

# Regulating mitochondrial donation

**Strategic delivery:**       Setting standards       Increasing and informing choice       Demonstrating efficiency economy and value

## Details:

Meeting	Authority
Agenda item	7
Paper number	HFEA (16/09/2015) 764
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## Output:

For information or decision?	For decision
Recommendation	Agree recommendations for the regulation of mitochondrial donation.
Resource implications	Staff resource implications (across the Executive)
Implementation date	29 October 2015
Communication(s)	Clinic Focus and Code of Practice update, 29 October 2015
Organisational risk	<input type="checkbox"/> Low <input type="checkbox"/> Medium <input checked="" type="checkbox"/> High
Annexes	<p>Annex 1: Regulating mitochondrial donation: stakeholder feedback report</p> <p>Annex 2: Summary of Standing Orders changes</p> <p>Annex 3: Draft mitochondrial donation Code of Practice guidance note</p> <p>Annex 4: Draft general directions:</p> <ul style="list-style-type: none"> <li>• 0001 - Gamete and Embryo donation</li> <li>• 0005 - Collecting and recording information for the HFEA</li> <li>• 0007 - Consent</li> <li>• 0008 - Information to be submitted to the HFEA as part of the licensing process</li> <li>• 0012 - Retention of records</li> </ul>

Annex 5: Draft forms and guidance (to note), including the:

- Licence variation form
- Mitochondrial donation follow-up information sheet
- Patient application form
- Clinical expert review form
- Decision trees for the Statutory Approvals Committee
- Mitochondrial donation: explanatory note for Statutory Approvals Committee
- Consent forms

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## 1. Introduction

- 1.1. In February 2015 Parliament approved The Human Fertilisation and Embryology (Mitochondrial Donation) Regulations 2015 ('the Regulations') to permit the use of maternal spindle transfer (MST) and pronuclear transfer (PNT) to avoid serious mitochondrial disease. The regulations will come into force on 29 October 2015.
- 1.2. In [May 2015](#) the Authority approved draft proposals for licensing mitochondrial donation and key areas to seek focused stakeholder feedback. Since then, the Executive has continued to work with members to develop and refine these proposals and to take into account expert views from key stakeholders and legal advice. A summary of stakeholder feedback is provided at annex one.
- 1.3. Mitochondrial donation to avoid serious mitochondrial disease has not been offered at any clinic in the world before. The statutory provisions governing this new treatment are set out in the Regulations and prescribe the steps UK clinics must take before they can offer this new treatment.
- 1.4. As with any new treatment it is important that it is judged to be safe and effective before it is made available. The [HFEA expert panel](#) has considered the safety and efficacy of MST and PNT in three reports and it has recommended a number of tests which it believes should be completed before the treatment is offered. There is no statutory requirement that these tests must be met before MST or PNT is offered in treatment but in passing the Regulations, Parliament expected this to happen before the HFEA could consider licensing the first clinic.
- 1.5. Accordingly, once these tests have been carried out, we will convene the expert panel to consider the results, and their report will be presented to the Authority. If the panel is satisfied and the Authority accepts their recommendations, we will amend the list of authorised processes that clinics are permitted to use. This will trigger the licensing process and enable clinics to apply to be licensed to offer the treatment. In order to grant a licence, the Authority must be satisfied that the clinic has the relevant skills and competence to carry out the treatments safely and effectively, and if licensed, they will need to seek approval for each patient they propose to treat.
- 1.6. This paper sets out the three broad stages under the new proposed system that a clinic wishing to offer mitochondrial donation must follow:
  1. How to seek approval to carry out mitochondrial donation
  2. How to run a good quality service, and
  3. What to do after treatment.
- 1.7. The Authority is asked to approve the final proposals for regulating mitochondrial donation (and the attached documents set out in annexes two to four) for implementation on 29 October 2015. The draft forms and supporting guidance incorporating the new requirements are attached at annex five. These forms are to note only – they do not require formal Authority approval.

