PGT-M: NEW CONDITION/TYPE

ADMINISTRATIVE REQUIREMENTS

- Has it been confirmed that the **condition/type is not already on the list**?

No ✗ | Yes ✓

PURPOSE OF TESTING

Would testing be for **at least one of the following**?

- S2 1ZA (1) (a) – to establish whether the embryo has a gene, chromosome, or mitochondrion abnormality that may affect its **capacity to result in a live birth**

If this applies, is the Committee **satisfied that the abnormality for which the embryo is to be tested may indeed affect capacity to result in a live birth?**

- S2 1ZA (1) (b) – to establish, where there is a particular risk, whether an embryo has an **abnormality** or any other gene, chromosome, or mitochondrion abnormality
- S2 1ZA (1) (c) – to establish the **sex of the embryo** in cases where there is a particular risk that any resulting child will have or develop
  - i. A gender-related serious physical or mental disability
  - ii. A gender-related serious illness
  - Iii. Any other gender-related serious medical condition.

And, **if testing is not for a condition**:

- S2 1ZA (1) (e) – in a case where **uncertainty has arisen** as to whether the embryo is one of those whose creation was brought about by using the gametes of particular persons, establishing whether it is.

No

REFUSE AUTHORISATION – with reasons
OR
ADJOURN - and seek further information

PARTICULAR RISK

i.e. mode of inheritance

Is there a **particular risk** that the embryo may **have an abnormality; OR** is there a **particular risk** that any resulting **child will have or develop a gender-related** serious physical or mental disability, serious illness or other serious medical condition? *(Give reasons why there is a particular risk.)*

No

Yes

Is the testing for either S2 1ZA (1) (b) (abnormality) or S2 1ZA (1) (c) (sex testing)?

Yes

No

AUTHORISE

HAVE YOU EXPLAINED >>>

Decision to authorise/not
Reasoning re. risk and seriousness
Which types (if applicable)
Precisely what should be added to the list of approved conditions
Your considerations regarding any Executive recommendations

SIGNIFICANCE & SERIOUSNESS

Is there a **significant risk** 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? *(Give reasons why there is a significant risk.)*

AND

Would an affected person have or develop a **serious physical or mental disability, a serious illness, or any other serious medical condition**? *(Give reasons why this condition/type is deemed serious.)*

No

Yes

Is the testing for S2 1ZA (1) (c) (sex testing)?

No

Yes

FURTHER CONSIDERATIONS

For conditions for which sex testing is relevant:

Does the physical or mental disability, illness or other medical condition **affect only one sex? OR** does it affect **one sex significantly more** than the other?

Yes

No

Human Fertilisation and Embryology Authority
Pre-Implantation Genetic Testing ("PGT-M")
Explanatory Note For Statutory Approvals Committee

1. Preamble

The Statutory Approvals Committee of the Human Fertilisation and Embryology Authority has produced this explanatory note to set out its approach to the statutory criteria of "risk" and "seriousness" which it is required to assess when considering applications to undertake PGT-M. This explanatory note should be read in conjunction with the PGT-M Decision Tree.

The approach set out in this explanatory note was first approved by the Authority on 8 September 2010 and the explanatory note was first adopted by the Chair of the Licence Committee on 28 October 2010. This explanatory note is effective from 9 May 2018, following Authority approval. It was updated in June 2021 to reflect the change in terminology from PGD to PGT-M (approval not required).

2. Introduction

2.1 The Authority has delegated the function of considering PGD applications to the Statutory Approvals Committee. The Authority has adopted a condition based approach to the approval of applications which means that the Statutory Approvals Committee will usually consider applications to perform PGD for an abnormality based on the condition rather than the particular circumstances of any individual or family.

2.2 Once the Statutory Approvals Committee has approved an application to perform PGD for a particular abnormality, any licensed PGD centre in the UK can offer PGD for that abnormality. However, centres will still need to assess, on an individual family basis, whether a particular request for PGD is appropriate. The Code of Practice provides guidance on how such decisions should be made.

2.3 When considering PGD applications, the Statutory Approvals Committee will take into account material provided with the application, including evidence from the applicant, peer reviewers and, where available, from patients and patient groups.

3. The Statutory Requirements

3.1 Paragraph 1ZA of Schedule 2 (Annex A) sets out the statutory criteria which the Statutory Approvals Committee must consider before deciding whether or not a PGT-M application should be granted.

