HFEA Licence Committee Meeting

31 May 2012

Finsbury Tower, 103-105 Bunhill Row, London, EC1Y 8HF

Minutes – Item 2

Centre 0017 (Newcastle Fertility Centre at Life) – PGD for Kearns Sayre Syndrome (KSS)/ Pearsons Marrow-Pancreas Syndrome (PMPS) (OMIM #530000 &557000)

Members of the Committee: David Archard (lay) Chair Mair Crouch (lay) Rebekah Dundas (lay) – VC Expert Adviser – Dagan Wells	Committee Secretary: Lauren Crawford Legal Adviser: Juliet Oliver, Field Fisher Waterhouse

Declarations of Interest: members and the expert adviser 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 Enclosed for consideration:

- Executive Summary
- LC minutes (09/03/2012)
- Additional information from centre in response to Committee comments (20/03/2012)
- Redacted additional comment provided by the peer reviewer (17/04/2012)
- Centre Response to peer reviewers additional comments (15/05/2012)

Papers Enclosed for reference:

- Previous set of papers
    - Executive Summary
    - PGD Application Form
    - Redacted Peer Review
    - Genetic Alliance Opinion

The Committee also had before it

- HFEA Protocol for the Conduct of Licence Committee Meetings and Hearings

- 8th edition of the HFEA Code of Practice
- Human Fertilisation and Embryology Act 1990 (as amended)
- Decision trees for granting and renewing licences and considering requests to vary a licence (including the PGD decision tree); and
- Guidance for members of Authority and Committees on the handling of conflicts of interest approved by the Authority on 21 January 2009.
- Guidance on periods for which new or renewed licences should be granted
- Standing Orders and Instrument of Delegation
- Indicative Sanctions Guidance
- HFEA Directions 0000 – 0012
- Guide to Licensing
- Compliance and Enforcement Policy
- Policy on Publication of Authority and Committee Papers
- HFEA Pre-Implantation Diagnostic Testing ("PGD") Explanatory Note For Licence Committee

Background

1. Centre 0017 is licensed to provide PGD and had had previously submitted an application for embryo testing for Kearns Sayre Syndrome (KSS)/ Pearsons Marrow-Pancreas Syndrome (PMPS) (OMIM #530000 & 557000).

2. An application from centre 0017 was considered for this condition on the 1st March 2012 and minutes published (09/03/2012). The application was adjourned as the Committee requested additional information to support the application.

3. The Committee's reasons for the adjournment of the item were:
    - No clear recommendation from the Peer Reviewer and concerns expressed by the Peer Reviewer.
    - No clear statement by the Centre or Peer Reviewer on degree of penetrance and any additional factors that may affect this in specific families.
    - Insufficient information on the seriousness of the condition and the particular risk of an embryo having an abnormality.
    - Insufficient assurances that other centres within the UK that would be licensed to carry out PGD for this condition would be qualified and competent to do so.

4. The Committee noted that the Centre and the Peer Reviewer have provided additional comments following the publication of the minutes and addressing the request from the Committee

5. The Committee also had before them an expert geneticist to advise on clinical and scientific aspects of the application.

Decision

6. The Committee had regard to its Decision Tree. The Committee noted that the Centre is licensed to carry out PGD. The Committee was also satisfied that the Centre has much experience of carrying out PGD and that generic patient information about its PGD programme and associated consent forms had previously been received by the HFEA.

7. The Committee noted that the Centre's proposed purpose of testing the embryos was as set out in paragraph 1ZA(1)(b) of schedule 2 of the Act, ie. 'where there is a particular risk that the embryo may have any gene, chromosome or mitochondrion abnormality, establishing whether it has that abnormality or any other gene, chromosome or mitochondrion abnormality'.

8. The Committee noted that mitochondria act as tiny batteries within every cell, providing energy vital for the cell's normal function. These mitochondria have their own DNA (mtDNA) which holds a small amount of key information necessary to make important parts of the mitochondrion. Unfortunately mtDNA is error prone and one such error results in mtDNA having a large portion missing (a large-scale single deletion). If enough mtDNA are affected in this way then disease will occur.

