HFEA Licence Committee Meeting

05 May 2011

21 Bloomsbury Street London WC1B 3HF

Minutes – Item 4

Centre 0119 (Birmingham Women's Hospital) – PGD to perform all subtypes of Hereditary Nonpolyposis Colorectal Cancer

Members of the Committee:	Committee Secretary:
David Archard (lay) – Chair Debbie Barber (professional) Jane Dibblin (lay) Rebekah Dundas (lay) (via videoconference) Sue Price (professional)	Terence Dourado Legal Adviser: Tom Rider, Field Fisher

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:

- Executive Summary
- PGD Application form
- PGD application form appendix
- Redacted Peer Review
- Genetic Alliance opinion
- Review article provided in evidence by the centre: 'Hereditary and Familial Colon Cancer', Jasperson, Tuohy et al. (2010), Gastroenterology 138(6): 2044-2058).

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

1. The Committee had regard to its Decision Tree. The Committee was satisfied that the Centre is licensed to provide PGD.

2. The Committee noted that it had previously licensed two subtypes of Hereditary Nonpolyposis Colorectal Cancer: Lynch Syndrome / HNPCC (MSH2 gene) OMIM #120435, and Lynch Syndrome/ HNPCC (MLH1 gene) 609310.

3. 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’.

4. The Committee considered that the condition was not clearly defined and that it was better understood in terms of the mechanism of cancer predisposition. It is caused by changes in DNA mismatch repair genes. The Committee noted that there was a range of penetrance but that the diagnosis was nonetheless serious for those affected and that the condition had a range of risks of developing a range of serious symptoms.

5. Nonpolyposis Colorectal Cancer and its subtypes are inherited in an autosomal dominant manner. Only one copy of the affected gene is sufficient to cause the disorder, ie. There is a 1 in 2 chance of the embryo having the abnormality in a family where one parent is affected and the other is unaffected.

6. The degree of penetrance is very high, as noted by the peer reviewer, and so the Committee considered that there is a significant risk that a person with the abnormality will develop a serious medical condition.

7. The Committee considered that the condition is serious because many people with these genetic changes will develop bowels polyps that can

progress to bowel cancer. Women have a significant risk of gynaecological cancer, and cancer risk for a wider range of organ types is increased. The Committee noted that if a mutation is identified in one of these genes there is a high lifetime risk of colon cancer of up to 80%. Early onset can be expected between the ages of 40 and 50 years, although 5% will occur before the age of 30 years, compared to 60 – 70 years in the general population. Carriers of the mutation also have an increased susceptibility to other multiple primary cancers, such as endometrial, gastric, biliary tract, urinary tract, and ovarian cancer. Further, in individuals with an identified mutation, accelerated carcinogenesis has been reported within 2 – 3 years in Lynch syndrome compared to 8 – 10 years in the general population. The Committee further noted that there is no preventative treatment for the condition and that screening must continue throughout the affected person's life time. Surgery as a treatment option for colon cancer may result in a colostomy, which has social, psychological as well as negative physical consequences.

8. The Committee took in to account 5.5 of its Explanatory Note which states '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.'

9. The Committee noted paragraph 10.5 of the Code of Practice (8th edition)/ HFEA guidance for Centres: 'The use of PGD should be considered only where there is a significant risk of a serious genetic condition being present in the embryo. When deciding if it is appropriate to provide PGD in particular cases, the seriousness of the condition in that case should be discussed between the people seeking treatment and the clinical team. The perception of the level of risk for those seeking treatment will also be an important factor for the centre to consider.'

10. On the basis of the information presented, the Committee 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.

11. The Committee agreed that the licence should be varied to authorise the testing of embryos for all subtypes of Hereditary Nonpolyposis Colorectal Cancer and that no conditions should be put on the licence in relation to the variation. The Committee confirmed that this condition will be added to the published list of conditions for which PGD may be carried out.

Signed Date: 19/05/11

David Archard (Chair)