HFEA Licence Committee Meeting

29 March 2012

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

Minutes – Item 5

Centre 0044 (Centre for Reproductive and Genetic Health) – PGD for Holt Oram Syndrome (OMIM #142900)

Members of the Committee:	Committee Secretary:
David Archard (lay) Chair Anna Carragher (lay) Rebekah Dundas (lay) (videoconference) Mair Crouch (lay) (videoconference) Sue Price (professional) Debbie Barber (professional)	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 Holt Oram Syndrome (OMIM #142900) is a disorder that is inherited in an autosomal dominant manner. There is a 1 in 2 chance of an embryo being affected by this condition where a parent is affected.

4. The Committee noted Holt Oram Syndrome is caused by mutations in the TBX5 gene. If the offspring inherits that genetic change, there is a high chance (75%) that there will be at least some cardiac impairment. All people with this disorder have at least one limb abnormality that affects bones in the wrist. Affected individuals may have additional limb abnormalities. The Committee noted that the effects of the genetic mutation will be present from before birth, and that the variability of symptoms is currently unpredictable.

5. The Committee noted Holt Oram Syndrome (HOS) is characterized by the following problems: Abnormalities of the limb that can vary from carpal (wrist) bone anomalies, underdevelopment of the thumb, underdevelopment of a limb including, forearm, arm, collar and shoulder bone anomalies. Physiotherapy and occupational therapy to help with disability in severe cases is often needed. Surgical management in some

cases to improve function of the affected limb is also considered; Heart problems such as defects in the septum such as VSD or ASD. Complex congenital heart conditions have also been described in HOS. Careful monitoring and surgical management will often be needed; Cardiac conduction disorders leading to abnormal tracing of the heart (abnormal ECG). This may present as progressive heart block, sinus bradycardia and sometimes atrial fibrillation requiring interventions such as pacing. Careful monitoring for these complications and treatment will be needed to avoid complications such as pulmonary hypertension, arrhythmias and heart failure. Progressive conduction abnormalities of the heart leading to long term monitoring and treatment of the congenital heart problems.

6. The Committee noted that the condition is serious because the physical disability, invasive treatment and long term monitoring with frequent hospital admissions can severely affect the quality of life. An individual may have only an unusual (unopposable) thumb or may effectively have only one arm and one rudimentary one and heart defects, requiring medication and surgery. Although there is no intellectual impairment, the effects of hospitalisation and the possible lack of at least one functioning upper limb will have far reaching effects.

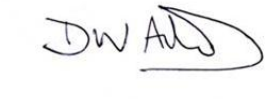
7. The Committee noted that the application is supported by the Peer Reviewer as well as by Genetic Alliance UK.

8. 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, 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.

9. 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).

10. The Committee agreed to authorise the testing of embryos for Holt Oram Syndrome (OMIM #142900). The Committee confirmed that this condition will be added to the published list of conditions for which PGD may be carried out.

Signed: Date: 12/04/2012



David Archard (Chair)