9. The Committee noted that Kearns Sayre Syndrome (KSS)/ Pearson's Marrow-Pancreas (PMPS) (OMIM #530000 & 557000) are rare disorders caused by the same molecular defect; a large-scale single deletion in mitochondrial DNA (mtDNA) .The risk of inheriting the disorders are estimated at 1 in 24. The Committee noted Peer Reviewer states that 'If the embryo contains the mtDNA rearrangement at a high level then there is a high risk of the embryo inheriting the abnormality'.

10. The Committee noted that the severity of the disease can vary from a fatal disorder affecting new born babies causing bone marrow failure and pancreatic failure (PMPS), through severe childhood-onset disease with heart failure, irregular heartbeat, profound muscle weakness, diabetes, adrenal failure and restricted eye movements with drooping eyelids (KSS), to an adult-onset milder condition associated with restricted eye movements, drooping eyelids and some muscle weakness (Chronic Progressive External Ophthalmoplegia +).

11. The Committee noted that unlike many errors in mtDNA, large-scale deletions are often not inherited down the female line of the family, but when this does happen the consequences are grave, resulting in either KSS or PMPS. There is no cure for mitochondrial disease and treatment is supportive: This may include hormone replacement – insulin, cortisol, thyroid; anticonvulsants; cardio-protective therapy – beta blockers and ACE inhibitors.

12. The Committee noted that PMPS is usually fatal in early infancy and those few that do survive go on to develop KSS a debilitating, progressive, life-limiting multi-system disorder. KSS can arise independently of PMPS. KSS onset occurs before 20 years, with first symptoms often before 10 years.

13. The Committee noted from the information provided by the Expert Adviser that the severity of this disorder is variable and in the most serious cases can result in early death. The disorder is extremely unpredictable even within families.

14. The Expert Adviser addressed the concerns raised in Paragraph 3, as follows.
    - The disease was in his opinion definitely serious enough to warrant PGD
    - The disease is unpredictable: If a person inherits a large proportion of affected mitochondria then penetrance will be 100%. If fewer, the penetrance will be incomplete or they will experience milder effects. In his opinion the degree of Penetrance would have to be measured on a case by case basis by the centres themselves, looking at the family history of patients, and also taking into account the variability of expression within families
    - He confirmed that the disorder in the most severe cases can result in death..The risk is at least 1 in 24.
    - In his opinion, to perform this type of PGD, specialist knowledge and equipment is necessary. Most centres with this specialist equipment should be competent and able to carry out this type of testing, and could be expected to seek the opinion of an expert in mitochondria.

15. The Committee noted that the application is supported by the Peer Reviewer as well as by Genetic Alliance UK.

16. The Committee had regard to its explanatory note, in particular paragraphs 5.4 '*Where a condition has a range of penetrance (e.g. 40-60%), the*

Licence Committee will base its decision on the highest penetrance figure' and 5.5 '*Where a condition has variable symptoms, the Licence Committee will base its determination of how serious the disability, illness or condition is, on the worst possible symptoms'*, and noted that on the basis of the information presented, given the conditions' worst symptoms and the range of penetrance, it was satisfied that there is a significant risk that a person with the abnormality will have or develop a serious physical or mental disability, a serious illness or any other serious medical condition. Accordingly, it was appropriate to grant the application under paragraph 1ZA(1)(b) of Schedule 2 to the Act.

17. The Committee noted that while they may grant approval, the centre providing PGD for the condition must also ensure that each individual case treated fulfills the severity criteria of Schedule 2 paragraph 1ZA of the HFE Act 1990 (as amended).

18. The Committee agreed to authorise the testing of embryos for Kearns Sayre Syndrome (KSS)/ Pearsons Marrow-Pancreas (PMPS) (OMIM #530000 & 557000). The Committee confirmed that these conditions will be added to the published list of conditions for which PGD may be carried out.

Signed: Date: 18/06/2012

David Archard (Chair)