Item 2

Statutory Approvals Committee – minutes

Centre 0102 (Guys Hospital)

Pre-implantation Genetic Diagnosis (PGD) application for X-linked Heterotaxy-1 (HTX1) - ZIC3 associated congenital heart defects and heterotaxy, OMIM #306955

Thursday, 27 July 2017

Church House Westminster, Dean's Yard, Westminster SW1P 3NZ

Committee members	Margaret Gilmore (Chair) Anne Lampe Tony Rutherford Ruth Wilde Bobbie Farsides	
Members of the Executive	Dee Knoyle Paula Robinson	Committee Secretary Head of Planning & Governance
External adviser	Dr Peter Turnpenny	
Legal Adviser	Dawn Brathwaite	Mills & Reeve LLP
Observers		

Declarations of interest

- Members of the committee declared that they had no conflicts of interest in relation to this item.

The committee had before it:

- 8th edition of the HFEA Code of Practice
- Standard licensing and approvals pack for committee members.

The following papers were considered by the committee:

- Executive Summary
- PGD Application Form
- Redacted peer review
- Genetic Alliance opinion

1. Consideration of application

1.1. The committee welcomed the advice of its specialist adviser, Dr Peter Turnpenny, who confirmed that the condition was as described in the papers.

1.2. The committee noted that the description in the application for X-linked Heterotaxy-1 (HTX1) - ZIC3 associated congenital heart defects and heterotaxy, OMIM #306955, is consistent with the Peer Review.

1.3. The committee noted that the Genetic Alliance opinion provided a patient perspective and supported the application.

1.4. 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.

1.5. The committee noted that the condition being applied for is not on the list of approved PGD conditions.

1.6. 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'.

1.7. The committee noted that HTX1 is inherited in an X-linked pattern. This means that a woman who carries a causative mutation has a 25% chance of having an affected child (male) in each pregnancy. For a woman who is a carrier, the risk of male offspring being affected is 50% and the risk of female offspring being a carrier is 50%. There are reports of female carriers being affected.

1.8. The committee noted that HTX1 is a very rare form of heterotaxy, involving different arrangement of the internal organs. Symptoms are likely to develop in utero or in infancy.

1.9. The committee noted that Heterotaxy is associated with a range of congenital anomalies, including a higher than usual incidence of congenital heart disease. Complications can include spinal, kidney and anal abnormalities, abdominal situs inversus (where the major internal organs are reversed or mirrored from their normal positions), abnormal spleen function and atrial septal defect (where there is an abnormal opening of the wall that divides the upper filling chambers of the heart). Affected individuals may also have an enlarged heart, dextrocardia (where the heart points towards the right instead of the left side) and affected children can fail to thrive. As this is a very rare condition, the degree of penetrance is unknown but all heterotaxy syndromes demonstrate variable expression and incomplete penetrance. It is not possible to predict severity from genetic testing.

1.10. The committee noted that some cardiac defects are amenable to open heart surgery but this will rarely be able to fully correct the anatomy. Other defects may also require surgery. Lifespan is often limited and many males with HTX1 die from the complications of their heart defect in utero, in infancy or in childhood.

1.11. The committee noted the inspectorate's request to consider whether HTX1, OMIM #306955, should be approved for inclusion on the PGD List. The committee agreed to consider the application on this basis.

2. Decision

2.1. The committee considered that HTX1, OMIM #306955, is serious, given that the symptoms develop in utero or in infancy. Babies are born with heart defects and heterotaxy, involving different arrangement of the internal organs with the possibility of open heart surgery being required, although this is unlikely to fully correct the defect. Life expectancy is limited. Other complications can include spinal, kidney and anal abnormalities, abdominal situs inversus, abnormal spleen function and atrial septal defect. The committee noted the compelling personal accounts of the condition given by parents of affected children, which was provided by Genetic Alliance. The committee considered the potential physical and mental impact on the lives of affected individuals and their families and that there is no cure for this condition and children may fail to thrive.

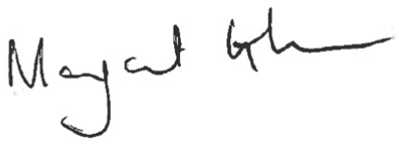
2.2. The committee had regard to its decision tree and noted that on the basis of the information presented, given the condition's worst symptoms, it was satisfied that there is a significant risk that a person with the abnormality will have or develop a serious physical or mental disability, a serious illness or any other serious medical condition. The committee was therefore satisfied that the condition of X-linked Heterotaxy-1 (HTX1) – *aka* ZIC3 associated congenital heart defects and heterotaxy, OMIM #306955, does meet the criteria for testing under paragraph 1ZA(1)(b) and (2) of Schedule 2 of the Act.

2.3. The committee agreed to authorise the testing for X-linked Heterotaxy-1 (HTX1) - ZIC3 associated congenital heart defects and heterotaxy, OMIM #306955.

3. Chair's signature

3.1. I confirm this is a true and accurate record of the meeting,

Signature



Name

Margaret Gilmore

Date

24 August 2017