Pre genetic diagnosis(“PGD”)

For PGD to be feasible, techniques must be available which allow for the diagnosis of a particular gene defect from just one or two cells. Some research projects aim to extend existing technologies to allow PGD to be applied to a greater range of diseases and to develop new technology to

improve the process of biopsy and embryo selection, with the ultimate aim of increasing the clinical success of the treatment.

3. Egg and Embryo Freezing

Some research projects aim to identify new methods of freezing eggs and embryos (such as vitrification) to reduce the risk of damage sustained during the freeze/thaw process and thereby to improve the national success rates for obtaining a baby using frozen eggs or embryos in the treatment cycle.

4. Egg Activation

Some research projects aim to give new insight into the very early events occurring in fertilization, which may lead to the development of new diagnostic and treatment regimes.

5. In Vitro Maturation of Eggs

This research involves comparative studies of IVM and IVF to determine whether embryos created from in vitro matured eggs are healthy and develop normally.

6. Mitochondrial Disease

These research projects are aimed at establishing techniques for identifying defects in mitochondrial DNA in human embryos created by IVF and techniques to prevent the transmission of mitochondrial disease.

7. Human Embryonic Stem Cell Lines

These research projects involve the derivation of stem cell lines.

8. Cell Nuclear Replacement

These research projects are aimed at understanding the science underlying this technology.

43. Before submitting an application for a research licence, the majority of researchers contact the Authority to discuss their proposed research. Existing licence holders liaise directly with the Authority's compliance department on renewals and evaluations.

44. The Authority expects that researchers should have sought and been granted research ethics approval by a properly constituted ethics committee before submitting an application for a research licence to the Authority.
45. The administration fee is currently £500 for most projects. Projects involving the derivation of human embryonic stem cells or cell nuclear replacement incur an administration fee of £750 which reflects the increased complexity and rigour required for the licensing of such projects.
46. The application must nominate a “Person Responsible” who is required to provide Curriculum Vitae of all staff engaged directly in the project; all relevant clinical and laboratory protocols; patient information relating to the proposed project; consent forms regarding the use of gametes and embryos and the most recent three scientific publications.
47. The Person Responsible must also provide a “lay summary” of the proposed project of research and detailed information relating to the expected use of any gametes or embryos in the project. The lay summary has to include the aims of the project; the activities involved; and how those activities will address the stated aims of the project. The application is also required to address how the project fits in to the current state of knowledge about the subject area.
48. Lastly, the application must set out the methodology and experimental design of the project and how the results are to be analysed.

Peer Review

49. Upon receipt of a complete application, the Authority commissions peer reviews of that application. The Authority normally commissions about two or three peer reviews of each application.
50. The Authority uses a panel of national and international experts in the field of reproductive technologies and infertility to conduct the peer reviews. The names of these Peer Reviewers are published as an appendix to the Authority’s Annual Report and Accounts.
51. The purpose of the peer review is to determine whether the proposed project of research:-
 - a) fulfills the statutory requirements of the Act;

- b) requires human embryos to fulfill its aims and objectives;
- c) requires the numbers and types of embryos described in the application;
- d) meets the requirements of the Authority's Code of Practice;
- e) has been done before; and
- f) is an important contribution to other research in the field.

The necessary or desirable test

52. In accordance with paragraph 3A of Schedule 2 to the Act, the Research Licence Committee must be satisfied that the activity to be authorised is **necessary or desirable** for one of the purposes specified in Schedule 2 to the Act, or in Regulations.

53. These purposes are:-

- a) increasing knowledge about serious disease or other serious medical conditions;
- b) developing treatments for serious disease or other serious medical conditions;
- c) increasing knowledge about the causes of any congenital disease or congenital medical condition;
- d) promoting advances in the treatment of infertility;
- e) increasing knowledge about causes of miscarriage;
- f) developing more effective techniques of contraception;
- g) developing methods of detecting the presence of gene, chromosome or mitochondrion abnormalities in embryos before implantation;
- h) increasing knowledge about development of embryos;
- i) providing knowledge that, in the view of the HFEA, may be capable of being applied to any of the purposes listed above.

Use of embryos in research

54. In addition, under paragraph 3(5) of Schedule 2 to the Act, the Research Licence Committee can not grant a licence for a project of research using embryos or human admixed embryos, unless it is satisfied that the use of embryos or human admixed embryos is **necessary**.

55. In accordance with Directions issued by the HFEA, centres undertaking a project of research licensed by the HFEA must make a provisional report to the HFEA within three months of the end of the project. The provisional report must set out the results and conclusions of the research project. Centres must also provide the HFEA with a final referenced report as soon as practicable after the conclusion of the research project. (Directions D0002).

56. The Authority publishes periodic thematic reports, entitled "Human Embryo Research in the UK", on its website. The next report is anticipated to be published in 2010.

Control sheet

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