HFEA Licence Committee Meeting

27 September 2012

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

Minutes – Item 6

Centre 0044 (Centre for Reproductive and Genetic Health (CRGH)) – PGD for Machado Joseph Disease (MJD) or Spinocerebellar ataxia 3 (SCA 3) (OMIM #1091500)

Members of the Committee:	Committee Secretary:
David Archard (lay) Chair Sue Price (professional) Jane Dibblin (lay) Anna Carragher (lay) Mair Crouch (lay) Rebekah Dundas (lay) –Videoconference	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

- 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 Machado Joseph Disease (MJD) or Spinocerebellar ataxia 3 (SCA 3) (OMIM #1091500) is a disorder that is inherited in an autosomal dominant manner. There is a 1 in 2 chance of an embryo inheriting this condition from an affected parent..

4. The Committee noted that Machado Joseph Disease may begin in adolescence; however the more severe forms may present at an earlier age. In severely-affected people, life expectancy may be around the mid-30s. The main characteristics are progressive cerebellar ataxia, spasticity, and ocular movement abnormalities. These are apparent as a lack of muscle control and coordination of the upper and lower extremities. It is nearly fully-penetrant when the critical CAG triplet repeat expansion is present.

5. The Committee noted that there are five sub-types of MJD and that these are characterized by differences in the age of onset and range of symptoms. The sub-types illustrate a wide variety of symptoms that patients can experience; however, assigning individuals to a specific subtype of the disease is of limited clinical significance.

    - Type I - distinguished by arrival between the ages of 10 and 30. It usually has fast development and severe rigidity and dystonia.

- Type II - most common sub-type and typically begins between 20 and 50 years of age. It has an intermediate progression and causes symptoms that include spasticity, exaggerated reflex responses and spastic gait, ataxia and upper motor neuron signs.
- Type III – There is a slow progression. Patients typically have an onset between the ages of 40 and 70. Symptoms include muscle twitching, tingling, cramps, unpleasant sensations such as numbness, pain in the feet, hands and limbs and muscle atrophy. Nearly all patients experience a decline in their vision such as blurred vision, double vision, inability to control eye movements, and loss of capability to distinguish colour. Some patients also experience Parkinsonian symptoms.
- Type IV - distinguished by Parkinsonian symptoms that respond particularly well to drug (levodopa) treatment.
- Type V- appears to resemble Hereditary Spastic Paraplegia; however, more research is needed to conclude the relationship between these two.

6. The Committee noted that symptoms of MJD are memory deficits, spasticity, difficulty with speech and swallowing, weakness in arms and legs, clumsiness, frequent urination and involuntary eye movements. Symptoms can begin in early adolescence and they get worse over time. Eventually, MJD leads to paralysis; however, intellectual functions usually remain the same.

7. The Committee noted that although there is no cure, symptoms may be alleviated with anti-spasm drugs, special glasses and walking aids. For example, spasticity can be reduced with antispasmodic drugs. Parkinsonian symptoms can be treated with drug therapy. Prism glasses can reduce diplopic symptoms. Physiotherapy can help patients by prescribing mobility aids to increase the patients' independence, providing gait training, and prescribing exercises to maintain the mobility of various joints and general health to decrease the likelihood of falls or injuries as a result of falls. Walking aids and wheelchairs can greatly help the patient with everyday tasks. Some patients will experience difficulties with speech and swallowing, so speech therapy can assist. However, the mutation is very likely to cause the disease, which has wide-ranging neurological degenerative effects, commonly resulting in premature death and always in impaired physical function.

8. The Committee considered the condition is serious because it is a variable neurodegenerative disorder that can have onset from teenage years to midlife. As the genetic change underlying the disorder is a triplet repeat expansion the disorder can show anticipation (be worse in sucessive generations) due to an increase in the repeat number. The disorder is a

neurodegenerative condition that can have onset from as early as mid-childhood to midlife. It can progress over 15-20 yrs or the course can be longer than this. It is almost completely penetrant. The condition shows relentless progression with many patients having the last few years of life with very poor quality. The test would only determine whether the gene had been inherited, not how severly affected an individual can be as the variation of sub-type is unpredictable.

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 Machado Joseph Disease (MJD) or Spinocerebellar ataxia 3 (SCA 3) (OMIM #1091500) The Committee confirmed that this condition will be added to the published list of conditions for which PGD may be carried out.

Signed: Date: 09/10/2012

David Archard (Chair)