Statutory Approvals Committee – minutes

Centre 0119 (Birmingham Women's Hospital)

Pre-implantation Genetic Diagnosis (PGD) application for

Primary Ciliary Dyskinesia Type 3 (CILD3), OMIM #608644

Thursday, 30 November 2017

HFEA, 10 Spring Gardens, London, SW1A 2BU

Committee members	Margaret Gilmore (Chair) Anne Lampe Anthony Rutherford Bobbie Farsides	
Members of the Executive	Bernice Ash Dee Knoyle Frances Metcalf-Head	Committee Secretary Committee Secretary (Observing) Inspections and Logistics Officer (Observing)
External adviser	Dr Alison Male	
Legal Adviser	Philip Grey	Mills & Reeve LLP
Observers		

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
- Genetic Alliance UK Statement
- Email from the centre's PGD coordinator, on behalf of the PR, to include all autosomal recessive forms of Primary Ciliary Dyskinesia within the application

1. Consideration of application

1.1. The committee welcomed the advice of its Specialist Adviser, Dr Alison Male, who confirmed that the condition was as described in the papers.

1.2. The committee noted that the description in the application for Primary Ciliary Dyskinesia Type 3 (CILD3), OMIM #608644 is consistent with the peer review.

1.3. The committee noted that the Genetic Alliance opinion provided a patient perspective and supported the application.

1.4. 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.

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

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 the condition is inherited in an autosomal recessive pattern, which means there is a 25% chance of an embryo being affected with the condition, if both parents have a relevant mutation.

1.8. The committee noted that PCD results from abnormal structure and/or function of cilia. Cilia are found in every cell and are involved in moving substances; they have multiple functions, so defects lead to a wide range of problems. Around 50% of the time, these involve major errors in the early stages of embryonic development such as incorrect placement and development of organs. In other situations, the failure of cilia movement causes severe functional compromise in tissues and organs, for example, the movement of cilia from the lungs.

1.9. In PCD, mucus and bacteria are not cleared properly resulting in respiratory distress in 75% of newborns and frequent chest infections. Frequent chest infections lead to bronchiectasis and lung scarring, with the symptoms of chronic cough with reduced exercise ability and sometimes a need for supplementary oxygen. Repeated sinus infections are common. Males are often infertile.

1.10. The committee noted that the condition is 100% penetrant if a child inherits mutations from both parents.

1.11. The committee noted that there is no curative treatment for this condition.

1.12. The committee noted the peer reviewer’s suggestion that it might consider licensing all autosomal recessive genetic causes of Primary Ciliary Dyskinesia. The PGC coordinator at the centre, on behalf of the Person Responsible (PR) had agreed to include Primary Ciliary Dyskinesia condition types, as below, to be included on the list of PGD conditions for which PGD can be applied;

Condition	OMIM	Causative mutation (OMIM)	Inheritance pattern
CILD1	#244400	DNAI1 gene (604336)	Autosomal recessive (AR)
CILD2	#606763	DNAAF3 gene (614566)	AR
CILD5	#608647	HYDIN gene (610812)	AR
CILD6	#610852	TXNDC3 gene (607421)	AR
CILD7	#611884	DNAH11 gene (603339)	AR
CILD9	#612444	DNAI2 gene (605483)	AR
CILD10	#612518	DNAAF2 gene (612517)	AR
CILD11	#612649	RSPH4A gene (612647)	AR
CILD12	#612650	RSPH9 gene (612648)	AR
CILD13	#613193	DNAAF1 gene (613190)	AR
CILD14	#613807	CCDC39 gene (613798)	AR
CILD15	#613808	CCDC40 gene (613799)	AR
CILD16	#614017	DNAL1 gene (610062)	AR
CILD17	#614679	CCDC103 gene (614677)	AR
CILD18	#614874	DNAAF5 gene (614864)	AR
CILD19	#614935	LRRC6 gene (614930)	AR
CILD20	#615067	CCDC114 gene (615038)	AR
CILD21	#615294	DRC1 gene (615288)	AR
CILD22	#615444	ZMYND10 gene (607070)	AR
CILD23	#615451	ARMC4 gene (615408)	AR
CILD24	#615481	RSPH1 gene (609314)	AR
CILD25	#615482	DYX1C1 gene (608706)	AR
CILD26	#615500	C21ORF59 gene (615494)	AR
CILD27	#615504	CCDC65 gene (611088)	AR
CILD28	#615505	SPAG1 gene (603395)	AR
CILD29	#615872	CCNO gene (607752)	AR
CILD30	#616037	CCDC151 gene (615956)	AR
CILD32	#616481	RSPH3 gene (615876)	AR
CILD33	#616726	GAS8 gene (605178)	AR
CILD34	#617091	DNAJB13 gene (610263	AR
CILD35	#617092	TTC25 gene (617095)	AR
CILD37	#617577	DNAH1 gene (603332).	AR

