# Statutory Approvals Committee – minutes

## Centre 0102 (Guy's Hospital)

## Pre-implantation Genetic Diagnosis (PGD) application for Severe / Profound Global Developmental Delay and Epilepsy (GRM7 gene, OMIM *604101)

Thursday, 30 August 2018

HFEA, 10 Spring Gardens, London, SW1A 2BU

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| Committee members | Margaret Gilmore (Chair)<br>Bobbie Farsides (Deputy Chair)<br>Anne Lampe<br>Ruth Wilde<br>Anthony Rutherford | |
| Members of the Executive | Bernice Ash<br>Paula Robinson<br>Catherine Burwood | Committee Secretary<br>Head of Planning and Governance (Observer)<br>Senior Governance Manager (Observer) |
| Specialist Adviser | Professor Peter Turnpenny | |
| Legal Adviser | Jane Williams | Mills & Reeve LLP |
| Observers | Stevan Cirkovic | Policy Officer (Induction) |

## 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
- Two academic papers (one with an annex) regarding the condition
- SAC minutes, 30 March 2017, PGD for multiple early infantile epileptic encephalopathy types
- SAC minutes, 29 June 2017, PGD for early infantile epileptic encephalopathy type 48

## 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 the application from the centre was for Severe / Profound Global Developmental Delay and Epilepsy (GRM7 gene), OMIM *604101. An OMIM number for the phenotype has not yet been allocated for this condition. Thus, the OMIM number provided (604101) is for the GRM7 gene only. Therefore, the number should be expressed as *604101, rather than as it appears in the application form (#604101).

**1.3.** The Specialist Adviser confirmed that the status of this OMIM number, and the lack of a designated phenotype number within OMIM, is likely to be due to the recent description of the condition in the medical literature, as well as its rarity. Currently, there is also no proposed or accepted name for this condition. The committee agreed to the condition being named as Severe / Profound Global Developmental Delay and Epilepsy (GRM7 gene), OMIM *604101.

**1.4.** The committee noted that the description in the application of Severe / Profound Global Developmental Delay and Epilepsy (GRM7 gene), OMIM *604101 is consistent with the peer review.

**1.5.** The committee noted that an opinion on this application and the impact of the condition on individuals, families and carers was requested from Genetic Alliance UK. At the time of submission of the papers to the committee, the opinion had not been provided,

**1.6.** 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.

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

**1.8.** 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'.

**1.9.** The committee noted that the condition 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 both parents have a relevant mutation.

**1.10.** The committee noted that Severe / Profound Global Developmental Delay and Epilepsy (GRM7 gene), OMIM *604101 is a very rare condition resulting from homozygous mutations in the Glutamate Receptor Metabotropic 7 (GRM7) gene. Only three affected families have been reported so far, each with different mutations but a similar phenotype, as described in the two academic papers submitted by the centre making the application. Mutations in the GRM7 gene cause severe to profound global developmental delay, hypotonia (poor muscle tone) and seizures, with progressive abnormalities of the brain. Babies present with epilepsy in early infancy and have shortened life expectancy

**1.11.** The main symptoms of the condition are severe epilepsy, profound hypotonia, severe to profound developmental delay, microcephaly and progressive brain anomalies (hypomyelination and brain atrophy). Affected individuals will never learn to walk or talk. Penetrance appears to be 100%.

**1.12.** The committee noted that this is a very serious, incurable condition that causes severe to profound intellectual disability and epilepsy. Treatment is symptomatic only.

**1.13.** The executive noted that there is no OMIM entry for the condition, given its rarity and recent characterisation, and no subtypes are listed. The condition as described in the application and by the peer reviewer appears to be similar to early infantile epileptic encephalopathies (EIEE), multiple types of which are already approved for PGD. The committee noted the minutes of these decisions, acknowledging that Severe / Profound Global Developmental Delay and Epilepsy (GRM7 gene), OMIM *604101 may not necessarily be associated with early death in the manner of some of the EIEE types, though there is a paucity of information in this respect at present.

**1.14.** The committee noted the inspectorate's request to consider whether Severe / Profound Global Developmental Delay and Epilepsy (GRM7 gene), OMIM *604101 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, in the worst case scenario, Severe / Profound Global Developmental Delay and Epilepsy (GRM7 gene), OMIM *604101 is a serious condition given its early onset and the possible shortened life expectancy. Symptoms are debilitating, progressive and severe. The committee considered this condition would severely impact on the individual's quality of life.

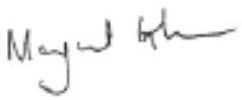
**2.2.** The committee had regard to its explanatory note and confirmed that, on the basis of the information presented, it was satisfied that there is a particular risk that an embryo may have the abnormality in question and that there is a significant risk, given the condition's worst symptoms, that 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 condition Severe / Profound Global Developmental Delay and Epilepsy (GRM7 gene), OMIM *604101 meets the criteria for testing under paragraph 1ZA(1)(b) and (2) of Schedule 2 of the Act and agreed to authorise testing.

**2.3.** The committee agreed to authorise testing for Severe / Profound Global Developmental Delay and Epilepsy (GRM7 gene) OMIM *604101.

## 3. Chairs signature

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

### Signature



### Name

Margaret Gilmore

### Date

26 September 2018