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## 2. How to seek approval to carry out mitochondrial donation

- 2.1. Before any HFEA-licensed clinic can undertake mitochondrial donation for treatment purposes it must follow a two-stage process:
1. it will need to apply to vary its licence to include specific permission to carry out MST and/or PNT. Such applications will be considered by the Licence Committee. If the application is approved, the clinic will be licensed and will not need to repeat this step (unless they wish to seek approval to change their embryologists, see paragraph 2.5 below).
  2. it will then need to apply for approval to treat a specific patient. Such applications will be considered by the Statutory Approvals Committee (SAC). This step must be completed for each individual patient.
- 2.2. These proposals require changes to the Authority's Standing Orders which are highlighted (at annex two).

### Licence variation process

- 2.3. A clinic must first submit a completed licence variation application form and the necessary supporting evidence, to their HFEA Inspector. The Inspectorate will then assess the competence of the clinic and suitability of its premises and processes. We will use the same inspection methodology to assess a mitochondrial donation application as we do to assess an application to vary a licence for other reasons. We will carry out a detailed assessment against all relevant standards, including the new Code of Practice guidance. The Inspectorate will carry out an additional onsite inspection focused on the licence variation which will not affect the clinic's normal inspection cycle. Once a variation has been granted, the Inspectorate will continue to monitor the clinic as part of the usual compliance cycle.
- 2.4. Today the Authority is asked to approve General Directions 0008 which sets out the necessary evidence needed to support a licence variation (at annex four). These directions require the clinic's Person Responsible (PR) to submit the following evidence:
- suitable validation of their clinic's equipment and processes
  - their process for monitoring children born following mitochondrial donation, where patients have consented to follow-up - covering what links the clinic has with research groups or mitochondrial disease specialists, what follow-up will involve (eg, the method and frequency of contact) and what information the clinic will provide to their patients about follow-up
  - competency of the clinic staff and suitability of its premises and processes with specific reference to PNT and/or MST - all staff either directly involved in mitochondrial donation techniques, or staff involved with patients receiving such treatment, must be suitably qualified, trained and assessed as competent for the tasks they perform
  - competency of the clinic's MST/PNT embryologist(s), including:
    - their specific experience of carrying out MST or PNT in treatment, training or research on human eggs or embryos (eg, embryo survival

rates, blastocyst development, and rate of carryover of mutant mitochondria, in line with key performance indicators) references to support their experience and knowledge, and

- any other information that may demonstrate competence (such as their experience of performing micro-manipulation on human or animal (eg, mice) eggs or embryos).

- 2.5.** A PR wishing to make any changes to their list of authorised embryologists will need to apply to vary the clinic's licence and will be required to submit the relevant competency information for each proposed embryologist for consideration by a Licence Committee.

### **Developing the proposal for assessing embryologist competency**

- 2.6.** The proposed approach of assessing the competence of MST/PNT embryologists goes further than our usual approach to assessing staff competency and beyond the criteria set out in the Regulations. In developing this rigorous approach we have taken account of the views of Authority members and stakeholders in particular from the scientific community, who have all acknowledged that the competence of the individual performing the techniques has a direct bearing on the rate of carry-over of mutant mitochondria. The ability of the embryologist to create embryos following MST or PNT with a low rate of carryover of mutant mitochondria will directly affect whether or not the child is born free from mitochondrial disease – which is the primary purpose of the Regulations and of course the primary reason for patients seeking this new treatment.
- 2.7.** Stakeholders have emphasised the novel nature of the techniques and difficulty of performing the techniques such that a low carry over rate is consistently achieved. In order for the Authority to maintain public confidence in the regulation of new techniques such as this and provide patients with assurance, it is considered crucial that only those embryologists who have been able to demonstrate that they have the requisite skills and experience should be permitted to conduct the two techniques. The two techniques that only the authorised embryologists can do are those defined in Regulations 4 and 7.
- 2.8.** Therefore, for the time being, it is proposed that not only should the PR be required to demonstrate that their MST/PNT embryologists have experience of performing the techniques on human gametes and embryos, but the PR must also demonstrate that the individual can perform the techniques in line with a pre-determined set of performance indicators: embryo survival rates, blastocyst development, and rate of carryover of mutant mitochondria. These performance indicators will be determined by the Authority, taking into account the advice of an expert panel following consideration of the latest research (when it meets to assess the outcomes of the final safety and efficacy tests, as outlined in 1.4-1.5 above). These performance indicators will be added to General Directions 0008 once agreed by the Authority (see recommendation at 2.10).

