HFEA Licence Committee Meeting

29 March 2012

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

Minutes – Item 1

Centre 0102 (Guys Hospital) – PGD for Familial Paraganglioma Syndrome (PGL1) (OMIM #168000)

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 Familial Paraganglioma Syndrome (PGL1) (OMIM #168000) 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.

4. The Committee noted that PGL1 has a varying degree of penetrance depending on which parent passed on the gene (it demonstrates the "parent of origin effect" in that it is generally only children who inherit the gene from their father who develop symptoms). Penetrance is 48% by the age of 30, 73% by the age of 40 and 86% by the age of 50 years.

5. The Committee noted that Paragangliomas are mostly non-functioning tumours which present with symptoms caused by growing in a confined space, usually in the head and neck. They can cause tinnitus (white noise or ringing in the ears) and conductive hearing loss (deafness), hoarseness of the voice or difficulty swallowing. Symptoms of phaechromocytomas commonly include a rapid pulse, palpitations, headaches, nausea, vomiting, anxiety, chest pain, visual disturbances, fainting, abdominal pain and constipation depending where the tumours are situated.

6. The Committee noted that treatment is available for PGL1 through surgical removal of the tumours but if malignant transformation has occurred then the treatment is palliative. Affected individuals will need MRI, CT and PET to localize the tumours, followed by surgery and possible radiotherapy, or radiosotope therapy. If tumours are removed before they have spread (metastatized) then surgery can be curative, but if not then only 50% of those affected will survive for 5 years. The Committee also noted the evidence from Genetic Alliance UK that surgery to remove paragangliomas carry a risk of nerve damage and therefore a "wait and see" policy is commonly adopted

~~7.~~ The Committee considered that the condition is serious because although the majority of paragangliomas are not malignant, they cause significant problems by compressing nerves, blood vessels and functioning structures in the head and neck area. This can have a broad range of effects on patients including hearing loss, tinnitus, problems swallowing and other problems due to interference with nerves. Affected individuals will require lifelong surveillance (from the age of 7 years old) and there is also the possibility of death if tumours metastasize.

8. The Committee noted that the application both the Peer Reviewer and Genetic Alliance UK consider the condition to be serious.

9. The Committee had regard to its explanatory note, in particular paragraphs 5.4 *Where a condition has a range of penetrance (eg. 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'*. The Committee noted that on the basis of the information presented, given the highest degree of penetrance and 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 another 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 Familial Paraganglioma Syndrome (PGL1) (OMIM #168000). 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)