Statutory Approvals Committee – minutes

Centre 0102 (Guys Hospital)

Pre-implantation Genetic Diagnosis (PGD) application for Primary Microcephaly 1 (MCPH1) OMIM #251200; (MCPH2), OMIM #604317; (MCPH3), OMIM #604804; (MCPH4), OMIM #604321; (MCPH5), OMIM #608716; (MCPH6), OMIM #608393; (MCPH7), OMIM #612703; (MCPH8), OMIM #614673; (MCPH9), OMIM #614852; (MCPH10), OMIM #615095; (MCPH11), OMIM #615414; (MCPH12), OMIM #616080; (MCPH13), OMIM #616051; (MCPH14), OMIM #616402; (MCPH15), OMIM #616486; (MCPH16), OMIM #616681; (MCPH17), OMIM #617090; (MCPH18), OMIM #617520; (MCPH19), OMIM #617800; (MCPH20), OMIM #617914; (MCPH21), OMIM #617983; (MCPH22), OMIM #617984; (MCPH23), OMIM #617985; (MCPH24), OMIM #618179; (MCPH25), OMIM #618351.

Thursday, 31 October 2019

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

Committee members	Margaret Gilmore (Chair) Rachel Cutting Emma Cave	
Members of the Executive	Moya Berry Catherine Burwood	Committee Officer Licensing Manager
Specialist Adviser	Professor Mary Porteous	
Legal Adviser	Ros Foster	Brown Jacobson LLP
Observer	Alistair Robertson	DAC Beachcroft LLP

Declarations of interest

- Members of the committee declared that they had no conflicts of interest in relation to this item.

Apologies:

- Apologies were received from Tony Rutherford and Bobbie Farsides.

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

1. Consideration of application

1.1. The committee welcomed the advice of its specialist adviser, Professor Mary Porteous, who confirmed that the conditions were as described in the papers.

1.2. The committee noted that the description in the PGD application for Primary Microcephaly 1 (MCPH1), OMIM #251200; MCPH2, OMIM #604317; MCPH3, OMIM #604804; MCPH4, OMIM #604321; MCPH5, OMIM #608716; MCPH6, OMIM #608393; MCPH7, OMIM #612703; MCPH8, OMIM #614673; MCPH9, OMIM #614852; MCPH10, OMIM #615095; MCPH11, OMIM #615414; MCPH12, OMIM #616080; MCPH13, OMIM #616051; MCPH14, OMIM #616402; MCPH15, OMIM #616486; MCPH16, OMIM #616681; MCPH17, OMIM #617090; MCPH18, OMIM #617520; MCPH19, OMIM #617800; MCPH20, OMIM #617914; MCPH21, OMIM #617983; MCPH22, OMIM #617984; MCPH23, OMIM #617985; MCPH24, OMIM #618179; and MCPH25, OMIM #618351 is consistent with the peer review.

1.3. The committee agreed that the Primary Microcephaly conditions as listed in section 1.2 will be termed collectively as MCPH 1-25 for the purpose of these minutes.

1.4. The committee noted that the conditions being applied for are not on the list of approved PGD conditions.

1.5. The committee noted that the Genetic Alliance UK statement provided a perspective on the impact of the conditions on patients, their families and carers.

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 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'.

1.8. The committee noted that MCPH 1-25, with the exception of MCPH18, are inherited in an autosomal recessive pattern, which means there is a 25% chance of an embryo being affected by the condition in each pregnancy if each parent has a relevant mutation. MCPH18

is inherited in autosomal dominant pattern, which means there is a 50% chance of an embryo being affected by the condition in each pregnancy if either parent has a relevant mutation.

1.9. The committee noted the penetrance of the conditions can be 100%.

1.10. The MCPH 1-25 conditions are characterised by abnormal brain development and the head and brain are severely reduced in size from birth. Those affected may develop epilepsy, moderate to severe intellectual disability and demonstrate delayed development of speech and motor skills.

1.11. There is no cure for these conditions and treatment is supportive.

1.12. The committee noted the recommendation of the peer reviewer not to include the following conditions on the list for which PGD can be applied. These are: MCPH11, OMIM #615414, MCPH 12, OMIM #616080, MCPH 23, OMIM #617985 and MCPH 24, OMIM #618351 as these conditions are of a milder phenotype or have only been reported in one family and might not have been caused by the gene in question. MCPH18, OMIM #617520 is also not recommended for inclusion as this condition is also associated with macrocephaly and is of a milder phenotype.

1.13. The committee noted and agreed to the executive's request to consider MCPH 1-25, with the exception of MCPH11, OMIM #615414; MCPH12, OMIM #616080; MCPH18, OMIM #617520; MCPH23, OMIM #617985; and MPCH24, OMIM #618179.

2. Decision

2.1. The committee considered that, in the worst-case scenario MCPH 1-10, 13-17, 19-22 and 25 are serious neurological conditions which present prenatally or at birth. There is no cure for these conditions. The committee considered the possible adverse impact on the quality of life for patients living with these conditions.

2.2. The committee agreed that as MCPH11, OMIM #615414; MCPH12, OMIM #616080; MCPH18, OMIM #617520; MCPH23, OMIM #617985; and MPCH24, OMIM #618179 are different to the above MCPH conditions, it was not appropriate to consider these types under this application.

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 abnormalities in question and that there is a significant risk, that a person with such an abnormality will, given the conditions' worst symptoms, have or develop a serious physical disability, a serious illness or any other serious medical condition.

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

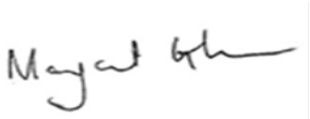
- Primary Microcephaly 1 (MCPH1), OMIM #251200
- Primary Microcephaly 2 (MCPH2), OMIM #604317
- Primary Microcephaly 3 (MCPH3), OMIM #604804
- Primary Microcephaly 4 (MCPH4), OMIM #604321
- Primary Microcephaly 5 (MCPH5), OMIM #608716
- Primary Microcephaly 6 (MCPH6), OMIM #608393
- Primary Microcephaly 7 (MCPH7), OMIM #612703

- Primary Microcephaly 8 (MCPH8), OMIM #614673
- Primary Microcephaly 9 (MCPH9), OMIM #614852
- Primary Microcephaly 10 (MCPH10), OMIM #615095
- Primary Microcephaly 13 (MCPH13), OMIM #616051
- Primary Microcephaly 14 (MCPH14), OMIM #616402
- Primary Microcephaly 15 (MCPH15), OMIM #616486
- Primary Microcephaly 16 (MCPH16), OMIM #616681
- Primary Microcephaly 17 (MCPH17), OMIM #617090
- Primary Microcephaly 19 (MCPH19), OMIM #617800
- Primary Microcephaly 20 (MCPH20), OMIM #617914
- Primary Microcephaly 21 (MCPH21), OMIM #617983
- Primary Microcephaly 22 (MCPH22), OMIM #617984
- Primary Microcephaly 25 (MCPH25), OMIM #618351

3. Chairs signature

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

Signature



Name
Margaret Gilmore

Date
18 November 2019