Statutory Approvals Committee - minutes

Centre 0101 (CARE Nottingham)

Preimplantation Genetic Testing for Monogenic Disorders (PGT-M) - application for:

Charcot-Marie-Tooth Disease, Type 4C (CMT4C), OMIM #601596
Charcot-Marie-Tooth Disease, Type 4A (CMT4A), OMIM #214400
Charcot-Marie-Tooth Disease, Type 4B1(CMT4B1), OMIM #601382
Charcot-Marie-Tooth Disease, Type 4B2 (CMT4B2), OMIM #604563
Charcot-Marie-Tooth Disease, Type 4B3 (CMT4B3), OMIM #615284
Charcot-Marie-Tooth Disease, Type 4D (CMT4D), OMIM #601455
Charcot Marie-Tooth Disease, Type 4E (CMT4E), OMIM #602253
Charcot-Marie-Tooth Disease, Type 4F (CMT4F), OMIM #614895
Charcot-Marie-Tooth Disease, Type 4G (CMT4G), OMIM #605285
Charcot-Marie-Tooth Disease, Type 4H (CMT4H), OMIM #609311
Charcot-Marie-Tooth Disease, Type 4J (CMT4J), OMIM #611228
Charcot-Marie-Tooth Disease, Type 4K (CMT4K), OMIM #616684

Date:	26 August 2021
Venue:	HFEA, 2nd Floor, 2 Redman Place, London E20 1JQ via Microsoft Teams
Committee Members:	Margaret Gilmore (Chair) Emma Cave Anne Lampe Ruth Wilde Tim Child
Specialist Adviser:	Alan Fryer
Legal Adviser:	Tom Rider - FieldFisher LLP
Members of the Executive:	Moya Berry - Committee Officer Catherine Burwood - Licensing Manager
Apologies:	No apologies were received for the meeting

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:

- HFEA Code of Practice 9th edition
- Standard Licensing and Approvals Pack

The following papers were considered by the committee:

- Executive Summary
- PGT-M Application Form
- Redacted Peer Review
- 2021-03-25 Statutory Approvals Committee Minutes for Charcot Marie Tooth Disease, Type 4J, OMIM #611228

1. Consideration of application

1.1. The committee welcomed the advice of its specialist adviser, Dr Alan Fryer, who confirmed that the conditions were as described in the papers.

1.2. The committee noted that the description in the PGT-M application of Charcot-Marie-Tooth Disease, Type 4C (CMT4C), OMIM #601596; Charcot-Marie-Tooth Disease, Type 4A (CMT4A), OMIM #214400; Charcot-Marie-Tooth Disease, Type 4B1(CMT4B1), OMIM #601382; Charcot-Marie-Tooth Disease, Type 4B2 (CMT4B2), OMIM #604563; Charcot-Marie-Tooth Disease, Type 4B3 (CMT4B3), OMIM #615284; Charcot-Marie-Tooth Disease, Type 4D (CMT4D), OMIM #601455; Charcot Marie-Tooth Disease, Type 4E (CMT4E), OMIM #602253; Charcot-Marie-Tooth Disease, Type 4F (CMT4F), OMIM #614895; Charcot-Marie-Tooth Disease, Type 4G (CMT4G), OMIM #605285; Charcot-Marie-Tooth Disease, Type 4H (CMT4H), OMIM #609311; Charcot-Marie-Tooth Disease, Type 4J (CMT4J), OMIM #611228 and Charcot-Marie-Tooth Disease, Type 4K (CMT4K), OMIM #616684 is consistent with the peer review.

1.3. The committee noted that the conditions being applied for are not on the list of approved PGT-M conditions with the exception of Charcot-Marie-Tooth Disease, Type 4J (CMT4J), OMIM #611228, which is on the approved PGT-M list and therefore an application is not required.

