Statutory Approvals Committee – minutes

Centre 0119 (Birmingham Women's Hospital)

Pre-implantation Genetic Diagnosis (PGD) application for

Orofaciodigital Syndrome 1 (OFD1), OMIM #311200

Orofaciodigital Syndrome 7 (OFD7), OMIM #608518

Joubert Syndrome Type 10, OMIM #300804

Simpson-Golabi-Behmel Syndrome Type 2, OMIM #300209

Retinitis Pigmentosa 23, OMIM #300424

Thursday, 26 April 2018

HFEA, 10 Spring Gardens, London, SW1A 2BU

Committee members	Margaret Gilmore (Chair) Bobbie Farsides (Deputy Chair) Anne Lampe Anthony Rutherford	
Members of the Executive	Dee Knoyle Bernice Ash Paula Robinson Catherine Burwood Clare Ettinghausen	Committee Secretary Committee Secretary (Observer) Head of Planning & Governance (Observer) Senior Governance Manager (Observer) Director of Strategy & Corporate Affairs (Observer)
External adviser	Professor Peter Turnpenny	
Legal Adviser	Gerard Hanratty	Browne Jacobson 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
- Comment from centre regarding peer review
- Genetic Alliance opinion
- Statutory Approvals Committee Minutes, 5 August 2016, PGD for Joubert Syndrome types 1-4, 7-9, 13-18 and 20-26
- Statutory Approvals Committee Minutes, 20 November 2014, PGD for Retinitis Pigmentosa 7
- Statutory Approvals Committee Minutes, 25 September 2014, PGD for Retinitis Pigmentosa 11
- Licence Committee Minutes, 28 October 2010, PGD for Autosomal Dominant Retinitis Pigmentosa
- Merged Licence Committee Minutes, 16 December 2010, PGD for Simpson Golabi Behmel Syndrome Type 1

1. Consideration of application

1.1. The committee welcomed the advice of its Specialist Adviser, Professor 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 Orofaciodigital syndrome 1 (OFD1), OMIM #311200 is consistent with the peer review.

1.3. The committee noted that Genetic Alliance 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 OFD1 is caused by mutations in the OFD1 gene on the X-chromosome. The condition is inherited in an X-linked dominant manner, which means there is 50% chance of an embryo being affected in each conception where the mother is a carrier. Male embryos that inherit the faulty gene (a 50% risk for male embryos, 25% risk overall) will miscarry during pregnancy, while female embryos that inherit the faulty gene (50% risk for female embryos, 25% risk overall) will be viable and affected by the condition.

1.8. The committee noted that this condition is generally considered to be prenatally lethal to male embryos/foetuses. Females with the genetic abnormality are likely to develop symptoms before or at birth, and exhibit them throughout life.

1.9. The committee noted that symptoms of the condition in affected females, with incidence rates in brackets when known, include polycystic kidney disease (50%), microcephaly (small brain and head), facial asymmetry, hearing loss, cleft palate, dentition problems, cardiac anomalies, fibrocystic liver (45%), finger (45%) and toe (25%) anomalies (webbing or extra digits), central nervous system malformations (40%) and intellectual disability (40%). Penetrance is high. There is however variability in the range and severity of symptoms in affected females and while affected male foetuses generally miscarry, occasional births of affected males have been reported.

1.10. The committee noted that the lifespan of those affected by OFD1 is shortened. Some symptoms in females, such as cleft palate, are surgically treatable. Polycystic kidney disease can lead to end stage renal failure which might require dialysis or kidney transplant. However, there are no treatments that alleviate all aspects of condition. Affected individuals have difficulties which are wide ranging and depend on their clinical presentation, but can range from intellectual disability and seizures secondary to brain malformations, through to the physical issues with hands, feet and dentition, which all affect quality of life.

1.11. The committee noted the inspectorate's request to consider whether the following condition should be approved for inclusion on the PGD List:

- Orofaciodigital Syndrome 1 (OFD1), OMIM #311200

1.12. The committee noted that the inspectorate also requests that the following conditions which belong to a group of conditions with similar phenotype, all caused by mutations in the OFD1 gene should also be considered for inclusion on the PGD List:

- Orofaciodigital Syndrome 7 (OFD7), OMIM #608518
- Joubert Syndrome Type 10, OMIM #300804
- Simpson-Golabi-Behmel Syndrome Type 2, OMIM #300209
- Retinitis Pigmentosa 23, OMIM #300424

The committee noted that multiple Joubert syndrome and Retinitis pigmentosa types and Simpson-Golabi-Behmel Syndrome Type 1 have already been approved for inclusion on the PGD List.

The committee noted that current evidence suggests that Retinitis Pigmentosa 23, OMIM #300424 could be the result of an unusual DNA change (intronic) which is 'private' to one reported family.

1.13. The committee agreed to consider this application for inclusion on the PGD List.

2. Decision

2.1. The committee considered that, in the worst case scenario, Orofaciodigital Syndrome 1 (OFD1), OMIM #311200 is a serious condition. The age of onset is before or after birth and the condition is fatal, particularly to males, shortening the lifespan of those affected. This is a multi-system disorder which affects major organs such as the brain, heart, liver and kidneys and also affects the central nervous system. Affected individuals also have malformations to the face and digits and may have intellectual disability and hearing loss. Some symptoms of the condition require surgery such as cleft palate. Individuals with kidney disease may require dialysis and eventually a kidney transplant. The condition severely impacts on an individual's quality of life.

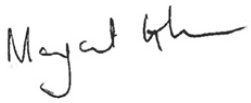
2.2. The committee had regard to its explanatory note and confirmed that, on the basis of the information presented, it was satisfied that there is a particular risk that an embryo may have the abnormality in question and that there is a significant risk, given the condition's worst symptoms, that a 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 conditions listed below meet the criteria for testing under paragraph 1ZA(1)(b) and (2) of Schedule 2 of the Act and agreed to authorise testing for these conditions:

- Orofaciodigital Syndrome 1 (OFD1), OMIM #311200
- Orofaciodigital Syndrome 7 (OFD7), OMIM #608518
- Joubert Syndrome Type 10, OMIM #300804
- Simpson-Golabi-Behmel Syndrome Type 2, OMIM #300209.

3. Chair's signature

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

Signature



Name

Margaret Gilmore

Date

17 May 2018