1.13. The committee noted the inspectorate's request to consider whether Primary Ciliary Dyskinesia Type 3 (CILD3), OMIM # 608644, should be approved for inclusion on the PGD List. The inspectorate also requested that the committee consider approving all autosomal recessive genetic causes of Primary Ciliary Dyskinesia (PCD), given that it is not possible to distinguish clinically between PCD caused by mutations in different causative genes. The committee agreed to consider the application on this basis.

2. Decision

2.1. The committee considered that Primary Ciliary Dyskinesia Type 3 (CILD3), OMIM # 608644, is serious given that there is a significant risk of death in infancy, heart and lung disease, alongside bacterial infections. The condition is socially isolating and severely impacts on the family and 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 Primary Ciliary Dyskinesia Type 3 (CILD3), OMIM # 608644 meets 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 Ciliary Dyskinesia Type 3 (CILD3), OMIM # 608644. The committee also agreed to authorise testing for the following conditions:

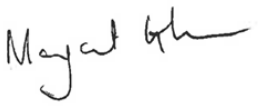
Primary Ciliary Dyskinesia Type 1 (CILD1), OMIM #244400
Primary Ciliary Dyskinesia Type 2 (CILD2), OMIM #606763
Primary Ciliary Dyskinesia Type 5 (CILD5), OMIM #608647
Primary Ciliary Dyskinesia Type 6 (CILD6), OMIM #610852
Primary Ciliary Dyskinesia Type 7 (CILD7), OMIM #611884
Primary Ciliary Dyskinesia Type 9 (CILD9), OMIM #612444
Primary Ciliary Dyskinesia Type 10 (CILD10), OMIM #612518
Primary Ciliary Dyskinesia Type 11 (CILD11), OMIM #612649
Primary Ciliary Dyskinesia Type 12 (CILD12), OMIM #612650
Primary Ciliary Dyskinesia Type 13 (CILD13), OMIM #613193
Primary Ciliary Dyskinesia Type 14 (CILD14), OMIM #613807
Primary Ciliary Dyskinesia Type 15 (CILD15), OMIM #613808
Primary Ciliary Dyskinesia Type 16 (CILD16), OMIM #614017
Primary Ciliary Dyskinesia Type 17 (CILD17), OMIM #614679
Primary Ciliary Dyskinesia Type 18 (CILD18), OMIM #614874
Primary Ciliary Dyskinesia Type 19 (CILD19), OMIM #614935
Primary Ciliary Dyskinesia Type 20 (CILD20), OMIM #615067
Primary Ciliary Dyskinesia Type 21 (CILD21), OMIM #615294
Primary Ciliary Dyskinesia Type 22 (CILD22), OMIM #615444
Primary Ciliary Dyskinesia Type 23 (CILD23), OMIM #615451
Primary Ciliary Dyskinesia Type 24 (CILD24), OMIM #615481
Primary Ciliary Dyskinesia Type 25 (CILD25), OMIM #615482
Primary Ciliary Dyskinesia Type 26 (CILD26), OMIM #615500
Primary Ciliary Dyskinesia Type 27 (CILD27), OMIM #615504
Primary Ciliary Dyskinesia Type 28 (CILD28), OMIM #615505
Primary Ciliary Dyskinesia Type 29 (CILD29), OMIM #615872
Primary Ciliary Dyskinesia Type 30 (CILD30), OMIM #616037

Primary Ciliary Dyskinesia Type 32 (CILD32), OMIM #616481
Primary Ciliary Dyskinesia Type 33 (CILD33), OMIM #616726
Primary Ciliary Dyskinesia Type 34 (CILD34), OMIM #617091
Primary Ciliary Dyskinesia Type 35 (CILD35), OMIM #617092
Primary Ciliary Dyskinesia Type 37 (CILD37), OMIM #617577

3. Chairs signature

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

Signature



Name

Margaret Gilmore

Date

19 December 2017