1.4. The committee noted that a Genetic Alliance (UK) statement had not been provided for this application.

1.5. The committee had regard to its decision tree. The committee noted that the centre is licensed to carry out PGT-M. The committee was also satisfied that the centre has experience of carrying out PGT-M and that generic patient information about its PGT-M 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 Charcot-Marie-Tooth Disease, Type 4C (CMT4C), OMIM #601596; Charcot-Marie-Tooth Disease, Type 4A (CMT4A), OMIM #214400; Charcot-Marie-Tooth Disease, Type 4B1(CMT4B1), OMIM #601382; Charcot-Marie-Tooth Disease, Type 4B2 (CMT4B2), OMIM #604563; Charcot-Marie-Tooth Disease, Type 4B3 (CMT4B3), OMIM #615284; Charcot-Marie-Tooth Disease, Type 4D (CMT4D), OMIM #601455; Charcot Marie-Tooth Disease, Type 4E (CMT4E), OMIM #602253; Charcot-Marie-Tooth Disease, Type 4F (CMT4F), OMIM #614895; Charcot-Marie-Tooth Disease, Type 4G (CMT4G), OMIM #605285; Charcot-Marie-Tooth Disease, Type 4H (CMT4H), OMIM #609311 and Charcot-Marie-Tooth Disease, Type 4K (CMT4K), OMIM #616684 are inherited in an autosomal recessive manner which means there is 25% chance of having an affected child in each pregnancy if each parent has a relevant mutation.

1.8. The committee noted that the penetrance of the conditions is close to 100%.

1.9. Charcot-Marie-Tooth Disease, Type 4C (CMT4C), OMIM #601596; Charcot-Marie-Tooth Disease, Type 4A (CMT4A), OMIM #214400; Charcot-Marie-Tooth Disease, Type 4B1(CMT4B1), OMIM #601382; Charcot-Marie-Tooth Disease, Type 4B2 (CMT4B2), OMIM #604563; Charcot-Marie-Tooth Disease, Type 4B3 (CMT4B3), OMIM #615284; Charcot-Marie-Tooth Disease, Type 4D (CMT4D), OMIM #601455; Charcot Marie-Tooth Disease, Type 4E (CMT4E), OMIM #602253; Charcot-Marie-Tooth Disease, Type 4F (CMT4F), OMIM #614895; Charcot-Marie-Tooth Disease, Type 4G (CMT4G), OMIM #605285, Charcot-Marie-Tooth Disease, Type 4H (CMT4H), OMIM #609311and Charcot-Marie-Tooth Disease, Type 4K (CMT4K), OMIM #616684, are characterised by the onset of progressive muscle weakness and sensory abnormalities in childhood. Type 4C is notably characterized by severe spine deformities (scoliosis or kyphoscoliosis) and foot deformities (pes cavus, pes planus, or pes valgus) that typically present in the first decade of life or early adolescence and can be disabling and may require surgery. Other findings can include cranial nerve involvement (most commonly tongue involvement, facial weakness, hearing impairment, dysarthria – unclear speech) and respiratory problems/insufficiency. Limb involvement usually develops in the first decade or adolescence, but occasionally manifests as delay in onset of independent ambulation in early childhood. The neuropathy is slowly progressive with some individuals becoming wheelchair dependent because of involvement of the proximal lower limbs.

1.10. The other types of CMT4 are characterised by progressive limb involvement, with affected children and teenagers often becoming wheelchair dependent as a result of muscle weakness and deformities of the feet and spine. Sensory abnormalities can result in complex pain syndromes and render joints more susceptible to trauma. Scoliosis (curvature of the spine), kyphosis (exaggerated, forward rounding of the back), and deformation of the bones of the feet can occur and cause significant pain and disability. Involvement of respiratory muscles may contribute to premature death whilst tongue paralysis may cause significant speech and swallowing problems. Congenital glaucoma occurs in type 4B2.

1.11. There is no cure for the conditions and those affected may require multiple medical and surgical interventions to help ameliorate the symptoms.

