HFEA Licence Committee Meeting

1 November 2012

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

Minutes – Item 1

Centre 0044 (Centre for Reproductive and Genetic Health) – PGD for Donohue Syndrome (OMIM #246200)

Members of the Committee: David Archard (lay) Chair Sue Price (professional) Debbie Barber (professional) Jane Dibblin (lay) Anna Carragher (lay) Mair Crouch (lay) – VC Rebekah Dundas (lay) – VC	Committee Secretary: Lauren Crawford Legal Adviser: Graham Miles, Morgan Cole

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

- Cover sheet
- 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

Discussion

1. 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 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.

2. 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'.

3. The Committee noted Donohue Syndrome (OMIM #246200) is a disorder that is inherited in an autosomal recessive manner. Therefore there is a 1 in 4 chance that an embryo will have the condition if both parents are carriers.

4. The Committee noted that an affected individual will have inherited two abnormal copies of the gene which codes for the insulin receptor, resulting in an extremely rare form of diabetes mellitus. Donohue syndrome affects both males and females. The symptoms of the disorder are uncontrolled diabetes, abnormal growth of many organs including the heart, stunted growth (including during gestation), enlarged genitals, and facial features characteristic of the disorder including prominent and low-set ears, flared nostrils and thick lips.

5. The Committee noted that Donohue syndrome is a genetic disorder of the insulin receptor and presents soon after birth with severe problems in maintaining blood sugar levels. Effective insulin production and action is vital for blood sugar control and if the insulin receptor does not function as it should, glucose levels become very difficult to manage. These children have very high levels of insulin and these high levels can activate other receptors which look like insulin receptors but have other actions. These other receptors include insulin-like growth factor 1 receptors. Activation of these receptors leads to abnormal growth of many organs including the heart. Possible therapies include continuous nasogastric feeding and recombinant human IGF-1 therapy but there has been little progress in developing an effective

treatment regimen and most affected children die before the age of 2 years after a very turbulent period of care.

6. The Committee noted that there is very little effective treatment for those affected with Donohue syndrome. Managing the condition with insulin is largely ineffective (as it has to signal through the affected insulin receptor), and treatment with high dose insulin can result in cardiomyopathy, as well as nephrocalcinosis and proteinuria. Possible therapies include continuous nasogastric feeding and recombinant human IGF-1 therapy. However, as most therapies are largely ineffective, the disease is usually managed with strict dietary control.

7. The Committee considered the condition is serious because the condition is fully penetrant in both sexes, the majority of babies die in the first few months, there are severe dietary control issues and there is little or no effective treatment.

8. The Committee noted that the application is supported by the Peer Reviewer and the Genetic Alliance UK.

9. The Committee had regard to its explanatory note, in particular paragraph 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, it was also 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.

10. The Committee agreed to authorise the testing of embryos for Donohue Syndrome (OMIM #246200)**.** The Committee confirmed that this condition will be added to the published list of conditions for which PGD may be carried out.

Signed: Date: 15/11/2012

David Archard (Chair)