Statutory Approvals Committee - minutes

Centre 0101 (CARE Nottingham)

Preimplantation Genetic Diagnosis (PGD) application for Application to perform PGD for Nephronophthisis 2 (NPHP 2), OMIM #602088

Date:	25 February 2021
Venue:	Microsoft Teams Meeting
Committee Members:	Margaret Gilmore (Chair) Emma Cave Ruth Wilde
Specialist Adviser:	Alan Fryer
Legal Adviser:	Sarah Ellson - FieldFisher LLP
Members of the Executive:	Moya Berry - Committee officer Catherine Burwood - Licensing Manager
Observers:	Sarah Steadman - Inspector (Induction) Karen Campbell - Inspector (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 Licencing and Approvals Pack

The following papers were considered by the committee:

- Executive Summary
- PGD Application form
- Redacted Peer Review
- Peer Review - summary of other nephronophthisis condition types

1. Consideration of application

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

1.2. The committee noted that the description in the PGD application for Nephronophthisis 2, (NPHP2), OMIM #602088 is consistent with the peer review.

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

1.4. The committee noted that no Genetic Alliance (UK) statement had 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 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.

1.6. 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 Nephronophthisis 2, (NPHP2), OMIM #602088, is inherited in an autosomal recessive manner, 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.

1.8. The committee noted that the penetrance of the condition is 100%.

1.9. Nephronophthisis 2, (NPHP2), OMIM #602088 is a rare form of nephronophthisis, a condition characterised by progressive loss of kidney function. In NPHP2, children typically present with the “infantile” form of nephronophthisis. They may present in utero with oligohydramnios (reduced amniotic fluid around the baby during pregnancy), which can lead to post-natal respiratory failure and death in a small proportion of cases. More commonly survivors present with growth failure and anaemia due to renal impairment with resulting metabolic acidosis and rapidly progress to end-stage renal failure by the age of 3 years. A few patients with the condition can also exhibit non-renal features (so-called “syndromic nephronophthisis”) including retinopathy (damage to the retina of the eye), heart defects, bronchial infections, and developmental delay. Some patients present with a juvenile-onset – these children have similar symptoms and develop end stage renal failure at a median age of 13 years.

1.10. Kidney problems in children can be treated by correction of water and electrolyte imbalance, treating high blood pressure with medication, and treating anaemia. However, once progression to end stage kidney failure has occurred, they require dialysis or transplantation. If successful, transplantation can lead to life-long dependence on anti-rejection medication. If children do not receive dialysis or renal transplantation, life expectancy is extremely short, stretching to only a few years.

1.11. The committee noted the executive’s request to consider Nephronophthisis 2, (NPHP2), OMIM #602088, for inclusion on the list of conditions approved for PGD. The committee agreed to consider the application on this basis.

1.12. The committee also noted the recommendation of the peer reviewer to consider fourteen other types of conditions for inclusion on the list for which PGD can be applied and agreed to consider the application on this basis.

1.13. The condition types which are all inherited in an autosomal recessive pattern (except for Nephronophthisis 14, OMIM #614844, which may possibly exhibit both an autosomal dominant and a recessive pattern of inheritance. It was noted that those patients reported with a possible autosomal dominant mode of inheritance nevertheless had a severe syndromic form of nephronophthisis). The conditions are likely to have a penetrance close to 100% and have a high risk of end stage renal disease in childhood or early adulthood. Life expectancy is extremely short if those affected by these conditions do not receive dialysis or renal transplantation. For some of these conditions, the disorder has always been a syndromic form of nephronophthisis with involvement notably of the brain and retina. The fourteen conditions are:

- Nephronophthisis 1, (NPHP1), OMIM #256100
- Nephronophthisis 3, (NPHP3), OMIM #604387
- Nephronophthisis 4, (NPHP4), OMIM #606966
- Nephronophthisis 7, (NPHP7), OMIM #611498
- Nephronophthisis 11, (NPHP11), OMIM #613550
- Nephronophthisis 12, (NPHP12), OMIM #613820
- Nephronophthisis 13, (NPHP13), OMIM #614377
- Nephronophthisis 14, (NPHP14), OMIM #614844
- Nephronophthisis 15, (NPHP15), OMIM #614845
- Nephronophthisis 16, (NPHP16), OMIM #615382
- Nephronophthisis 18, (NPHP 18), OMIM #615862
- Nephronophthisis 19, (NPHP 19), OMIM #616217
- Nephronophthisis 20, (NPHP 20), OMIM #617271
- Nephronophthisis-like nephropathy1, OMIM #613159

2. Decision

2.1. The committee considered that, in the worst-case scenario, Nephronophthisis 2, (NPHP2), OMIM #602088, is a devastating and potentially life-limiting condition that can present in utero or early infancy. Children born with the condition will require a high level of intervention through dialysis and /or kidney transplantation, which is not without risk. The committee considered the serious implications and impact on the quality of life for those affected with the condition.

2.2. The committee considered that the following conditions can present from birth and in the worst-case scenario can result in end stage renal failure and premature death, even when patients receive treatment. The committee considered the serious physical and psychological impact on those affected with the conditions. The conditions are:

- Nephronophthisis 1, (NPHP1), OMIM #256100
- Nephronophthisis 3, (NPHP3), OMIM #604387
- Nephronophthisis 4, (NPHP4), OMIM #606966
- Nephronophthisis 7, (NPHP7), OMIM #611498
- Nephronophthisis 11, (NPHP11), OMIM #613550
- Nephronophthisis 12, (NPHP12), OMIM #613820
- Nephronophthisis 13, (NPHP13), OMIM #614377

- Nephronophthisis 14, (NPHP14), OMIM #614844
- Nephronophthisis 15, (NPHP15), OMIM #614845
- Nephronophthisis 16, (NPHP16), OMIM #615382
- Nephronophthisis 18, (NPHP 18), OMIM #615862
- Nephronophthisis 19, (NPHP 19), OMIM #616217
- Nephronophthisis 20, (NPHP 20), OMIM #617271
- Nephronophthisis-like nephropathy1, OMIM #613159

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 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.

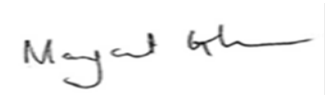
2.4. The committee was therefore satisfied that the following conditions meet the criteria for testing under paragraph 1ZA(1)(b) and (2) of Schedule 2 of the Act. The committee agreed to authorise testing for:

- Nephronophthisis 1, (NPHP1), OMIM #256100
- Nephronophthisis 2, (NPHP2), OMIM #602088
- Nephronophthisis 3, (NPHP3), OMIM #604387
- Nephronophthisis 4, (NPHP4), OMIM #606966
- Nephronophthisis 7, (NPHP7), OMIM #611498
- Nephronophthisis 11, (NPHP11), OMIM #613550
- Nephronophthisis 12, (NPHP12), OMIM #613820
- Nephronophthisis 13, (NPHP13), OMIM #614377
- Nephronophthisis 14, (NPHP14), OMIM #614844
- Nephronophthisis 15, (NPHP15), OMIM #614845
- Nephronophthisis 16, (NPHP16), OMIM #615382
- Nephronophthisis 18, (NPHP 18), OMIM #615862
- Nephronophthisis 19, (NPHP 19), OMIM #616217
- Nephronophthisis 20, (NPHP 20), OMIM #617271
- Nephronophthisis-like nephropathy1, OMIM #613159

3. Chair's signature

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

Signature



Name

Margaret Gilmore

Date

17 March 2021