## **Recommendation**

- 2.9.** The Authority is asked to approve the proposed approach for varying a clinic's licence to perform mitochondrial donation set out at paragraphs 2.3-2.8 above, including the information that clinics need to submit as set out in General Directions 0008 (at annex four) and the consequential changes to Standing Orders (at annex two).
- 2.10.** Members are also asked to note the delegation of later amendments to General Directions 0008, to include performance indicators for MST/PNT embryologists, to a sub-set of Authority members.

### **Mitochondrial donation licence conditions**

- 2.11.** Before the HFEA can issue a licence specifically permitting the clinic to carry out mitochondrial donation the clinic must acknowledge the licence conditions in the usual manner. The new licence conditions specific to mitochondrial donation must be agreed by the Authority today. The proposed conditions relevant to mitochondrial donation are outlined below. It is worth noting that the existing conditions (T1 to T123) are considered sufficiently comprehensive and we therefore need only introduce a small number of new conditions specific to mitochondrial donation. Crucially, we have not sought to impose conditions which merely restate what is contained in the Regulations.

- 2.12.** The new conditions are as follows:

- T124**
- a.** No clinic may carry out either the process of pronuclear transfer\* (PNT) or maternal spindle transfer\* (MST) or part of either process, unless express provision has been made on the clinic's licence permitting it to undertake either or both processes.
  - b.** Neither PNT nor MST may be carried out under third party, satellite or transport agreements.
  - c.** No clinic may provide treatment using gametes or embryos which have been created using PNT or MST unless express provision has been made on the clinic's licence permitting the clinic to undertake either or both processes.

\*Wherever reference is made in this licence to PNT or MST or the process of PNT or MST, that is the process defined in Regulation 4 or Regulation 7 of the Human Fertilisation and Embryology (Mitochondrial Donation) Regulations 2015.

- T125.** PNT and MST must only be carried out on premises of clinics licensed to undertake mitochondrial donation ('MD'). These processes must not be carried out on the premises of a clinic that is operating under a third party, satellite or transport agreement with a clinic that holds a licence to undertake MD.

- T126** Donors of gametes for use in PNT and or MST must be screened for pathogenic mitochondrial DNA mutations and an assessment of the risk of transmission of inherited conditions known to be present in the maternal line must be carried out, after consent is obtained. Complete

information on the associated risk and on the measures undertaken for its mitigation must be clearly communicated and explained to the recipient.

- T127**
- a. No alterations may be made to the nuclear or mitochondrial DNA of an egg created by means of the application of MST;
  - b. No alterations may be made to the nuclear or mitochondrial DNA of an embryo created by means of the application of PNT and no cell may be added to an embryo created by means of the application of PNT other than by the division of the embryo's own cells.
- T128.** In the case of treatment involving mitochondrial donation the clinic must ensure that it only carries out the process of PNT or MST for a particular, named patient once the Authority has issued a determination that:
- there is a particular risk that any egg extracted from the ovaries of the named woman or any embryo created by the fertilisation of an egg extracted from the ovaries of the named woman may have mitochondrial abnormalities caused by mitochondrial DNA and
  - there is a significant risk that a person with those abnormalities will have or develop a serious mitochondrial disease.
- T129** Only those embryologists assessed as competent by the Authority to undertake PNT, MST or both, and named on the front of this licence, are permitted to undertake those processes or any part thereof.

## Recommendation

- 2.13.** The Authority is asked to approve the new Licence Conditions at paragraph 2.12 of this paper.

### Individual patient approval process

- 2.14.** Before a clinic licensed to do MST and/or PNT is permitted to carry out the treatment for a specific patient, it will need to apply to the HFEA for approval. These applications will be considered by the Statutory Approvals Committee (SAC). If granted, approval can only be given for the treatment to be applied for the particular patient, in the circumstances described in the Regulations. Two decision trees for SAC reflecting the regulations have been developed to aid its decision making (at annex five).
- 2.15.** Step one of the approval is the assessment of whether there is a 'particular risk' of the egg or embryo having a mitochondrial abnormality caused by mitochondrial DNA. The biology of mitochondrial disease means that for any woman carrying mutant mitochondrial DNA (mtDNA), even if very low levels of affected mtDNA are present, there is almost a 100% risk that her eggs will have mitochondrial abnormalities caused by mitochondrial DNA. Therefore the presence of a mutation in the female patient's mtDNA alone is sufficient to satisfy the test for 'particular risk.'

