HFEA Statutory Approvals Committee

29 May 2014

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

Minutes – Item 2

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:
	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
- Tabled Document – 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) ("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 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.

4. 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.

5. 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.

6. 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

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

8. 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.

9. The Committee were not satisfied at this time that the condition met the test in regards to seriousness and turned to their explanatory note in particular paragraph 5.3, which states:

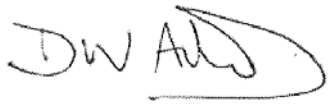
> When assessing the seriousness of the disability, illness or condition, the Licence Committee will take into account the following factors:
>
> *a) Age of onset.*
> Is the condition congenital or does it manifest later in life? If it does manifest later, at what stage (childhood, early adulthood, later)?
> b) *Symptoms of the disease*.
> What are the symptoms of the condition and is it fatal, life threatening or life limiting?
> *c) Whether the condition is treatable*
> *d) What type of treatment is available for those conditions that can be treated*
> What is the extent of the treatment available? How invasive is the treatment or likely treatment?
> *e) Effect of the condition on quality of life*
> This will include any evidence about the speed of degeneration in progressive disorders and the extent of any physical and /or intellectual impairment.
> *f) Variability of symptoms*
> Symptoms associated with the same condition can vary from family to family (and from individual to individual), and can range from the mild to the severe.
> Where the condition has variable symptoms, the Licence Committee will take account of:

- what the range of variability is; and
- whether the range suggests that some forms of the condition are so mild that they might not meet the ‘serious’ test.

10. The Committee considered that at this time that they did not have enough information provided in this paperwork to make an informed decision on the seriousness of this condition. The information provided does not contain enough detail in regards to the severity of the symptoms of the disorder – in particular the growth, skeletal and spinal symptoms – and the severity of those symptoms in the worst case. The information did not allow the Committee to judge the growth centile as there was no final heights given. There was also insufficient information on the surgical interventions required to treat the conditions. The Committee also noted the discrepancy between the details in the application and the peer review’s assessment of the worse case scenario being mild short stature.

11. The Committee urged the centre to provide more supporting information in regards to this application and agreed to adjourn consideration of this item in order for this further information to be obtained from the centre

Signed: Date: 12/06/2014



David Archard (Chair)