HFEA Licence Committee Meeting

19 July 2012

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

Minutes – Item 1

Centre 0201 (Edinburgh Assisted Conception Unit) – PGD for Dravet Syndrome (OMIM #607208)

Members of the Committee: David Archard (lay) Chair Anna Carragher (lay) Sue Price (professional) Debbie Barber (professional) Rebekah Dundas (lay) - VC	Committee Secretary: 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
- Additional Information provided by the centre (29th June 2012)
- 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 Dravet Syndrome (OMIM #607208) 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 where a parent is affected. However, given the severity of the condition, a parent may be mosaic for the mutation with a maximum risk of 1 in 2.

4. The Committee noted Dravet Syndrome is associated with mutations in the SCN1A gene. Symptoms include prolonged seizures and a variable degree of intellectual disability. Occasionally childhood death can occur. The risk of this is lower but still significant if the SCN1A mutation leads to partial rather than complete loss of function of the gene.

5. The Committee noted that Dravet Syndrome is an epilepsy syndrome with onset in the first year of life. Children are initially normal but then present with prolonged lateralised, often febrile seizures, that often require ITU admission. Developmentally they remain normal over the first year. In the second year of life they present with further seizure types – generalised tonic clonic seizures, focal seizures and myoclonic jerks. There is then developmental slowing; many make little if any cognitive progress.

6. The Committee noted that treatment is currently not curative. Specific antiepileptic treatments are known to be more beneficial than others – eg

stiripentol with clobazam and/or sodium valproate and topiramate. Others are known to possibly aggravate seizures eg carbamazepine, lamotrigine and phenytoin. It has been suggested that this is an epileptic encephalopathy, and that the epileptic activity is at least in partly responsible for the developmental problems. However this is not well understood; there is little evidence to suggest optimal treatment changes outcome, and that genetic background (yet to be determined) is likely to influence neurodevelopmental outcome. Long term cognitive outcome is unlikely to be above a 3 year level in the majority.

7. The Committee noted that the seizures associated with Dravet are prolonged and often refractory to conventional anticonvulsant medications. Dravet syndrome has a profound and negative effect on the life of the affected individual and their family.

8. The Committee noted that the condition is serious because for the first few years of life, children with Dravet Syndrome are subject to frequent and regular seizures. The form that these can take can be variable. Some children have many small consecutive seizures, others have episodes of epileptic status. It is not uncommon for a child to have more than a dozen seizures a day. The typical seizures of Dravet Syndrome are difficult to control. Most medicines traditionally used to control seizures are ineffective, and some make the syndrome worse. Care provision for children affected by Dravet Syndrome is most usually provided locally in the UK, and not by specialised care providers. Children with Dravet Syndrome have no prospect of an independent life, and have lower than average life expectancy. Musculo-skeletal problems can eventually lead to wheelchair dependence.

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

10. The Committee noted that the Peer Reviewer did not feel it was appropriate to recommend PGD for this condition as they felt they needed further information on phenotype and genotype correlation. They also state that the condition is inherited in an autosomal recessive manner, which is contradictory to the application form.

11. The Committee noted the additional information sent by the centre, in response to the Peer Reviewers comments, which states “There are no reports of autosomal recessive inheritance of SCN1A pathogenic mutations that we are aware of. There is a significant level of phenotype-genotype correlation in SCN1A associated disease with heterozygous nonsense being commonly associated with severe disease”.

12. The Committee was therefore 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. In reaching this decision, the Committee had regard to its Explanatory Note and in particular, paragraph 5.5 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'*. Accordingly, it considered that it was appropriate to grant the application under paragraph 1ZA(1)(b) of Schedule 2 to the Act.

13. 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).

14. The Committee agreed to authorise the testing of embryos for Dravet Syndrome (OMIM #607208). The Committee confirmed that this condition will be added to the published list of conditions for which PGD may be carried out.

Signed: Date: 30/07/2012

David Archard (Chair)