Statutory Approvals Committee – minutes

Item 1

Centre 0102 (Guys Hospital)

Pre-implantation Genetic Diagnosis (PGD) application for Combined Oxidative Phosphorylation Deficiency Type 7 (COXPD7), OMIM #613559

Thursday, 28 March 2019

HFEA Spey Meeting Room, Level 2, 10 Spring Gardens, London, SW1A 2BU

Committee members	Margaret Gilmore (Chair) Bobbie Farsides (Deputy Chair) Emma Cave Anne Lampe Tony Rutherford	
Members of the Executive	Moya Berry Catherine Burwood	Committee Secretary Licensing Manager (Observer)
Specialist Adviser	Dr Alison Male (PGD)	
Legal Adviser	Tom Rider	Fieldfisher LLP
Observers	Hannah Carpenter	Policy Officer

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:

- 9th 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 UK statement
- 2017-04-27 Statutory Approvals Committee Minutes - Item 5 - COXPD5 -OMIM #611719
- 2015-09-24 SAC Minutes - Item 2 - PGD Mitochondrial Complex 1 Deficiency mutation in ACAD9 gene OMIM #611126 – centre 0102
- 2015-12-17 SAC Minutes - Item 1 - PGD for Mitochondrial complex 1 deficiency OMIM #252010
- 2017-07-27 Statutory Approvals Committee - caused by mutation in the NDUFB3 gene OMIM #603839
- 2017-08-31 Statutory Approvals Committee- Autosomal Recessive Mitochondrial Complex 1 Deficiency

1. Consideration of application

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

1.2. The committee noted that the description in the PGD application for Combined Oxidative Phosphorylation Deficiency Type 7 (COXPD7) OMIM # 613559, was consistent with the peer review.

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

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

1.5. 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.

1.6. 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 COXPD7 is inherited in an autosomal recessive pattern, which means there is a 25% chance of an embryo being affected with the condition in each pregnancy if each parent carries a relevant mutation.

1.8. The committee noted penetrance of the condition is 100%.

1.9. The committee welcomed the advice of the specialist adviser who explained COXPD7 is an extremely rare and severe genetic condition, caused by a mutation in the C12orf65 gene. It affects the mitochondria therefore having a broad impact on multiple body systems with onset at birth. COXPD7 is a progressive disorder where an affected baby may develop normally, then deteriorate during infancy and early childhood. The condition is life limiting.

1.10. COXPD7 is a multisystem disorder that can cause damage to the brain, brain stem and spinal cord, eventually resulting in extensive brain damage. The condition also progressively affects the vision, causing abnormal and involuntary eye movements, paralysis of the muscles within or surrounding the eye, and severely reduced vision. Affected children have a lack of muscle coordination and weakness which affects physical movements. This may cause difficulty swallowing, speaking and chewing, paralysis of the face, and progressive wasting of the body muscle. Patients may become wheelchair dependent. Thought processes and physical movements deteriorate over time and patients have a shortened life expectancy.

1.11. There is currently no curative treatment available for COXPD7. The management of the condition is limited, and may involve the use of a wheelchair, feeding tube, and eventually reliance on a mechanical ventilator to breathe, as well as certain medications.

1.12. The committee noted that COXPD7 is one of over 35 similar types of the condition. The committee noted the recommendation of the peer reviewer, that a further 33 additional subtypes of COXPD should be considered alongside the application for COXPD7.

1.13. The committee noted the advice of the specialist advisor who stated that COXPD types 1-4 and 7-36 all share a similar phenotype and are all inherited in an autosomal recessive manner (with the exception of type 6, which has not been included in the application for PGD approval). The specialist adviser confirmed that as the additional 33 sub types all have a similar phenotype it would be reasonable to consider their application on this basis.

1.14. The committee also noted the peer reviewer's suggestion that Spastic Paraplegia 55 OMIM #615035, is also considered alongside this application. Spastic Paraplegia 55 is associated with a mutation in the C12orf65gene and a milder phenotype than COXPD7, which can lead to significant visual and motor disability even if not necessarily life-shortening.

