Statutory Approvals Committee - minutes

Centre 0201 (Edinburgh Assisted Conception Unit)

Preimplantation Genetic Diagnosis (PGD) application for Bullous Ichthyosiform Erythroderma (Epidermolytic Ichthyosis), OMIM #113800, Cyclic Ichthyosis with Epidermolytic Hyperkeratosis, OMIM #607602, Epidermolytic Palmoplantar Keratoderma, OMIM #144200, Non-epidermolytic Palmoplantar Keratoderma, OMIM #600962 and Curth-Macklin Type Ichthyosis, OMIM #145900

Date:	29 April 2021
Venue:	Microsoft Teams Meeting
Committee Members:	Margaret Gilmore (Chair) Emma Cave Ruth Wilde Jason Kasraie
Specialist Adviser:	Jenny Carmichael
Legal Adviser:	Darryn Hale – DAC Beachcroft LLP
Members of the Executive:	Moya Berry - Committee officer Catherine Burwood - Licensing Manager
Observers:	Julia Chain - HFEA Chair (Induction) Tim Child - HFEA Authority Member (Induction) Neil Ward - Mills & Reeve LLP (New Legal Adviser) (Induction)
Apologies:	No apologies were received for the meeting
Declarations of Interest:	Anne Lampe declared a conflict of interest and was not present at the meeting for this item. No other members declared a conflict 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
- PGD Application form
- Redacted Peer review
- Genetic Alliance (UK) Statement
- 2015-11-26 Licence Committee Minutes - Icthyosis histrix of Curth-Macklin, OMIM #146590
- Supporting Document provided by the Peer Reviewer - Rout et al, 2019

1. Consideration of application

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

1.2. The committee noted that the description in the PGD application for the conditions Bullous Ichthyosiform Erythroderma (Epidermolytic Ichthyosis), OMIM #113800, Cyclic Ichthyosis with Epidermolytic Hyperkeratosis, OMIM #607602, Epidermolytic Palmoplantar Keratoderma, OMIM #144200, Non-epidermolytic Palmoplantar Keratoderma, OMIM #600962 and Curth-Macklin Type Ichthyosis, OMIM #145900 are consistent with the peer review.

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

1.4. The committee also noted that in the application, an incorrect OMIM number had been assigned to Curth-Macklin Type Ichthyosis (OMIM #145900). The committee noted that the OMIM number should be OMIM #146950, and that the condition had already been approved for PGD on the 15 November 2015. Therefore, the application for Curth-Macklin Type Ichthyosis OMIM #146950 required no further progression.

1.5. The committee noted that on the OMIM website, the primary name for the condition Bullous Ichthyosiform Erythroderma, OMIM #113800 is Epidermolytic hyperkeratosis (EHK), OMIM #113800, the primary name for the condition Cyclic Ichthyosis with Epidermolytic Hyperkeratosis, OMIM #607602 is Ichthyosis, cyclic, with epidermolytic hyperkeratosis, OMIM #607602, the primary name for the condition Epidermolytic Palmoplantar Keratoderma, OMIM #144200 is Palmoplantar keratoderma, epidermolytic; EPPK OMIM #144200, and the primary name for the condition Non-epidermolytic Palmoplantar Keratoderma, OMIM #600962 is Palmoplantar keratoderma, non-epidermolytic (NEPPK), OMIM #600962.

As the OMIM website entry lists primary names for conditions, the conditions, for the purposes of this application, will be termed:

- Epidermolytic hyperkeratosis, EHK, OMIM #113800
- Ichthyosis, cyclic, with epidermolytic hyperkeratosis, ICEHK, OMIM #607602
- Palmoplantar keratoderma, epidermolytic; EPPK, OMIM #144200
- Palmoplantar keratoderma, non-epidermolytic; NEPPK, OMIM #600962

1.6. The committee noted that the Genetic Alliance (UK) statement provided a perspective on the impact of the condition on patients, their families, and carers.

1.7. 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.