3.2 These criteria include the requirements that:

a) there should be a particular risk that an embryo may have a gene, chromosome or mitochondrion abnormality; and

b) there should be a significant risk that the person with abnormality will have or develop a serious physical or mental disability, a serious illness or any other serious medical condition.

4. Particular Risk

4.1 When considering whether or not there is a particular risk that an embryo may have an abnormality, the Statutory Approvals Committee will take into account whether or not the abnormality is heritable and if so, what the mode of inheritance is.

4.2 This is an objectively measurable criterion. For example, if a genetic abnormality is "autosomal dominant", there will be a one in two chance of an embryo carrying the abnormality. However, if the abnormality is "autosomal recessive", there will be a one in four chance of an embryo carrying that abnormality.

5. Significant Risk and Seriousness

5.1 When considering the significance of the risk, the Statutory Approvals Committee will take into account the penetrance of the condition.

5.2 The penetrance of a condition is an estimate, in percentage terms, of the likelihood that someone with the abnormality would develop the condition in question. Penetrance is a population based statistic which represents the accumulation of available studies of the incidence of that abnormality in populations of people who carry the relevant gene mutation.

The options are:

- full penetrance (100% - i.e. it is a certainty that a person with the abnormality will develop the condition in question), or
- incomplete penetrance, which is usually presented as a range of percentages (e.g. 40 – 60%) i.e. only a subset of people with the abnormality will develop the condition.

5.3 When assessing the seriousness of the disability, illness or condition, the Statutory Approvals Committee will take into account the following factors: .

a) Age of onset.

Is the condition congenital or does it manifest later in life? If it does manifest later, at what stage (childhood, early adulthood, later)?

b) Symptoms of the disease.

What are the symptoms of the condition and is it fatal, life threatening or life limiting?

c) Whether the condition is treatable

d) What type of treatment is available for those conditions that can be treated

What is the extent of the treatment available? How invasive is the treatment or likely treatment?

e) *Effect of the condition on quality of life*

This will include any evidence about the speed of degeneration in progressive disorders and the extent of any physical and /or intellectual impairment.

f) Variability of symptoms

Symptoms associated with the same condition can vary from family to family (and from individual to individual), and can range from the mild to the severe.

5.4 Where the condition has variable symptoms, the Statutory Approvals Committee will take account of:

- what the range of variability is; and
- whether the range suggests that some forms of the condition are so mild that they might not meet the 'serious' test.

5.5 Where a condition has a range of penetrance (e.g. 40-60%), the Statutory Approvals Committee will base its decision on the highest penetrance figure.

5.6 Where a condition has variable symptoms, the Statutory Approvals Committee will base its determination of how serious the disability, illness or condition is, on the worst possible symptoms.

6. Reasons

6.1 The Statutory Approvals Committee will give reasons for the decisions it makes. The reasons will set out clearly the matters that the Statutory Approvals Committee took into account in deciding whether or not to grant the application to perform PGT-M.

ANNEX A

1ZA

(1) A licence under paragraph 1 cannot authorise the testing of an embryo, except for one or more of the following purposes--

(a) establishing whether the embryo has a gene, chromosome or mitochondrion abnormality that may affect its capacity to result in a live birth,

(b) in a case 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,

(c) in a case where there is a particular risk that any resulting child will have or develop--

(i) a gender-related serious physical or mental disability,

(ii) a gender-related serious illness, or

(iii) any other gender-related serious medical condition,

establishing the sex of the embryo,

(d) in a case where a person ("the sibling") who is the child of the persons whose gametes are used to bring about the creation of the embryo (or of either of those persons) suffers from a serious medical condition which could be treated by umbilical cord blood stem cells, bone marrow or other tissue of any resulting child, establishing whether the tissue of any resulting child would be compatible with that of the sibling, and

(e) in a case where uncertainty has arisen as to whether the embryo is one of those whose creation was brought about by using the gametes of particular persons, establishing whether it is.

(2) A licence under paragraph 1 cannot authorise the testing of embryos for the purpose mentioned in sub-paragraph (1)(b) unless the Authority is satisfied--

(a) in relation to the abnormality of which there is a particular risk, and

(b) in relation to any other abnormality for which testing is to be authorised under sub-paragraph (1)(b),

that there is a significant risk 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.

(3) For the purposes of sub-paragraph (1)(c), a physical or mental disability, illness or other medical condition is gender-related if the Authority is satisfied that--

(a) it affects only one sex, or

(b) it affects one sex significantly more than the other.

