HFEA Licence Committee Meeting
14 June 2012

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

Minutes – Item 6

Centre 0102 (Guys Hospital) – PGD for Argininosuccinic Aciduria – (OMIM #207900)

Members of the Committee:	Committee Secretary:
David Archard (lay) Chair Mair Crouch (lay) Sue Price (professional) Debbie Barber (professional) Jane Dibblin (lay)	Lauren Crawford Legal Adviser: Juliet Oliver, 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

- 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 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.

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 Argininosuccinic Aciduria (OMIM #207900) is a disorder that is inherited in an autosomal recessive manner. There is a 1 in 4 chance of an embryo being affected by this condition where both parents are carriers.

4. The Committee noted Argininosuccinic Aciduria is an inherited disorder that causes ammonia to accumulate in the blood. Ammonia, which is formed when proteins are broken down in the body, is toxic if the levels become too high. The nervous system is especially sensitive to the effects of excess ammonia. Argininosuccinic aciduria usually becomes evident in the first few days of life. An infant with argininosuccinic aciduria may be lacking in energy (lethargic) or unwilling to eat, and have poorly controlled breathing rate or body temperature. Some babies with this disorder experience seizures or unusual body movements, or go into a coma and die. Complications from argininosuccinic aciduria may include developmental delay and intellectual disability. Progressive liver damage and skin lesions may occur.

5. Occasionally, an individual may inherit a later onset form of the disorder in which ammonia accumulates in the bloodstream only during periods of illness or other stress. This can cause learning difficulties, attention deficit disorders, seizures, liver involvement and high blood pressure.

6. The Committee noted there are treatments available, but these are for control of symptoms rather than cure. Treatment of the initial symptoms is with rapid control of the excess levels of ammonia by stopping oral protein and giving

intravenous glucose and lipids, and special arginine and nitrogen therapy. More long term treatment involves special diets and possibly liver transplantation. Scrupulous attention to the diet is essential and life long.

7. The Committee noted that the condition is serious because affected individuals usually become unwell within the first week of life with a progressive encephalopathy. Permanent brain damage can occur. Additionally liver disease, developmental delay and epilepsy are frequent. Treatment which consists of a protein restricted diet and life long medication is usually effective in preventing the high ammonia but does not effect the other disease manifestations. Liver disease can progress to cirrhosis and learning difficulties range from moderate to severe.

8. The Committee noted that the application is supported by the Peer Reviewer as well as by 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 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 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).

11. The Committee agreed to authorise the testing of embryos for Severe Argininosuccinic Aciduria (OMIM #207900). The Committee confirmed that this condition will be added to the published list of conditions for which PGD may be carried out.

Signed: Date: 27/06/2012

David Archard (Chair)