Statutory Approvals Committee – minutes

Centre 0102 (Guy's Hospital)

Pre-implantation Genetic Diagnosis (PGD) application for

Intellectual Disability X-linked 102 (MRX102), OMIM #300958

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
- One additional academic paper from the centre
- One 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 X-linked Mental Retardation (DDX3X gene), OMIM #300958 is consistent with the peer review. The committee noted that the Peer Reviewer referred to the condition as DDX3X associated intellectual disability, while the condition is named on the OMIM website as Mental Retardation, X-linked 102 (MRX102), OMIM #300958. The committee agreed that the condition should be named Intellectual Disability, X-linked 102 (MRX102), OMIM #300958.

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 X-linked pattern which means there is a 50% chance of a child inheriting the affected X chromosome. 50% of males will be affected and 50% of females will be carriers, although symptoms of varying severity are also seen in female carriers.

1.8. The committee noted that the condition is an inherited form of intellectual disability characterised by serious limitations in intellectual functioning and adaptive behaviour, starting from infancy. The condition is caused by a mutation in the DDX3X gene on the X chromosome. As an X-linked condition, it affects males more than females, indeed all males inheriting a DDX3X mutation will be affected with the condition

1.9. The main symptom of the condition is intellectual disability. Affected individuals can also present with features including: hypotonia (low muscle tone), microcephaly (smaller head), movement disorders, brain structure anomalies, epilepsy, dysmorphic features, cleft lip and palate, hearing loss and visual problems.

1.10. The committee noted that based on the limited data currently available, the condition appears to be fully penetrant.

1.11. There is no curative treatment for X-Linked Intellectual Disability. Medication can be given for epilepsy and cleft lip and palate can be surgically repaired. Treatment cannot however address most other symptoms of the condition, such as intellectual disability and microcephaly, although support therapies can sometimes assist. The condition is not treatable and the associated features can make the functions of day-to-day living extremely difficult. Significantly, affected individuals lack independence and their quality of life can be poor.

1.12. The committee noted the inspectorate's request to consider whether Intellectual Disability, X-linked 102 (MRX102), OMIM #300958 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 noted that this is a rare condition with very few cases reported in the literature. Given the limited data, but also what is known about the possibility of x-linked conditions potentially giving rise to serious disability, illness, or other medical conditions in worst case scenarios in females as well as in males, the committee decided that any decision to authorise testing should apply to testing embryos regardless of sex.

2.2. The committee considered that Intellectual Disability, X-linked 102 (MRX102), OMIM #300958 is serious given the combination of symptoms associated with the condition, including hearing loss, brain structure anomalies and epilepsy. The committee considered that this condition would have a severe impact on the life of the affected individual and their family.

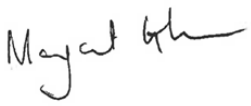
2.3. The committee had regard to its explanatory note and confirmed that, on the basis of the information presented, it was satisfied that there is a particular risk that an embryo may have the abnormality in question and that there is a significant risk, given the condition's worst symptoms, that a 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 Intellectual Disability, X-linked 102 (MRX102), OMIM #300958 meets the criteria for testing under paragraph 1ZA(1)(b) and (2) of Schedule 2 of the Act.

2.4. The committee agreed to authorise testing for Intellectual Disability, X-linked 102 (MRX102), OMIM #300958.

3. Chair's signature

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

Signature



Name

Margaret Gilmore

Date

9 April 2018