# Statutory Approvals Committee – minutes

## Centre 0102 (Guy's Hospital)

## Pre-implantation Genetic Diagnosis (PGD) application for Kabuki Syndrome Type 1, OMIM #147920 and Kabuki Syndrome Type 2, OMIM #300867

Thursday, 25 October 2018

HFEA, 10 Spring Gardens, London, SW1A 2BU

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| Committee members | Margaret Gilmore (Chair)<br>Bobbie Farsides (Deputy Chair)<br>Anne Lampe<br>Anthony Rutherford<br>Ruth Wilde | |
| Members of the Executive | Bernice Ash<br>Dee Knoyle<br>Paula Robinson<br>Catherine Burwood | Committee Secretary<br>Committee Secretary (Observer)<br>Head of Planning and Governance (Observer)<br>Senior Governance Manager (Observer) |
| Specialist Adviser | Professor Mary Porteous | |
| Legal Adviser | Gerard Hanratty | Browne Jacobson LLP |
| Observers | Emma Cave | (New Member Induction) |

## 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

## 1. Consideration of application

**1.1.** The committee welcomed the advice of its Specialist Adviser, Professor Mary Porteous who confirmed that the condition was as described in the papers.

**1.2.** The committee noted that the description in the application for PGD Kabuki Syndrome Type 1, OMIM #147920 and Kabuki Syndrome Type 2, OMIM #300867 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 Kabuki Syndrome Type 1 is inherited in an autosomal dominant pattern which means there is a 50% chance of an embryo being affected with the condition in each pregnancy, if either parent has a relevant mutation.

**1.8.** The committee noted that Kabuki Syndrome Type 2 is inherited in an X-linked recessive pattern which means there is a 50% chance of a child inheriting the relevant mutation, if the mother is a carrier.

**1.9.** Kabuki Syndrome Type 2 may lead to a female carrier experiencing phenotypic symptoms, depending on the pattern of X chromosome inactivation in the individual.

**1.10.** The committee noted that the penetrance of Kabuki Syndrome, Type 1 and Type 2, appears to be 100% although there is variable expressivity of symptoms between patients. The condition causes mild to moderate intellectual disability, postnatal growth deficiency as well as gastrointestinal, cardiovascular, endocrine and muscular disorders to varying degrees. Patients are also at an increased risk of infections, autoimmune disorders and hearing loss. Kabuki Syndrome, Type 1 and Type 2, cannot be cured, and treatment requires a multi-disciplinary approach to manage symptoms.

**1.11.** The Peer Reviewer noted that previous studies have found that 55-80% of Kabuki Syndrome cases are caused by mutations in KMT2D (i.e. Kabuki Syndrome Type 1) and less than 5% of cases are caused by KDM6A mutations (i.e. Kabuki Syndrome Type 2). The remaining cases of Kabuki Syndrome are of an unknown genetic cause.

**1.12.** The committee noted the inspectorate's request to consider whether add Kabuki Syndrome Type 1, OMIM #147920 and Kabuki Syndrome Type 2, OMIM #300867 should be approved for inclusion on the PGD List. The committee agreed to consider the application on this basis.

## 2. Decision

**2.1.** The committee considered that, in the worst case scenario, Kabuki Syndrome Type 1, OMIM #147920 and Kabuki Syndrome Type 2, OMIM #300867 are serious as the conditions are multi-systemic, impacting on the heart and kidneys, and can require multiple surgeries. The condition severely impacts on the individual's quality of life and the family.

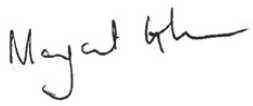
**2.2.** The committee had regard to its explanatory note and confirmed that, on the basis of the information presented, it was satisfied that there is a particular risk that an embryo may have the abnormality in question and that there is a significant risk, given the condition's worst symptoms, that 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 following conditions meet the criteria for testing under paragraph 1ZA(1)(b) and (2) of Schedule 2 of the Act and agreed to authorise testing:

- Kabuki Syndrome Type 1, OMIM #147920
- Kabuki Syndrome Type 2, OMIM #300867.

## 3. Chairs signature

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

### Signature



### Name

Margaret Gilmore

### Date

27 November 2018