- 2.16.** The second step is the assessment of whether there is a ‘significant risk’ that a child with those abnormalities will have, or develop, a ‘serious’ mitochondrial disease. The assessment of ‘seriousness’ should be based on the most severe symptoms that could be expected for a particular case. To support an application, a clinic will need to submit patient-specific information to enable an assessment of ‘significant risk’ and ‘seriousness’ to be made. This will include:
- the patient’s medical history
  - the patient’s mutant mtDNA load and mutation threshold
  - the patient’s family medical history of the mtDNA mutation or disease
  - scientific literature relevant to the mtDNA mutation or disease, and
  - any additional information which the clinician may consider is relevant to the application.

## Recommendation

- 2.17.** The Authority is asked to approve the proposed approach to assessing individual patient applications set out at paragraphs 2.14-2.16, including the information that clinics need to submit as set out in General Directions 0008 (at annex four).

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## 3. How to run a good quality service

- 3.1.** For a clinic licensed to carry out mitochondrial donation to run a good service, it will need to follow new guidance set out in the Code of Practice and directions, use new consent forms, and submit the prescribed information to the HFEA. This section sets out how a clinic should run a good quality service in line with the new regulatory requirements.

### Registration process

- 3.2.** Clinics must submit information to us on their patients, donors and treatments, according to General Directions 0005 (at annex four). In addition to the patient and partner (or sperm donor) registration information submitted for standard IVF cycles, registration of the mitochondrial donors and pronuclear transfer only sperm donors (where applicable) will also be required.
- 3.3.** The PNT-only registration will apply to a small number of cases where the male donor is only providing sperm for part of the PNT process (involving the creation of embryos with the mitochondrial donor) where he will not be genetically related to the child. This may happen if the male partner of the patient undergoing treatment cannot be used for this part of the PNT process because he is a close genetic relative of the mitochondria donor.

### Obtaining consent to treatment and donation

- 3.4.** Another step that must take place before treatment is offered is obtaining properly informed consent from the egg and sperm provider(s) and the mitochondrial donor. We have developed separate forms so that the questions

are tailored to these specific type of treatments, recognising the different information needs of the patients and donors, and reflecting the consent provisions in the Regulations.

- 3.5.** Female patients can consent to their eggs undergoing MST and embryos created from eggs following MST being used in their treatment, and/or for their eggs to be used to create embryos which will undergo PNT. The male partner of a woman having treatment can also either consent to his sperm being used to create embryos with eggs that have undergone MST, and/or for his sperm to be used in PNT. He can consent to both stages of the technique (creating embryos with his partner's eggs (the first stage) and the donor's eggs (the second stage), or consent to the first stage only. Again, each stage of the MST and PNT technique is explained before he is asked to give his consent. In both forms we explain what MST or PNT involves beneath each question and they broadly mirror the 'standard' fertility patient/partner treatment form.
- 3.6.** We have also developed a form for women donating their eggs and/or embryos created with their eggs for use in other women's mitochondrial donation treatment. They can consent to their eggs undergoing MST and for embryos created from eggs following MST being used for the treatment of others, and/or to their eggs being used to create embryos outside of the body which will undergo PNT. If a man is donating his sperm for use in PNT only (and not for 'standard' donation) he can provide consent to both stages of the PNT process (including creating embryos with the intended mothers eggs and donor eggs), or for the second stage only (with the donor eggs). Alternatively, we have developed a form which allows a man to consent to the use of his sperm for PNT in addition to 'standard' donation. These forms have been developed to reflect the different information needs of PNT donors as opposed to 'standard' donors.
- 3.7.** We propose that before any consents or samples are obtained from a prospective mitochondrial donor and patient, the recruiting clinic should provide information about screening and its implications, the procedure, legal parenthood, what information will be collected and held by the HFEA and what will be potentially disclosed to any person born following their donation (paragraphs 33.28-29). The consent requirements are outlined at paragraphs 33.30-33.32.
- 3.8.** In developing the consent forms we have sought legal advice and feedback from stakeholders, including from patient organisations, professional bodies and licensed clinics, to make sure they meet the requirements of the Regulations and Schedule 3 of the Human Fertilisation and Embryology Act 1990 and are as patient friendly as possible.
- 3.9.** The Authority is asked to approve this approach to consent to treatment and donation. The consent forms are for information (at annex five), and are as follows:

  - Women's consent to mitochondrial donation treatment and storage form (WMT form)

- Men's consent to mitochondrial donation treatment and storage form (MMT form)
- Your consent to mitochondrial donation (WDM form)
- Your consent to donating sperm for mitochondrial donation (for pronuclear transfer only) (MD - PNT only)
- Your consent to donating sperm, including for use in pronuclear transfer (MD including PNT)

### Code of Practice guidance

- 3.10.** We propose to introduce a standalone guidance note on mitochondrial donation and make a number of minor consequential changes to our existing guidance and requirements to cover the use of mitochondrial donation in clinical treatment. We sought stakeholder feedback on the key policy areas, which is incorporated in the summaries below. The mitochondria guidance note is at annex three.

### Staff to be involved in mitochondrial donation

- 3.11.** New Code of Practice guidance (paragraphs 33.1-33.8) sets out the licensing process outlined in stage one of this paper, including who should be involved in deciding whether a particular patient should receive mitochondrial donation treatment, who can perform the treatment, and who the treatment can be offered to.
- 3.12.** Paragraphs 33.9-33.11 describe how embryos following mitochondrial donation can be used. They state that embryos that have undergone either MST or PNT should not be transferred with any other embryos that have not undergone the same technique in the same treatment cycle. A clinic should not perform embryo biopsy (such as for the purpose of preimplantation genetic diagnosis (PGD) or preimplantation genetic screening (PGS)) on embryos that have undergone MST or PNT. It also states that a clinic should use the same sperm provider for both steps of PNT unless there is a good reason for not doing so (eg, if the mitochondria donor is a close genetic relative of the intended father).

### Provision of counselling and information

- 3.13.** New Code of Practice guidance (paragraphs 33.12-33.13) advises clinics that people seeking treatment should have access to mitochondrial disease specialists, clinical geneticists, genetic counsellors and, where appropriate, infertility counsellors. The clinic should work closely with the local genetics/mitochondrial disease clinic of those seeking treatment.
- 3.14.** The guidance also sets out what information clinics should provide to patients seeking mitochondrial donation (paragraphs 33.14-33.20). Most stakeholders agreed that these patients should receive similar information to other types of fertility patients but that they should also receive information specific to this form of treatment, including genetic and clinical information about the mitochondrial disease, the possible impact (if known) of the mitochondrial

disease on those affected and their families, and the experience of the clinic in carrying out the techniques.

- 3.15.** Similarly to sperm, egg and embryo donation, (paragraphs 33.21-33.22) clinics should tell people who seek mitochondrial donation treatment that it is best for any resulting child to be told about their origin early in childhood. We also propose that clinics inform patients of the potential risk of mitochondrial disease in future generations and the potential ways to avoid this (eg, that any female born following MST or PST that, should she wish to have children of her own, could have her eggs or early embryos analysed by PGD in order to select for embryos free of abnormal mitochondria).