(4) In sub-paragraph (1)(d) the reference to "other tissue" of the resulting child does not include a reference to any whole organ of the child.

STATUTORY APPROVALS COMMITTEE:

AUTHORISATION - MITOCHONDRIAL DONATION USING MATERNAL SPINDLE TRANSFER (MST)

ADMINISTRATIVE REQUIREMENTS

(Confirmation should be found in report summary)

Does the report confirm that the following administrative requirements have been met?

- Has the process of **maternal spindle transfer** been specified by the clinic in the application?
- Is the applicant centre **licensed** to carry out mitochondrial donation by MST, ie, has **express provision** been made on the licence?
- Are one or more **authorised embryologists** named on the licence, and if so, is there confirmation that only they will be **carrying out** the proposed MST in this case?

No ✗ | Yes ✓

PATIENT SELECTION CRITERIA

Would the **use of PGT-M** be considered **inappropriate or unlikely** to be successful in this patient's case? In reaching a view, the following should be considered:

- Any **evidence submitted by the clinic** which supports its view, or the view of PGT-M practitioners it has consulted, that PGT-M is not appropriate or is unlikely to be successful for this patient.
- Any evidence as to the **suitability or likelihood of success of PGT-M** for this patient which has been submitted by the **Executive and/or the independent expert reviewer**. *
- The guidance on patient selection criteria, in the Mitochondrial Donation **Explanatory Note.**

No ✗ | Yes ✓

* Refer to the requirements relating to heteroplasmy and homoplasmy at paragraph 2.5 and 7.1 of the Explanatory Note.

PARTICULAR RISK

In determining whether there is a particular risk, consider:

- The guidance on **particular risk**, set out in the Mitochondrial Donation **Explanatory Note**.
- All **evidence provided by the clinic** as to the particular risk.
- Any **evidence submitted by the Executive or the expert reviewer**.

Is there a particular risk that any egg extracted from the ovaries of the named woman may have mitochondrial abnormalities caused by mitochondrial DNA? Reg 5(a)(i)

No ✗ | Yes ✓

SIGNIFICANCE & SERIOUSNESS

In determining significance and seriousness, consider:

- The **guidance on significance and seriousness** set out in the Mitochondrial Donation Explanatory Note
- All **evidence provided by the clinic** as to significance and seriousness.
- Any **evidence submitted by the Executive and expert reviewer.**

Is there a **significant risk** that a person with those abnormalities **will have or develop serious mitochondrial disease**? **Reg 5(a)(ii)**

No ✗ | Yes ✓

REFUSE APPLICATION with reasons OR **ADJOURN** and seek further information

HAVE YOU EXPLAINED >>>

Determination yes/no

Reason re. risk and seriousness

Process to be used (MST)

Any redaction necessary to ensure patient confidentiality?

ISSUE DETERMINATION:
Authorisation is conditional on the egg subsequently being extracted from the ovaries of the named woman **(Reg 5(b)).**
This point must be included in the minutes.

STATUTORY APPROVALS COMMITTEE:

AUTHORISATION - MITOCHONDRIAL DONATION USING PRONUCLEAR TRANSFER (PNT)

ADMINISTRATIVE REQUIREMENTS

(Confirmation should be found in report summary)

Does the report confirm that the following **administrative requirements** have been met?

- Has the process of **pronuclear transfer** been specified by the clinic in the application?
- Is the applicant centre **licensed** to carry out mitochondrial donation by PNT, ie, has **express provision** been made on the licence?
- Are one or more **authorised embryologists** named on the licence, and if so, is there confirmation that only they will be **carrying out** the proposed PNT in this case?

No ✗ | Yes ✓

PATIENT SELECTION CRITERIA

Would the **use of PGT-M** in this case be considered **inappropriate or unlikely** to be successful in this patient's case? In reaching a view, the following should be considered:

- Any **evidence submitted by the clinic** which supports its view, or the view of PGT-M practitioners it has consulted, that PGT-M is not appropriate or is unlikely to be successful for this patient.
- Any evidence as to the **suitability or likelihood of success of PGT-M** for this patient which has been submitted by the **Executive and/or the independent expert reviewer**. *
- The guidance on patient selection criteria, in the Mitochondrial Donation **Explanatory Note.**

No ✗ | Yes ✓

* Refer to the requirements relating to heteroplasmy and homoplasmy at paragraph 2.5 and 7.1 of the Explanatory Note.

