HFEA Licence Committee Meeting

11 October 2012

ETC Venues, 8th Floor Tenter House, 45 Moorfields, London, EC2Y 9AE

Minutes – Item 3

Centre 0102 (Guy's Hospital) – PGD for Dentatorubral-Pallidoluysian Atrophy (DRPLA) (OMIM#125370)

Members of the Committee:	Committee Secretary:
David Archard (lay) Chair Sue Price (professional) Jane Dibblin (lay) Anna Carragher (lay)	Lauren Crawford Legal Adviser: Tom Rider, 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 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 Dentatorubral-Pallidoluysian Atrophy (DRPLA) (OMIM#125370) is a disorder that is inherited in an autosomal dominant manner. This means that any offspring of a person with an ATN1 mutation will be at 50% risk of inheriting an ATN1 mutation.

4. The Committee noted that, except for rare cases with a Mall expansion within the ATNI gene, DRPLA is considered to be fully penetrant.

5. The Committee noted that Dentatorubral-Pallidoluysian Atrophy (DRPLA is a progressive genetic disorder with onset of symptoms ranging from 1 year of age to the sixth decade. The average age of onset is 30 years. The age of onset strongly correlates with the size of the expanded CAG repeat within the ATN1 gene. Affected offspring typically have symptoms 26 to 29 years earlier than affected fathers and 14 to 15 years earlier than affected mothers.

6. The Committee noted that clinical presentation varies, depending on age of onset. Adult-onset symptoms typically include ataxia (poor muscle coordination), choreoathetosis (involuntary and uncontrollable movements) and dementia. Childhood-onset symptoms typically include ataxia (unstable balance), myoclonus (involuntary contraction of muscles), seizures and intellectual deterioration. DRPLA is sometimes initially misdiagnosed as Huntington's disease, owing to a number of similar progressive features

7. The Committee noted that treatment is limited to supportive care only. Treatments include prescribing standard antiepileptic drugs for seizures; appropriate psychotropic medications for psychiatric manifestations. Adaptation of environment and care to the level of dementia is required. Affected children will require special education. As the condition progresses, affected individuals' quality of life becomes increasingly compromised and they lose their independence and life expectancy is reduced. Because there is no cure for DRPLA, this may entail signifcant life decisions.

8. The Committee considered the condition is serious because there is no cure for this condition and it results in premature death (on average 13 years after symptom onset).

9. The Committee noted that the application is supported by the Peer Reviewer and the Genetic Alliance UK.

10. The Committee had regard to its explanatory note, in particular paragraph 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 condition's 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.

11. The Committee agreed to authorise the testing of embryos for Dentatorubral-Pallidoluysian Atrophy (DRPLA) (OMIM#125370)**.** The Committee confirmed that this condition will be added to the published list of conditions for which PGD may be carried out.

Signed: Date: 25/10/2012

David Archard (Chair)