HFEA Licence Committee Meeting

1 November 2012

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

Minutes – Item 3

Centre 0102 (Guy's Hospital) – PGD for X-Linked Lymphoproliferative Disease Type 2 (XLP2; XIAP gene) – (OMIM #300365)

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

1. HFEA Protocol for the Conduct of Licence Committee Meetings and Hearings
2. 8th edition of the HFEA Code of Practice
3. Human Fertilisation and Embryology Act 1990 (as amended)
4. Decision trees for granting and renewing licences and considering requests to vary a licence (including the PGD decision tree); and
5. Guidance for members of Authority and Committees on the handling of conflicts of interest approved by the Authority on 21 January 2009.
6. Guidance on periods for which new or renewed licences should be granted
7. Standing Orders and Instrument of Delegation
8. Indicative Sanctions Guidance
9. HFEA Directions 0000 – 0012

10. Guide to Licensing
11. Compliance and Enforcement Policy
12. Policy on Publication of Authority and Committee Papers
13. HFEA Pre-Implantation Diagnostic Testing ("PGD") Explanatory Note For Licence Committee

Background

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 considerable 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)(c) of schedule 2 of the Act, ie. 'to establish the sex of the embryo in case where there is a particular risk that any resulting child will have or develop a gender-related serious physical or mental disability, serious illness or serious medical condition' and also paragraph 1ZA(1)(b) of Schedule 2 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 that X-Linked Lymphoproliferative Disease Type 2 (XLP2; XIAP gene) – (OMIM #300365) is a disorder that is inherited in an X-linked manner. Couples with a family history of the condition have a 1 in 4 risk in each pregnancy of conceiving an affected child (half of all male children) as female carriers are symptom free.

4. The Committee noted that the centre's application was to test for two purposes under Schedule 2, both to establish the sex of the embryo and for the familial genetic change.

5. The Committee considered that there is a significant risk that a male with the abnormality will develop a serious medical condition because it is fully penetrant in affected males.

6. The Committee noted that X-Linked Lymphoproliferative Disease Type 2 (XLP2) is a hereditary immunodeficiency affecting males only. It is characterised by an inadequate immune response to infection with the Epstein-Barr virus (EBV). Affected boys typically present with haemophagocytic lymphohistiocytosis (HLH), a blood disorder often associated with EBV infection. Some males are asymptomatic and their long-

term prognosis is not known. Many affected boys die in infancy and childhood. HLH is the most common fatal complication, and typically leads to liver problems and profound bone marrow failure, which result in a mortality rate greater than 90%.

7. The Committee noted other causes of death include: life-threatening infections resulting from hypogammaglobulinemia (immune deficiency disorder), colitis (gastrointestinal disease), liver failure, and pneumonia. Prompt recognition of the disorder and aggressive treatment interventions are likely to improve survival. The only possible cure for XLP is bone marrow transplant. However, the therapy is not always successful and is not without significant risk and complications.

8. The Committee considered that XLP2 is serious because age of onset is most commonly in childhood with a mean age of death at 16 years. The condition presents with haemophagocytic lymphohistiocytosis (HLH), which may be triggered by Epstein-Barr virus infection or may occur in the absence of this. HLH leads to a hepatitis, hepatic necrosis and bone marrow failure. Mortality rates for HLH are in excess of 90% although prompt treatment may improve survival. Another manifestation of the condition is hypogammaglobulinaemia, in which there is a lack of one or more subclass of immunoglobulin leading to an immune deficiency. This may be treated with intravenous immunoglobulin. Approximately 13% of patients develop colitis, which is severe and has a mortality of 60%. Treatment of the manifestations is with cytotoxic agents, steroids and antibodies such as rituximab for HLH, and monthly intravenous immunoglobulins for hypgammaglobulinaemia. Bone marrow transplantation is the only curative treatment but this may not be successful (this is more successful in XLP1 linked to a different gene). The condition occurs in almost 100% of males who carry the gene mutation. It clearly has great potential to impair quality of life and significantly reduces life expectancy. Pachlopnik Schmid et al. (2011) reported that 43% reached adulthood.

9. 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 male 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 satisfied that this X-linked condition only affects males and therefore it was appropriate to grant the application under paragraph 1ZA(1)(b) and (c) of Schedule 2 to the Act.

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

11. The Committee agreed to authorise the testing of male embryos for X-Linked Lymphoproliferative Disease Type 2 (XLP2; XIAP gene) – (OMIM #300365). The Committee confirmed that this authorisation will be added to the published list of conditions for which PGD may be carried out.

Signed: Date: 15/11/2012

David Archard (Chair)