PARTICULAR RISK

In determining whether there is a particular risk, consider:

- The guidance on **particular risk**, set out in the Mitochondrial Donation **Explanatory Note**.
- All **evidence provided by the clinic** as to the particular risk.
- Any **evidence submitted by the Executive or the expert reviewer**.

Is there a particular risk that the embryo which is created by the fertilisation of an egg extracted from the ovaries of the named woman may have mitochondrial abnormalities caused by mitochondrial DNA? Reg 8(a)(i)

No ✗ | Yes ✓

SIGNIFICANCE & SERIOUSNESS

In determining significance and seriousness, consider:

- The **guidance on significance and seriousness** set out in the Mitochondrial Donation Explanatory Note
- All **evidence provided by the clinic** as to significance and seriousness.
- Any **evidence submitted by the Executive and expert reviewer.**

Is there a **significant risk** that a person with those abnormalities **will have or develop serious mitochondrial disease**? **Reg 8(a)(ii)**

No ✗ | Yes ✓

REFUSE APPLICATION with reasons OR **ADJOURN** and seek further information

HAVE YOU EXPLAINED >>>

Determination yes/no

Reason re. risk and seriousness

Process to be used (PNT)

Any redaction necessary to ensure patient confidentiality?

ISSUE DETERMINATION:
Authorisation is conditional on the embryo subsequently being created by the fertilisation of an egg extracted from the named woman **(Reg 8(b))**
This point must be included in the minutes.

Mitochondrial donation: Explanatory note for statutory approvals committee (Agreed December 2016)

1. Overview

1.1. The Statutory Approvals Committee of the Human Fertilisation and Embryology Authority will utilise this explanatory note to outline their approach to the statutory criteria of 'risk' and 'seriousness' which it is required to assess when considering applications to undertake mitochondrial donation. This explanatory note should be read in conjunction with the mitochondrial donation decision tree.

1.2. The approach set out in this explanatory note was approved by the Authority on 15 December 2016.

1.3. This explanatory note is effective for the Statutory Approvals Committee from 15 December 2016. In June 2021 it was updated to reflect a change in terminology from PGD to PGT-M (no re-approval required).

2. Introduction

2.1. Following the introduction of The Human Fertilisation and Embryology (Mitochondrial Donation) Regulations 2015 (the Regulations) on 29 October 2015 the Authority has delegated the function of considering mitochondrial donation applications to the Statutory Approvals Committee. The Regulations require the Authority to adopt a case by case based approach to the approval of applications which means that the Statutory Approvals Committee will consider applications to perform mitochondrial donation with reference to the particular circumstances of the patient.

2.2. Only clinics that have express provision on their licence to undertake mitochondrial donation can apply to undertake the process on behalf of a particular patient, and only those embryologist(s) approved by the HFEA are permitted to carry out the procedure.

2.3. When making applications to carry out mitochondrial donation, centres will need to assess, on an individual patient basis, whether the particular request for mitochondrial donation is appropriate. The Code of Practice provides guidance on how such decisions should be made.

2.4. When considering mitochondrial donation applications, the Statutory Approvals Committee will take into account material provided with the application, including evidence from the applicant, and any evidence from independent clinical experts and patient groups.

2.5. The Committee should ensure that the patient identified for treatment is (or is predicted to be) highly heteroplasmic or homoplasmic for a particular mtDNA mutation in their germ line and has undergone an assessment that deems PGT-M inappropriate or likely to be unsuccessful.

3. Statutory requirements

3.1. Paragraphs 5(a) and (b) and 8(a) and (b) of the Regulations (Annex A) prescribe the criteria that must be met before the Statutory Approvals Committee can issue a determination permitting the application of two mitochondrial donation techniques, pronuclear transfer (PNT) or maternal spindle transfer (MST).

3.2. These criteria include the requirements that:

- there should be a particular risk that an egg or embryo may have mitochondrial abnormalities caused by mitochondrial DNA, and
- there should be a significant risk that the person with the abnormalities will have or develop serious mitochondrial disease.

4. Particular risk

4.1. When considering whether or not there is a particular risk that an egg or embryo may have mitochondrial abnormalities caused by mitochondrial DNA (mtDNA), the Statutory Approvals Committee will take into account evidence of the genetic basis of the inherited disorder.

4.2. This is an objectively measurable criterion. Only a woman with an identified, pathogenic genetic alteration to her mtDNA can be determined to have a particular risk of transmitting this to her embryos.