2. Decision

2.1. The committee considered that, in the worst-case scenario COXPD7, OMIM #613559 is a serious multisystem disorder presenting at birth. It is a life limiting condition and presents with growth retardation, generalised muscle weakness, liver dysfunction, enlarged weak heart muscle with poor contraction and brain dysfunction presenting as epilepsy. There is no cure for the condition and patients have a shortened life expectancy. The condition is relentlessly progressive and can lead to death in infancy.

2.2. The committee considered the recommendation that COXPD types1-4 and 8-36 are also added to the list of conditions for which PGD can be applied. The committee noted the risk of inheriting these conditions is 25% in each pregnancy if each parent carries a relative mutation. In the worst-case scenario, these conditions are associated with features that can include growth retardation, microcephaly, intellectual disability, spasticity, cardiac and liver dysfunction and can result in death within the first weeks or years of life.

2.3. With regard to Spastic Paraplegia 55, the committee welcomed the advice of the specialist advisor and agreed that as this condition was of a different phenotype to COXPD types 1-4 and 7-36, it was not appropriate to consider this additional condition under this application.

2.4. 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, that a person with the abnormality will, given the conditions' worst symptoms, have or develop a serious physical disability, a serious illness or any other serious medical condition.

2.5. The committee was therefore satisfied that the following condition meets the criteria for testing under paragraph 1ZA(1)(b) and (2) of Schedule 2 of the Act. The committee agreed to authorise testing for:

- Combined oxidative phosphorylation deficiency 7 OMIM# 613559

The committee also agreed to authorise testing for the following conditions:

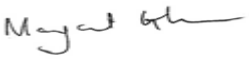
- Combined oxidative phosphorylation deficiency 1 OMIM# 609060
- Combined oxidative phosphorylation deficiency 2 OMIM# 610498
- Combined oxidative phosphorylation deficiency 3 OMIM# 610505
- Combined oxidative phosphorylation deficiency 4 OMIM# 610678

- Combined oxidative phosphorylation deficiency 8 OMIM# 614096
- Combined oxidative phosphorylation deficiency 9 OMIM# 614582
- Combined oxidative phosphorylation deficiency 10 OMIM# 614702
- Combined oxidative phosphorylation deficiency 11 OMIM# 614922
- Combined oxidative phosphorylation deficiency 12 OMIM# 614924
- Combined oxidative phosphorylation deficiency 13 OMIM# 614932
- Combined oxidative phosphorylation deficiency 14 OMIM# 614946
- Combined oxidative phosphorylation deficiency 15 OMIM# 614947
- Combined oxidative phosphorylation deficiency 16 OMIM# 615395
- Combined oxidative phosphorylation deficiency 17 OMIM# 615440
- Combined oxidative phosphorylation deficiency 18 OMIM# 615578
- Combined oxidative phosphorylation deficiency 19 OMIM# 615595
- Combined oxidative phosphorylation deficiency 20 OMIM# 615917
- Combined oxidative phosphorylation deficiency 21 OMIM# 615918
- Combined oxidative phosphorylation deficiency 22 OMIM# 616045
- Combined oxidative phosphorylation deficiency 23 OMIM# 616198
- Combined oxidative phosphorylation deficiency 24 OMIM# 616239
- Combined oxidative phosphorylation deficiency 25 OMIM# 616430
- Combined oxidative phosphorylation deficiency 26 OMIM# 616539
- Combined oxidative phosphorylation deficiency 27 OMIM# 616672
- Combined oxidative phosphorylation deficiency 28 OMIM# 616794
- Combined oxidative phosphorylation deficiency 29 OMIM# 616811
- Combined oxidative phosphorylation deficiency 30 OMIM# 616974
- Combined oxidative phosphorylation deficiency 31 OMIM# 617228
- Combined oxidative phosphorylation deficiency 32 OMIM# 617664
- Combined oxidative phosphorylation deficiency 33 OMIM# 617713
- Combined oxidative phosphorylation deficiency 34 OMIM# 617872
- Combined oxidative phosphorylation deficiency 35 OMIM# 617873
- Combined oxidative phosphorylation deficiency 36 OMIM# 617950

3. Chairs signature

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

Signature



Name

Margaret Gilmore

Date

24 April 2019