HFEA Statutory Approvals Committee

30 October 2014

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

Minutes – Item 7

Centre 0044 (Centre for Reproductive and Genetic Health) – PGD application for Focal Dermal Hypoplasia (FDH) #305600

Members of the Committee:	Committee Secretary:
David Archard (lay) Chair	Lauren Crawford, Committee Officer
Sue Price (professional)	
Debbie Barber (professional)	
Rebekah Dundas (lay)	Legal Adviser:
Jane Dibblin (lay)	Dawn Brathwaite, Mills & Reeve
Advisor: Dr Peter Turnpenny	

Declarations of Interest: The Members declared no conflicts in relation to this item.

The following papers were considered by the Committee:

- Executive summary
- PGD application form
- Redacted Peer Review form
- 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) ("the Act")
- 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 proposed purpose of testing the embryos was as set out in paragraph 1ZA(1)(b) of schedule 2 of the Act, i.e. '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 that Focal dermal hypoplasia (FDH) #305600 (also known as Goltz-Gorlin syndrome) is a severe multisystem disorder inherited in an X-linked dominant pattern. Affected people are nearly always female as non-mosaic males die in utero. There is a 1 in 2 chance of an embryo being affected at the point of conception.

4. The Committee noted that FDH it is due to mutations in PORCN. It almost always presents at birth with skin abnormalities including atrophic and hypoplastic areas of skin (thin skin) with herniation of fat through the skin defects. Cutis aplasia (missing areas of skin) can occur. There are often linear pigmentation defects. Papillomas (benign wart-like tumours) develop in the skin and mucous membranes (around the mouth, vulva, anus and eyes and in the larynx). Hair, nail and dental anomalies are common. Most have skeletal abnormalities, including syndactyly (webbing between digits), missing digits and split hand/foot malformation, which all impair function. Sometimes arm or leg bones are missing resulting in severe deformity. There is a risk of pathological fractures due to bone tumours or fibrous dysplasia of the bones. Spine abnormalities can occur leading to scoliosis (curvature of the spine) in later childhood. Diastasis pubis (separation of the symphysis pubis bone in the middle of the front of the pelvis) causes severe pain. Various eye abnormalities occur commonly and can cause blindness. Anophthalmia (absent eyes), occurs. Other features include: unusual facial features

including asymmetry, facial clefting, structural kidney abnormalities, hearing loss. Rare cases of abdominal and thoracic wall defects have been reported, where the intestines and sometimes liver and other abdominal organs, and heart develop outside the body. There are rare reports of mothers with PORCN mutations having babies with Pentalogy of Cantrell, a lethal condition with abdominal and thoracic wall defects and congenital heart defects.

5. The Committee noted that a significant number of severely affected cases die in infancy as a result of skin infections or severe congenital abnormalities (such as abdominal/thoracic wall defects). Survivors frequently suffer severe pain and itching from skin lesions. Limb abnormalities can result in severe disability, and pain occurs due to diastasis pubis or fractures. Some affected people are blind. Some have hearing loss. Often papillomas develop which can be painful and can occur in the larynx causing swallowing difficulties. The skin lesions and facial features often result in significant cosmetic concerns for affected patients. About 15% have developmental delay/cognitive impairment. In a small number of cases there is severe intellectual impairment.

6. The Committee noted that there is no cure. Treatment is aimed at reducing pain and skin infections by occlusive dressings and antiobiotics. Laser treatment can help some skin lesions. Surgery for papillomata affecting swallowing and to help improve function where there are severe limb defects. Analgesia for other pain.

7. The Committee welcomed the advice of its advisor, Dr Peter Turnpenny. Dr Turnpenny confirmed that the condition is as described in the papers. He advised that the level of the intellectual impairment is variable form mild to moderate to in some cases severe. He also advised that females can also develop serious intellectual impairment.

8. The Committee noted that the application is consistent with the Peer Review and is also supported by the Genetic Alliance.

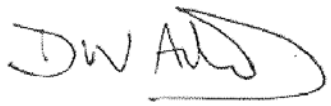
9. The Committee considered that the condition is serious because children are affected in utero, with male embryos dying in utero and affected females born have a combination of the serious symptoms listed above but have managed to survive.

10. The Committee had regard to its explanatory note and noted that on the basis of the information presented, given the condition's 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. The Committee was therefore satisfied

that the condition meets the criteria for testing under paragraph 1ZA(1)(b) and (2) of Schedule 2 to the Act.

11. The Committee agreed to authorise the testing of embryos for Focal dermal hypoplasia (FDH) #305600.

Signed: Date: 13/11/2014



David Archard (Chair)