4.3. Due to the intrinsic variability in the inheritance of those mitochondrial diseases caused by mutations to the mtDNA, the HFEA has determined that any woman harbouring such a genetic alteration is at particular risk of transmitting abnormal mitochondria to her eggs and embryos.

5. Seriousness: general information

5.1. Before the Statutory Approvals Committee can authorise mitochondrial donation treatment for a particular patient it must consider the risk to the patient's child, conceived in the absence of mitochondrial donation, of developing a serious mitochondrial disease.

5.2. In order to frame its assessment of this seriousness the Statutory Approvals Committee will first consider information from the scientific literature relating to the following factors:

a. Symptoms of the disease

It is important for the committee to recognise that the symptoms associated with the same genetic alteration to the mtDNA, can vary from family to family, and person to person, and can range from mild to severe.

The committee should therefore take into account the range of symptoms associated with the mitochondrial disease/genetic alteration, ensuring that they understand the symptoms that manifest when the disease is in its most severe form.

If the symptoms in this worst case scenario are not judged to be sufficiently serious, the Committee will not authorise mitochondrial donation for this patient.

b. Age of onset

As part of its consideration of the seriousness the committee should consider whether symptoms usually manifest at birth or later in life. If the symptoms do manifest later, at which stage (childhood, early adulthood, later)? If the disease is degenerative, how quickly does it progress?

c. Effect of the disease on quality of life of the patient

This will include any evidence about the speed of degeneration in progressive disorders and the extent of any physical and/or intellectual impairment.

d. Are treatments available for the disease or any of its symptoms?

If so, what is the type and extent of the treatments available? How invasive is the treatment or likely treatment?

6. Significant risk: general information

6.1. Mutations to the mtDNA can be present in all mitochondria or in only a proportion. Where all the mitochondria are affected this is known as homoplasmy. While if only a subset are affected this is known as heteroplasmy.

6.2. Where the mutation is heteroplasmic, the proportion of affected mitochondria versus unaffected mitochondria (known as the mutant mitochondrial load) often correlates with the symptoms, with higher loads associated with more severe symptoms. However this is not always the case.

6.3. Before the Statutory Approvals Committee can authorise mitochondrial donation treatment for a particular patient it must consider how significant the risk of developing a serious mitochondrial disease to is to the patient's child, if conceived in the absence of mitochondrial donation.

6.4. This risk will be influenced by the mutant mitochondrial load a child might inherit from its mother as well as the threshold beyond which the mutant mitochondrial load needs to pass in order to cause clinical symptoms.

6.5. In order to understand this risk the Statutory Approvals Committee will first consider information from the scientific literature, which provides information on:

- The usual threshold mutant mitochondrial load necessary to cause clinical manifestation of the mitochondrial disease.
- The degree to which mutant mitochondrial load usually correlates with severity of symptoms of the mitochondrial disease.
- Any cases indicating what the mutant mitochondrial loads were in women who have had children affected by the mitochondrial disease.

6.6. Due to the rare nature of some mitochondrial diseases and the paucity of publications characterising them, information on the threshold level of mtDNA harbouring a pathogenic genetic alteration required to result in the development of a mitochondrial disease may not be available.

6.7. This information is intended to provide a foundation upon which a judgement, based on the patient's individual circumstances, can be made.

6.8. The committee should bear in mind that the mutant mitochondrial load of the patient may not be the same as the load present in her eggs and embryos. This is because the inheritance of mitochondria between a woman and the eggs she produces is unpredictable. This results in women with heteroplasmic mutations producing eggs with a wide range of mutant mitochondrial loads, some of which would be sufficiently high to cause disease while some of which would not.

7. Significant risk and seriousness: patient information

7.1. The centre should only offer MST or PNT to patients who are (or are predicted to be) highly heteroplasmic or homoplasmic for a particular mtDNA mutation in their germ line and have undergone an assessment that deems PGT-M inappropriate or likely to be unsuccessful. In making this assessment the centre should take into account:

- the particular mutation involved,
- family history of affected individuals and their mutational load
- the likely clinical manifestations of disease and the efficacy of any previous treatments such as PGT-M

7.2. Based on the information from the scientific literature the Committee should hopefully have an understanding of the possible symptoms a particular mitochondrial disease/alteration to the mtDNA can cause, as well as the mutant mitochondrial load usually necessary to cause a clinical manifestation of disease.

7.3. However, in its assessment of 'significant risk' and 'seriousness', the Statutory Approvals Committee must take into account the circumstances of the individual patients.

