HFEA Statutory Approvals Committee

29 May 2014

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

Minutes – Item 1

Centre 0101 (CARE Nottingham) – PGD application for Waardenburg Syndrome Type I, IIa, IIb, IIc, IId, IIe, III, IVa, IVb, IVc OMIM #193500, #193510, #600193, #606662, #608890, #611584, #148820, #277580, #613265, #613266

Members of the Committee:	Committee Secretary:
David Archard (lay) Chair	Lauren Crawford
Sue Price (professional)	
Jane Dibblin (lay)	Legal Adviser:
	Dawn Brathwaite, Mills and Reeve
	Also in attendance:
	Sam Hartley, Head of Governance and Licensing, HFEA

Declarations of Interest: The Members declared no conflicts in relation to this item.

The following papers were considered by the Committee:

- Executive summary
- Application form
- Redacted Peer Review x4
- Public comment x2
- Tabled Document – Genetic Alliance Opinion
- Tabled Document – Email From Peer Reviewer (6 May 2014)

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) ("the Act")
- Decision trees for granting and renewing licences and considering requests to vary a licence (including the PGD decision tree)
- 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 proposed purpose of testing the embryos was as set out in paragraph 1ZA(1)(b) of schedule 2 of the Act, i.e. '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 Waardenburg syndrome Types I, IIa, IIb, IIc, IIe and IVc are inherited in an autosomal dominant manner, which means there is a 1 in 2 chance of having an affected child in each pregnancy where one parent is affected. Waardenburg syndrome Types III, IVa and IVb are also inherited in an autosomal dominant manner where one parent is affected, meaning there is a 1 in 2 chance of having an affected child in each pregnancy, OR are inherited in an autosomal recessive manner, meaning that there is a 1 in 4 chance of having an affected child in each pregnancy where both parents are carriers.

4. The Committee noted that Waardenburg syndrome (WS) in general, irrespective of subtype, is known to be highly variable even within a family with some members often much more severely affected than others despite all carrying the same gene change. Congenital bilateral profound sensorineural hearing loss and pigmentary disturbances of the iris, hair and skin are common characteristics. In addition, in WS type IVc can include Hirschsprung disease (where part or all of the large intestine are lacking innervation and can thus not contract/ relax and pass stool through it leading

to functional obstruction). In WS type IIe neurologic involvement canmental retardation, myelination defects (defect of insulating sheath around nerve cells), hypotonia (low muscle tone), absence of olfactory nerves (inability to smell) and ataxia (unsteadyness).

5. WS type IIe and IVc are inherited in an autosomal dominant way and are caused by mutations in SOX10; broadly speaking the more severe neurological disease is thought to be caused by mutations affecting the last exon of the gene and escaping the nonsense mediated decay pathway, however a three generation family with a SOX10 mutation causing hypopigmentation in maternal grandmother, hearing loss in the mother and WS type IVc in the proband illustrates the aforementioned extreme intrafamilial variability.

6. The Committee noted that not every case of Waardenburg syndrome expresses all clinical manifestations. Assignment of a specific clinical type, even when the genetic mutation is known, can be difficult.

7. The Committee noted that the likely genetic location for two of the conditions, type IIb and IIc, had been described but that the specific gene mutation had not yet been identified. Further to this there was no Peer Review written on these two types.

8. As a consequence the Committee noted that these two types of Waardenburg syndrome (IIb and IIc) were not ones for which genetic testing could be offered and excluded these types from the consideration of the condition.

9. The Committee noted this disorder is unpredictable in its expression and is usually present at birth although depending on how the disorder presents in an individual it can be diagnosed at a later date.

10. The Committee noted that associated abnormalities are treated symptomatically. Depending on the severity of the expression a multidisciplinary medical team will be required, involving an ear, nose and throat specialist, an audiologist, a speech therapist, a geneticist, an ophthalmologist, a dermatologist, a craniofacial surgeon and a gastrointestinal specialist. Affected individuals with profound deafness are candidates for cochlear implants. The majority of affected individuals will display moderate to profound hearing loss which can affect psychological and social development. The Committee notes that this was syndromic deafness, ie deafness associated with other symptoms. The characteristic white forelock and eye colouring can be very conspicuous and striking.

11. The Committee noted that the application is consistent with the Peer Review.

12. The Committee noted that the Peer Review mentions four additional conditions which are caused by mutations in the same gene and overlap with the Waardenburg syndrome phenotype. These conditions were not considered within this application.

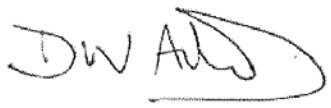
13. The Committee noted that it had two statements from people living with Waardenburg syndrome and were very grateful to the families for sending these in. It always helpful to hear how an individual can be affected.

14. The Committee considered that the condition is serious because it is a multi system neurological disorder with serious symptoms which affect people from birth.

15. 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 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 therefore satisfied that the condition meets the criteria for testing under paragraph 1ZA(1)(b) and (2) of Schedule 2 to the Act.

16. The Committee agreed to authorise the testing of embryos for Waardenburg Syndrome Type I, IIa, IId, IIe, III, IVa, IVb, IVc OMIM #193500, #193510, #608890, #611584, #148820, #277580, #613265, #613266.

Signed: Date: 12/06/2014



David Archard (Chair)