1.8. 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 Epidermolytic hyperkeratosis, EHK, OMIM #113800, Ichthyosis, cyclic, with epidermolytic hyperkeratosis, ICEHK, OMIM #607602, Palmoplantar keratoderma, epidermolytic; EPPK, OMIM #144200, and Palmoplantar keratoderma, non-epidermolytic (NEPPK), OMIM #600962 are generally inherited in an autosomal dominant manner, 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. However, some mutations causing Epidermolytic hyperkeratosis, EHK, OMIM #113800 may exhibit an autosomal recessive inheritance pattern, in which case there is 25% chance of having an affected child in each pregnancy if each parent has a relevant mutation.

1.10. The committee noted that the penetrance of the conditions is 100%.

1.11. Epidermolytic hyperkeratosis, EHK, OMIM #113800, Ichthyosis, cyclic, with epidermolytic hyperkeratosis, ICEHK, OMIM #607602, Palmoplantar keratoderma, epidermolytic; EPPK, OMIM #144200, and Palmoplantar keratoderma, non-epidermolytic (NEPPK), OMIM #600962 present at or soon after birth when the skin becomes reddened and inflamed. The natural skin barrier is missing, and the infant is extremely vulnerable to fluid loss and infections. As the baby gets older the pattern of the skin pathology changes, with blistering followed by the development of thickened hard scales. The hardened skin can crack leading to pain and the potential for infection. Whilst most infants survive, the condition is extremely painful and can be life threatening due to the risk of infection and fluid loss.

1.12. There is no cure for these conditions. Treatment includes the use of various emollients and topical keratolytics aimed at expediting desquamation of skin and enhancing appearance. These topical treatments require a significant investment of time on a regular, daily basis to ameliorate the symptoms. Keratolytic agents, particularly oral retinoids, must be taken with care as skin fragility may result. In addition, medications to control chronic pain associated with the condition may not always be effective.

1.13. The committee noted the executive's request to consider Epidermolytic hyperkeratosis, EHK, OMIM #113800, Ichthyosis, cyclic, with epidermolytic hyperkeratosis, ICEHK, OMIM #607602, Palmoplantar keratoderma, epidermolytic; EPPK, OMIM #144200, and Palmoplantar keratoderma, non-epidermolytic (NEPPK), OMIM #600962, for inclusion on the list of conditions approved for PGD. The committee agreed to consider the application on this basis.

2. Decision

2.1. The committee considered that, in the worst-case scenario, Epidermolytic hyperkeratosis, EHK, OMIM #113800, Ichthyosis, cyclic, with epidermolytic hyperkeratosis, ICEHK, OMIM #607602, Palmoplantar keratoderma, epidermolytic; EPPK, OMIM #144200, and Palmoplantar keratoderma, non-epidermolytic (NEPPK), OMIM #600962, are extremely painful skin conditions that present in infancy and can result in blisters and fissures (a breakage in the skin due to cracking or splitting), that can adversely affect the normal function of everyday life. The

conditions have no effective treatment and, in some cases, may result in death due to infection and life-threatening sepsis. The committee considered the serious implications for, and the physical and psychological impact on the quality of life of, those affected by the condition.

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 that a person with such an abnormality will, given the condition's worst symptoms, have or develop a serious physical disability, a serious illness, or any other serious medical condition.

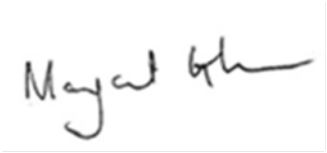
2.3. The committee was therefore satisfied that the following conditions meet the criteria for testing under paragraph 1ZA(1)(b) and (2) of Schedule 2 of the Act. The committee agreed to authorise testing for:

- Epidermolytic hyperkeratosis, EHK, OMIM #113800
- Ichthyosis, cyclic, with epidermolytic hyperkeratosis, ICEHK, OMIM #607602
- Palmoplantar keratoderma, epidermolytic; EPPK, OMIM #144200
- Palmoplantar keratoderma, non-epidermolytic; NEPPK, OMIM #600962

3. Chair's signature

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

Signature



Name

Margaret Gilmore

Date

1 June 2021