7.4. The Committee should consider the following questions:

a. Does the patient's medical history provide evidence of risk and seriousness?

- Does the patient have any symptoms? If so, how severe are they?
  - A patient with symptoms herself may be at significant risk of transmitting a mitochondrial disease with comparable or more serious symptoms to her children.

- Has the patient previously had any children affected by mitochondrial disease? If so, what were their symptoms? What was the age of onset? What was the effect on quality of life? Were any treatments available and what effect did they have? Would this manifestation of mitochondrial disease pass the seriousness test?
  - A patient who has had a child/children affected by a serious mitochondrial disease may be at significant risk of having another child affected by a mitochondrial disease of similar severity.
- Has the patient previously been treated with preimplantation genetic testing (PGT-M) to avoid transmission of mitochondrial disease? Was the PGT-M successful? What was the mutant mitochondrial load of the embryos tested? Did any of the embryos have a mutant mitochondrial load above the threshold level usually necessary for clinical manifestation of serious mitochondrial disease?
  - A patient who has had an unsuccessful PGT-M cycle because no embryos with sufficiently low mutant mitochondrial loads were found may be at significant risk of having eggs with mutant mitochondrial loads sufficiently high to cause a serious mitochondrial disease.

b. Does the patient's mutant mtDNA load provide evidence of risk and seriousness?

- Is the patient homoplasmic or heteroplasmic for the mutation? What is the patient's mutant mitochondrial load?
  - A patient who is homoplasmic for the mutation will only have eggs that are homoplasmic for the mutations. Therefore all her children are at risk of developing mitochondrial disease. Her children may have mitochondrial disease similar in severity to her own or that of her relatives.
  - A patient who is heteroplasmic for the mutation is likely to have eggs which are also heteroplasmic. However, the mutant mitochondrial load of the patient may not be the same as the load present in her eggs and embryos, which are likely to have considerable variability in mutant mitochondrial load. The committee should consider whether there is evidence from the scientific literature and/or family medical history showing that women with comparable mutant mitochondrial load have had a severely affected child.

c. Does the patient's family history provide evidence of risk and seriousness?

- Does the patient have a family history of mitochondrial disease? How prevalent is mitochondrial disease in the family ie, which family members are/have been affected by mitochondrial disease? How serious was the disease in affected family members: what were the symptoms, what was the age of onset, what was the effect on quality of life, were any treatments available and effect did they had?

- What were the mutant mitochondrial loads of affected family members with severe mitochondrial disease and what were the mutant mitochondrial loads of their mothers? Are the mutant mitochondrial loads of female family members who have had severely affected children comparable to the patient?
  - A patient with a family history of serious mitochondrial disease may be at significant risk of having a child with a similar severity of symptoms. This is especially the case if she has a comparable mutant mitochondrial load to that of her female relatives who have had an affected child.
- For affected family members, their symptoms, age of onset, effect on quality of life, their mutant mitochondrial load, if any treatment was available, what it was and what effect it had.

– Please note that clinics are asked to obtain consent from the affected family member before disclosing identifying medical history, or where that is not possible, to take steps to protect their confidentiality. For this reason, family history may have been provided as a narrative rather than describing individuals to a degree that they might be identified from the description.

8. Decision-making

8.1. The Statutory Approvals Committee will give reasons for the decisions it makes. The reasons will set out clearly the matters that the Statutory Approvals Committee took into account in deciding whether or not to grant approval to perform mitochondrial donation.

9. Publication of minutes

9.1. It is important for transparency that wherever possible documentation of the committee's decision-making process is published and available for public scrutiny. However, it is vital that patient confidentiality is upheld.

9.2. Some mitochondrial disease and genetic alterations to the mtDNA are very rare and as such it may be possible to identify a patient by some of the details recorded in the Statutory Approvals Committee minutes.

9.3. The committee should weigh up these two competing principals when deciding whether or not its minutes should be made publicly available, and consider publishing redacted minutes to preserve patient confidentiality where necessary, stating this as the reason.

Annex A: Extract from Regulations

5. Permitted egg: circumstances

The circumstances referred to in regulation 5(b) are that-

a) the Authority has issued a determination that-

   i. there is a particular risk that any egg extracted from the ovaries of a woman named in the determination may have mitochondrial abnormalities caused by mitochondrial DNA and
   ii. there is a significant risk that a person with those abnormalities will have or develop serious mitochondrial disease; and

b) egg B was extracted from the ovaries of the woman so named.

