Statutory Approvals Committee – minutes

Centre 0102 (Guys Hospital)

Pre-implantation Genetic Diagnosis (PGD) application for Ectrodactyly, Ectodermal Dysplasia and Cleft Lip / Palate syndrome 3 (EEC3), OMIM #604292

Thursday, 22 March 2018

HFEA, 10 Spring Gardens, London, SW1A 2BU

Committee members	Margaret Gilmore (Chair) Bobbie Farsides (Deputy Chair) Anne Lampe Ruth Wilde Anthony Rutherford	
Members of the Executive	Bernice Ash Dee Knoyle Paula Robinson Catherine Burwood	Committee Secretary Committee Secretary (Observer) Head of Planning and Governance (Observer) Senior Governance Manager (Observer)
Specialist Adviser	Dr Jenny Carmichael	
Legal Adviser	Sarah Ellson	FieldFisher 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 UK Statement
- Comment from the centre regarding peer review

1. Consideration of application

1.1. The committee welcomed the advice of its Specialist Adviser, Dr Jenny Carmichael, who confirmed that the condition was as described in the papers.

1.2. The committee noted that the description in the application for PGD for Ectrodactyly, Ectodermal Dysplasia and Cleft Lip / Palate syndrome 3 (EEC3), OMIM #604292 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 the condition is inherited in an autosomal dominant pattern which means there is a 50% chance of an embryo being affected with the condition, if either parent has a relevant mutation.

1.8. The committee noted EEC3 is a genetic condition characterised by multiple anomalies which presents with a variable clinical picture. Most features of the condition are apparent at birth, and some may be detected antenatally.

1.9. The committee noted that symptoms include facial clefts of the lip and/or palate which are frequently bilateral and severe, absent fingers /toes in the middle of the hands and feet, ectodermal abnormalities such as dry skin, thin/absent hair, underdeveloped or absent teeth, congenital anomalies of the genitourinary tract, short stature, hypogonadism and narrowing of the nasal passages.

1.10. The presence of cleft lip and palate may be associated with feeding difficulties. The cleft will require surgical repair, involving several different surgical procedures. Bone grafting and orthodontic treatment might be required later. Clefting may be associated with conductive hearing loss, speech, dental and psychological problems and will require multidisciplinary care and long term follow up over years.

1.11. The ectodermal dysplasia may be associated with increased risk of eye and chest infections and the dry skin condition will require treatment with moisturisers and topical creams. The urinary tract abnormalities require monitoring and prophylactic antibiotics and can sometimes lead to renal failure with the need for transplantation.

1.12. Limb defects will often require surgical intervention to improve function of the hands, but less treatment is available for significant abnormalities of the hands/feet. Feet can be broad with a central cleft and finding footwear may be difficult.

1.13. The committee noted that penetrance is almost 100%

1.14. The features of this condition are very visible and this can result in a high psychological burden. Multiple and extensive surgeries are often required, impacting on the family and quality of life.

1.15. The committee noted the Peer Reviewer described mutations in the same gene as is affected in EEC3 (TP63), causing similar conditions to EEC3, as well as another EEC subtype caused by an unknown gene mutation. These conditions are stated below:

Condition	OMIM	Gene affected
Ectrodactyly, Ectodermal Dysplasia, and Cleft Lip/Palate Syndrome 1; EEC1	#129900	Unknown chromosome 7
Rapp-Hodgkin Syndrome; RHS	#129400	TP63
ADULT Syndrome	#102385	TP63

1.16. The committee noted the Person Responsible (PR) at the centre had confirmed that they would like the conditions Rapp-Hodgkin Syndrome OMIM #129400 and ADULT Syndrome, OMIM #103285 to also be considered as conditions for which PGD can be applied, but not EEC1.

1.17. The committee noted the inspectorate's request to consider whether Ectrodactyly, Ectodermal Dysplasia and Cleft Lip/Palate syndrome 3 (EEC3), OMIM #604292 should be approved for inclusion on the PGD List. Thereafter, the inspectorate requested that the committee to consider approving the conditions Rapp-Hodgkin Syndrome, OMIM #129400 and ADULT Syndrome, OMIM #103285 for inclusion on the PDG list. The committee agreed to consider the application on this basis.

1.18. The committee noted the Executive's recommendation to not consider approving EEC1 for PGD as the mutated gene that causes the condition is unknown. The centre had also requested that the condition is not considered for PGD as part of the centre's application; the committee agreed with the Executive's recommendation.

2. Decision

2.1. The committee considered that, in the worst case scenario, Ectrodactyly, Ectodermal Dysplasia and Cleft Lip/Palate syndrome 3 (EEC3), OMIM #604292, is serious given the condition may result in multiple physical difficulties and can be associated with a high psychological burden, and can severely impact on the child's life, carrying through to adulthood. The impact of pain and multiple surgeries is also significant. The condition severely impacts quality of life and the family.

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 condition Ectrodactyly, Ectodermal Dysplasia and Cleft Lip/Palate syndrome 3 (EEC3), OMIM #604292, meets the criteria for testing under paragraph 1ZA(1)(b) and (2) of Schedule 2 of the Act.

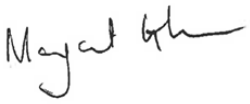
2.3. The committee agreed to authorise testing for Ectrodactyly, Ectodermal Dysplasia and Cleft Lip/Palate syndrome 3 (EEC3), OMIM #604292. The committee also agreed that given that they have a similar phenotype and are caused by mutations in the same gene, to authorise testing for the following conditions:

Rapp-Hodgkin Syndrome; RHS, OMIM #129400
Adult Syndrome, OMIM #103285

3. Chairs signature

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

Signature



Name

Margaret Gilmore

Date

9 April 2018