HFEA Research Licence Committee Meeting

15 July 2009

21 Bloomsbury Street London WC1B 3HF

Minutes – Item 9

Newcastle Fertility Centre at Life (0017) – application for variation of the current licence to include PGD for all mutations of the mitochondrial genome where a positive correlation between mutation load and disease severity has been established

Members of the Committee:

Emily Jackson (lay) – Chair
Richard Harries (lay)
David Archard (lay)
Lesley Regan (clinician)
Hossam Abdalla (clinician)

Committee Secretary:
Kristen Veblen

Legal Adviser:
Sarah Ellson, Field Fisher Waterhouse

Declarations of Interest: members of the Committee declared that they had no conflicts of interest in relation to this item.

The following papers were considered by the Committee:

- papers for licence committee (78 pages)
- no tabled papers.

The Committee also had before it:

- HFEA Protocol for the Conduct of Licence Committee Meetings and Hearings
- 7th edition of the HFEA Code of Practice
- Human Fertilisation and Embryology Act 1990 (as amended)
- HFEA (Licence Committees and Appeals) Regulations 1991 (SI 1991/1889)
- Decision Trees for Granting and Renewing Licences and Considering Requests to Vary a Licence; and
- Guidance for members of Authority and Committees on the handling of conflicts of interest approved by the Authority on 21 January 2009.

1. The Committee considered the papers, which included an executive summary, application, two peer reviews, and various supporting documents including patient information sheets and consent forms.
2. The Committee noted that this application was to vary the licence to include preimplantation genetic diagnosis (PGD) for all mutations of the mitochondrial genome where a positive correlation between mutation load and disease severity has been established. The Committee observed that these are conditions which had not been previously licensed. Further, the Committee noted that this application had not made for named patients.
3. The Legal Adviser reminded the Committee that the reason this application had been presented for consideration was to fulfil the requirements of Standard Licence Conditions A.13.8:

   With respect to any PGD programme the following conditions apply: (b) that, where the Centre wishes to carry out preimplantation testing which is not expressly authorised by the Centre's licence, the Centre must submit an application in the form specified in Directions for that purpose to the Authority. The preimplantation testing concerned must not be commenced until the Centre has received written confirmation from the Authority that the testing may be carried out under the Centre's licence.
4. Additionally, the Legal Adviser reminded the Committee that in accordance with Schedule 2, paragraph 1(3) of the HFE Act 1990 (as amended), a treatment licence could not authorise any activity unless it appeared to the Committee to be necessary or desirable for the purpose of providing treatment services.
5. The Committee recognised that faults or mutations in mitochondrial DNA disrupt the biological machinery and impair the energy conversion process, limiting the amount of energy available to the cell and that chronic neurological disease manifestations were directly related to the proportion of mutated mitochondrial DNA present, with higher levels leading to more severe disease. These maternally inherited mutations can come from asymptomatic mothers transmitting higher levels of mutation to children, which in some cases led to death or severe disability in infancy or early childhood.
6. It was also noted by the Committee that there was no cure for mitochondrial disease and that the most effective way to combat these diseases was to prevent transmission.
7. The Committee noted that there had been a query raised by one of the Peer Reviewers about who would be providing genetic counselling, however it was stated elsewhere in the papers that both Peer Reviewers support approval of PGD for this condition. Further the Committee noted that one of the Peer Reviewers was mistaken about the existing licence position as the Centre was already licensed to perform PGD.

8. The Committee also satisfied itself that the Centre has sufficient experienced embryo biopsy staff who had been part of the Centre's research group and who had been specifically working on mitochondrial disease.
9. The Committee noted that the Centre was applying to perform PGD for rare mutations of Mitochondrial DNA as well as four OMIM listed conditions.

The Committee's Decision

10. The Committee agreed that for the reasons discussed above and on the basis of the information provided, it was satisfied of the severity of the named diseases as required by 7th Code of Practice section G.12.3.2.
11. The Committee also considered the guidance given in the 7th Code of Practice at G.12.3.3 (c) and (d) and agreed that there was a high degree of suffering associated with these conditions and that currently there was no effective cure, nor was there any evidence an effective cure would be available in the foreseeable future.
12. The Committee noted the explanation offered by the Centre that the OMIM cataloguing system is not sufficiently specific for mitochondrial mutations to allow individual classification, and recognised that there are conditions other than the four named in the application that would be serious enough to warrant the use of PGD.
13. The Committee discussed the ramifications of granting authorisation for PGD for "all mutations of the mitochondrial genome where a positive correlation between mutation load and disease severity has been established" and concluded that they did not have enough information before them about the appropriateness and legality of varying a licence to allow PGD for a range of unnamed conditions.
14. Therefore, the Committee decided to vary the Licence to allow PGD for the following conditions, which had been named in the application:
    - NARP: Neurogenic muscle weakness, ataxia, retinitis pigmentosa (OMIM: 516060)
    - MELAS: Mitochondiral encephalomyopathy, lactic acidosis and stroke-like episodes (OMIM: 590050
    - Leigh's: Subacute necrotising encephalopathy of childhood (OMIM: 516000; 516002; 516005; 516006)
    - MERRF: Myoclonic epilepsy and ragged red fibres
15. Recognising that there are serious conditions associated with mitochondrial mutations other than the four named above, the Committee also decided to seek further information and advice:

- from the Peer Reviewers regarding unclassified mitochondrial mutations, their seriousness and whether or not it is possible to name or identify them and
- further legal and/or policy advice regarding the legality and appropriateness of allowing PGD for non-specific conditions defined only as "mutations of the mitochondrial genome where a positive correlation between mutation load and disease severity has been established".

Signed..... Date 22.7.09.
Emily Jackson (Chair)