8. Permitted embryo: circumstances

The circumstances referred to in regulation 8(b) are that-

a) the Authority has issued a determination that-

   i. there is a particular risk that any embryo which is created by the fertilisation of an egg extracted from the ovaries of a woman named in the determination may have mitochondrial abnormalities caused by mitochondrial DNA, and
   ii. there is a significant risk that a person with those abnormalities will have or develop serious mitochondrial disease, and

b) embryo B was created by the fertilisation of an egg extracted from the ovaries of the woman so named.

GB SPECIAL DIRECTIONS FOR IMPORT/EXPORT – from 1 Jul 2021 onwards

START

IS THE APPLICATION FOR IMPORT OR EXPORT?

Import | Export

* Defined as:
Gametes or embryos imported for the purposes of providing services to a particular person or persons on one occasion only. See Section 24 (4AE) of the 1990 HFE Act.

IMPORT

- Is the importing tissue establishment in possession of a **certificate** issued under Section 24 (4AD) and, other than in the case of one-off imports*, does the certificate name the third country supplier and does it list the **tissue type** (ie, gametes or embryos) as applicable to this particular application? And...
- In the case of a **one-off import**, can the requirements of GD0006v9 (GB) Sch 1 para 3(a-j), 4, 5 (a-e), 6(a-c) and 7(a-d) be met?
- In the case of imports that are **not one-offs**, can the requirements of GD0006v9 (GB) Sch 1 para 3(a-j), 4, 5(a-e) and 7(a-d) be met?

No ✗ | Yes ✓

EXPORT

- **Can the requirements of GD0006v9 (GB) Sch 2 para 1 (a-i) and para 2 of all be met?**

Yes ✓ | No ✗

No Special Direction required

REQUIREMENTS NOT MET

- **Is the Committee prepared to vary the General Directions to address problems with meeting the requirements?**

Factors to consider:
Where refusal to vary might interfere with an individual's/a couple's human rights, in particular **Articles 8** (the right to family life) **and 12** (the right to marry and found a family), interference **must be justified and fulfil a pressing social need, pursue a legitimate aim and be proportionate and non-discriminatory.**

No ✗ | Yes ✓

Import/Export **cannot take place.** *(Give reasons.)*

GRANT SDs and modify S12-14 as necessary to permit the import/export but to reflect relevant GD0006v9 (GB) schedule as closely as possible. *(Give reasons.)*

HAVE YOU EXPLAINED >>>
Decision to issue SDs or not.
Reasons for not agreeing with any Executive recommendation

NI - SPECIAL DIRECTIONS FOR IMPORT/EXPORT – 1 Jan 2021 onwards

NB: If this is an import to NI from GB, a separate decision tree applies.

START

LOCATION OF NON-UK CENTRE

- Is the non-UK centre **in the EEA?**

No ✗ | Yes ✓

If Import

If Export

IS THIS APPLICATION TO IMPORT OR EXPORT?

Export | Import

IMPORT

- Is the importing tissue establishment in possession of a **certificate** issued under Section 24 (4AD) and, other than in the case of one-off imports*, does the certificate name the third country supplier and does it list the **tissue type** (ie, gametes or embryos) as applicable to this particular application? And...
- In the case of a **one-off import**, can the requirements of GD0006v1 (NI) Sch 2 para 3 (a-j), 4, 5 (a-e), 6(a-c) and 7(a-d) be met?
- In the case of imports that are **not one-offs**, can the requirements of GD0006v1 (NI) Sch 2 para 3(a-j), 4, 5(a-e) and 7(a-d) be met?

No ✗ | Yes ✓

* Defined as:
Gametes or embryos imported for the purposes of providing services to a particular person or persons on one occasion only. See Section 24 (4AE) of the 1990 HFE Act.

No Special Direction required

EXPORT

- **Can the requirements of GD0006v1 (NI) Sch 4 para 1 (a-i) and para 2 all be met?**

Yes ✓ | No ✗

IMPORT

- Can the **requirements of GD0006v1 (NI) Sch 1 para 1 (a–g) and para 2 all be met**?

No ✗ | Yes ✓

No Special Direction required

COMPETENT AUTHORITY

- Is the non-UK centre **accredited, designated, authorised or licensed by the country's Competent Authority** under the EUTD?