1.12. The committee noted the executive's request to consider Charcot-Marie-Tooth Disease, Type 4C (CMT4C), OMIM #601596 Charcot-Marie-Tooth Disease, Type 4A (CMT4A), OMIM #214400 Charcot-Marie-Tooth Disease, Type 4B1(CMT4B1), OMIM #601382; Charcot-Marie-Tooth Disease, Type 4B2 (CMT4B2), OMIM #604563; Charcot-Marie-Tooth Disease, Type 4B3 (CMT4B3), OMIM #615284; Charcot-Marie-Tooth Disease, Type 4D (CMT4D), OMIM #601455; Charcot Marie-Tooth Disease, Type 4E (CMT4E), OMIM #602253; Charcot-Marie-Tooth Disease, Type 4F (CMT4F), OMIM #614895; Charcot-Marie-Tooth Disease, Type 4G (CMT4G), OMIM #605285; Charcot-Marie-Tooth Disease, Type 4H (CMT4H), OMIM #609311 and Charcot-Marie-Tooth Disease, Type 4K (CMT4K), OMIM #616684 for inclusion on the list of conditions approved for PGT-M. The committee agreed to consider the application on this basis.

2. Decision

2.1. The committee considered that, in the worst-case scenario, Charcot-Marie-Tooth Disease, Type 4C (CMT4C), OMIM #601596; Charcot-Marie-Tooth Disease, Type 4A (CMT4A), OMIM #214400; Charcot-Marie-Tooth Disease, Type 4B1(CMT4B1), OMIM #601382; Charcot-Marie-Tooth Disease, Type 4B2 (CMT4B2), OMIM #604563; Charcot-Marie-Tooth Disease, Type 4B3 (CMT4B3), OMIM #615284; Charcot-Marie-Tooth Disease, Type 4D (CMT4D), OMIM #601455; Charcot Marie-Tooth Disease, Type 4E (CMT4E), OMIM #602253; Charcot-Marie-Tooth Disease, Type 4F (CMT4F), OMIM #614895; Charcot-Marie-Tooth Disease, Type 4G (CMT4G), OMIM #605285 Charcot-Marie-Tooth Disease, Type 4H (CMT4H), OMIM #609311 and Charcot-Marie-Tooth Disease, Type 4K (CMT4K), OMIM #616684 are severe and slowly progressive conditions that present from early childhood, and can result in significant mobility issues. Those affected may become wheelchair dependent by adolescence. In some cases there is involvement of the facial nerves affecting both speech and swallowing. The committee considered the potential significant psychological, emotional, and physical implications on the quality of life of those affected by the conditions.

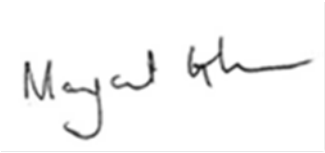
2.2. The committee was therefore satisfied that the following conditions meet the criteria for testing under paragraph 1ZA(1)(b) and (2) of Schedule 2 of the Act. The committee agreed to authorise testing for:

- Charcot-Marie-Tooth Disease, Type 4A (CMT4A), OMIM #214400
- Charcot-Marie-Tooth Disease, Type 4B1(CMT4B1), OMIM #601382
- Charcot-Marie-Tooth Disease, Type 4B2 (CMT4B2), OMIM #604563
- Charcot-Marie-Tooth Disease, Type 4B3 (CMT4B3), OMIM #615284
- Charcot-Marie-Tooth Disease, Type 4C (CMT4C), OMIM #601596
- Charcot-Marie-Tooth Disease, Type 4D (CMT4D), OMIM #601455
- Charcot Marie-Tooth Disease, Type 4E (CMT4E), OMIM #602253
- Charcot-Marie-Tooth Disease, Type 4F (CMT4F), OMIM #614895
- Charcot-Marie-Tooth Disease, Type 4G (CMT4G), OMIM #605285
- Charcot-Marie-Tooth Disease, Type 4H (CMT4H), OMIM #609311
- Charcot-Marie-Tooth Disease, Type 4K (CMT4K), OMIM #616684

3. Chair's signature

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

Signature



Name

Margaret Gilmore

Date

21 September 2021