HFEA Statutory Approvals Committee

28 August 2014

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

Minutes – Item 4

Centre 0199 (CRM London) – PGD application for Aarskog Syndrome (OMIM #305400)

Members of the Committee:	Committee Secretary:
David Archard (lay) Chair	Lauren Crawford
Sue Price (professional)	
Jane Dibblin (lay)	Legal Adviser:
Rebekah Dundas (lay)	Shelley Edwards, Fieldfisher
Advisor: Dr Peter Turnpenny	

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

The following papers were considered by the Committee:

- PGD application form
- Executive summary
- Redacted Peer Review
- Genetic Alliance Opinion
- Public comment
- Further information from centre with a covering email from the PR

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 noted that this application was previously adjourned for the receipt of further information as requested by the Committee.

2. The Committee noted that the additional information has been supplied from the Centre.

3. 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.

4. 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'.

5. The Committee noted that Aarskog Syndrome is inherited in an X-linked recessive manner which means there is a 1 in 4 chance of having an affected child in each pregnancy for a female carrier. Being inherited in an X-linked manner means there is a 1 in 2 chance of having an affected male child and a 1 in 2 chance of having a carrier female child in each pregnancy.

6. The Committee noted that symptoms of Aarskog syndrome vary from case to case, and may include short stature/, mild facial abnormalities, musculoskeletal and genital anomalies, and mild intellectual disability. Affected males often have a rounded face with a broad forehead. Additional characteristic facial features may also be present, as well as a variety of abnormalities affecting the ears and teeth.

Discussion

7. Affected males may also develop characteristic malformations of the skeletal system including disproportionate short stature, broad and short hands short

fingers, abnormally mobile finger joints, and wide flat feet with bulbous toes. In addition, males affected may have a sunken chest, protrusion of portions of the large intestine through an abnormal opening in the muscular lining of the abdominal cavity, and a prominent navel. Approximately 50% of individuals with Aarskog syndrome have spinal abnormalities. Males with Aarskog syndrome can be born with genital abnormalities. The urinary opening may be located on the underside of the penis and the scrotum may appear clefted or divided. Mild intellectual disability has occurred in some cases, but is not a consistent feature of the disorder.

8. In some cases, affected children may exhibit hyperactivity, fail to gain weight and grow at the expected rate, and develop chronic respiratory infections. Additional symptoms that may occur less frequently include congenital heart defects, scoliosis, additional pairs of ribs, a cleft palate and/or cleft lip, a mild webbing of the fingers and a short neck with or without webbing. Eye abnormalities may also be present including squint, far-sightedness and paralysis of certain eye muscles. Some female carriers of Aarskog syndrome might present milder features of the condition such as short stature or a widow's peak

9. The Committee noted that symptoms may develop by 1 year of age but sometimes symptoms may not be obvious until 3 years of age.

10. The Committee noted that there is no known cure for Aarskog syndrome. Treatment is limited to surgical procedures to treat conditions caused by the disorder and supportive treatment. Orthodontic treatment is often needed.

11. The Committee considered the additional information provided by the centre still appeared to be inconsistent with the original Peer Review of the condition.

12. The Committee asked Dr Peter Turnpenny, Expert Advisor to the Committee, for his views on the inconsistencies between the application and the peer review.

13. Dr Turnpenny confirmed that there is not a lot of information in the form of literature about this condition. He had found a 2010 paper which was a study of 60 patients presenting with symptoms of the condition. The paper actually only confirmed that 11 out of the 60 patients were confirmed to have the gene mutation for the disorder. Further out of the 11 patients with the gene only 5 had signs of mental retardation or mild learning difficulties. He explained that many older studies won't be backed up with molecular diagnosis and those that were considered to have had Aarskog, may not have had it and the learning difficulties may have been due to some other condition.

14. He had also found some further literature, but this paperwork also did not confirm that there was a significant risk of mental retardation or indicate how mild or severe the mental retardation could be. He noted that not everyone with Aarskog is short. Some can be above average height.

15. Dr Turnpenny also told the Committee that the condition was most likely undiagnosed in a lot of patients because most of the symptoms are not life threatening or serious enough to require attention. And therefore this could be why there is not a wider range of information about the condition.

16. Dr Turnpenny considered that the peer reviewer may have understated the symptoms of the condition, whereas the Applicant's descriptions were 'unusual' and did not describe most cases.

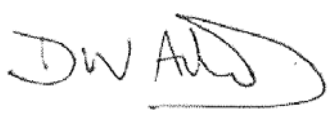
17. The Committee considered that most of the information about the condition may be based on case history and papers for which not all of those people studied were confirmed to have the gene, and therefore may have had other conditions.

18. The Committee had not been provided by the Centre with sufficient clear and consistent information on this condition as would allow the Committee to make a decision. It may be that the Centre cannot at present provide such information because of the current lack of confirmed patient studies.

19. The Committee accepted legal advice that if it did not consider that it had the information or evidence needed to decide the application, then the application should not be granted. The Committee noted that there was nothing to stop the Centre from providing additional information at some later time after further peer review and research.

20. The Committee considered that it was not necessary to go through the decision tree as it did not have the evidence required to make the decision needed.

Signed: Date: 17/09/2014



David Archard (Chair)