Yes ✓ | No ✗

Cannot import from or export to it

REQUIREMENTS NOT MET

- **Is the Committee prepared to vary the General Directions to address problems with meeting the requirements?**

Factors to consider:
Where refusal to vary might interfere with an individual's/a couple's human rights, in particular **Articles 8** (the right to family life) **and 12** (the right to marry and found a family), interference **must be justified and fulfil a pressing social need, pursue a legitimate aim and be proportionate and non-discriminatory.**

No ✗ | Yes ✓

Import/Export **cannot take place.** *(Give reasons.)*

HAVE YOU EXPLAINED >>>
Decision to issue SDs or not.
Reasons for not agreeing with any Executive recommendation

GRANT SDs and modify S12-14 as necessary to permit the import/export but to reflect relevant GD0006 schedule as closely as possible.
(Give reasons.)

NI - SPECIAL DIRECTIONS FOR IMPORT FROM GB – 1 Jan 2021 onwards

START

SUPPLYING GB CENTRE

- Is the supplying centre in GB licensed by the HFEA?

Yes

No

Cannot import from or export to it

IMPORT

- Is the importing tissue establishment in possession of an ITE certificate issued by the HFEA under Section 24 (4AD), and other than in the case of one-off imports* does the certificate name the centre in GB, and list the tissue type (gametes or embryos) as applicable to this application.
- In the case of a one-off import, can the requirements of GD0006v1 (NI) Schedule 3 para 3(a-h), 4, 5 (a-e), 6 (a-c) and 7 (a-c) be met?
- For all other imports, can the requirements of GD0006v1 (NI) Schedule 3 para 3(a-h), 4, 5 (a-e), and 7(a-c) be met?

Yes

No

No Special Direction required

* Defined as:
Gametes or embryos imported for the purposes of providing services to a particular person or persons on one occasion only. See Section 24 (4AE) of the 1990 HFE Act.

REQUIREMENTS NOT MET

- **Is the Committee prepared to vary the General Directions to address problems with meeting the requirements?**

Factors to consider:
Where refusal to vary might interfere with an individual's/a couple's human rights, in particular **Articles 8** (the right to family life) **and 12** (the right to marry and found a family), interference **must be justified and fulfil a pressing social need, pursue a legitimate aim and be proportionate and non-discriminatory.**

Yes

No

GRANT SDs and modify S12-14 as necessary to permit the import/export but to reflect relevant GD0006 schedule as closely as possible.
(Give reasons.)

Import/Export **cannot take place.**
(Give reasons.)

HAVE YOU EXPLAINED >>>
Decision to issue SDs or not.
Reasons for not agreeing with any Executive recommendation

PTT Decisions – made under paragraph 1ZA (1) (d) of the HFE Act

ELP starting point:

SAC starting point:

ADMINISTRATIVE REQUIREMENTS

- Has it been confirmed that the condition involved in the proposed PTT (preimplantation tissue typing) is on the list of approved PGT-M conditions?

No | Yes

PURPOSE OF PTT

Would testing be for the following purpose?

- S1 Z A (d) – **Establishing whether the tissue of any resulting child would be compatible with that of the sibling.**

No | Yes

SIBLING/EMBRYO

Is the sibling involved the **child of the people/person whose gametes were used** to bring about the creation of the embryo?

No | Yes

SERIOUS MEDICAL CONDITION

Does the **sibling suffer from a serious medical condition**?
(Give reasons why the condition is considered serious.)

As set out in the PGT-M Explanatory Note, relevant factors could be:

- **Effect of the condition on quality of life** – this will include any evidence about the speed of degeneration in progressive disorders and the extent of any physical and/or intellectual impairment.
- **Symptoms and prognosis** – what symptoms are present and what is the prognosis for the specific affected sibling? Are the current symptoms and/or those reflected in the prognosis, fatal, life-threatening or life limiting?
- **Whether the condition is treatable** other than by umbilical cord blood stem cells, bone marrow or other tissue.
- **What type of treatment is available** (for those conditions that can be treated) – what is the extent of treatment available? How invasive is the treatment, or likely treatment?

No | Yes

TREATMENT

Can the medical condition be treated by umbilical cord blood stem cells, bone marrow or other tissue from the child resulting from the embryo?

No | Yes

REFUSE AUTHORISATION – with reasons
OR
ADJOURN - and seek further information

HAVE YOU EXPLAINED >>>
Decision to authorise/not.
Reasoning why the condition the sibling has got is considered serious.
Reasons for not agreeing with any Executive recommendation

AUTHORISE