### **Disclosing non-identifying information about mitochondrial donors to patients and parents**

- 3.16.** The Authority is asked to consider whether to allow certain non-identifying information about the mitochondrial donor to be accessed by patients and/or parents of children born following mitochondrial donation before the child reaches the age of 16. This would mirror the access policy for sperm, egg and embryo donation.
- 3.17.** The Regulations require clinics to submit the following information about the mitochondria donor:
- (a) the screening tests carried out on the mitochondrial donor and information on that donor's personal and family medical history
  - (b) matters contained in any description of the mitochondrial donor as a person which that donor has provided, and
  - (c) any additional matter which the mitochondrial donor has provided with the intention that it be made available to a person who requests information under this section.
- 3.18.** This information can be accessed by a mitochondrial donor-conceived person, should they decide to access the information they are entitled to from the age of 16. Just as with standard gamete and embryo donation, there is no provision in the Act or Regulations to release this information to patients or parents of the resulting child. Legal advice suggests that if the Authority were to allow the disclosure of this information, it could disclose information about screening tests and medical history (see (a) above) and any description given by the donor ((b) above), but not information provided for the mitochondria donor-conceived person ((c) above).
- 3.19.** A key reason for encouraging clinics to disclose non-identifying donor information to patients and parents of donor-conceived people is to help parents share information about their child's genetic origins, and to prepare them for potentially meeting their donor once they can receive donor identifying information at 18. These Regulations introduce a different system for mitochondria donor-conceived children because it is recognised that a mitochondria donor does not determine the characteristics of a child in the

same way as with gamete donation and will not be the genetic parent of any child born. The Regulations specify that mitochondria donors cannot be identified, reflecting the policy view that mitochondrial donation is more akin to organ donation than egg or sperm donation.

- 3.20.** However, it is possible that patients or parents might find it beneficial to access certain information via the clinic or the HFEA about their mitochondrial donor. For example, the parent of a child born following mitochondrial donation with a medical condition may want to access information about their mitochondrial donor's family medical history. The Authority may wish to allow patients and parents to access this type of information, if they so wish. However, to recognise the clear differences with sperm and egg donation, we would not advise clinics to provide information about the mitochondria donor to prospective patients, in the same way as we do for egg and sperm donation.

### **Mitochondrial donor screening**

- 3.21.** Mitochondrial donors will provide their eggs in the same way as egg donors for treatment and as such the risk of infectious diseases being transmitted is likely to be the same. New mandatory requirements set out in box 33B requires clinics to follow the same requirements for laboratory tests and storage set out in [licence condition T52](#) (for sperm and egg donors), except for genetic screening. This part of T52 is not relevant because it relates to nuclear DNA based conditions. Instead, stakeholders suggested mitochondrial donors are screened for pathogenic mitochondrial DNA mutations to ensure, as far as possible, that the donor doesn't carry a mitochondrial disease. Clinics should therefore carry out genetic screening for pathogenic mitochondrial DNA mutations and carry out an assessment of the risk of transmitting inherited conditions known to be present in the maternal line, after consent is obtained. Complete information on the associated risk and on the measures undertaken for its mitigation should be communicated and clearly explained to the recipient.
- 3.22.** Following stakeholder feedback on the impact of continuing research in this area, we propose advising clinics to keep up to date with relevant literature and professional guidance, such as on refinements to the techniques, to improve their efficacy in treatment. Also, consistent with a recommendation of the scientific expert panel, clinics should keep up to date with emerging research relevant to mitochondria haplotype matching and consider matching the haplotypes of donors with recipients where possible.
- 3.23.** In addition, before accepting a mitochondrial donor, clinics should follow the broadly same requirements and guidance as set out in [guidance note 11 Donor recruitment, assessment and screening](#) (such as on assessing their suitability and the provision of information and counselling). This is proposed in paragraph 33.25 of the new guidance note.

### **Age limit for mitochondrial donors**

- 3.24.** Age should be a consideration when selecting mitochondrial donors as there is some evidence to suggest that mitochondrial DNA has a high mutation rate

resulting in numerous new mutations over a person's lifetime, and potentially resulting in decreased mitochondrial function. The age of the donor may also affect the number of viable eggs that are collected. Stakeholders had mixed views on our proposal to apply the same age limit for egg donors to mitochondrial donors. It was agreed that any limit applied needs to be scientifically justified.

- 3.25.** There is some evidence to suggest that mitochondria in a woman's eggs accumulate damage over time meaning the eggs of older donors may have reduced mitochondrial function. Age should therefore be taken into consideration (paragraph 33.26) when determining the suitability of a woman donating her eggs, in conjunction with an assessment of her reproductive health, such as an assessment of ovarian reserve.

### **The 10 family limit**

- 3.26.** The family limit refers to the number of families a single donor can help to create. The current limit is based on the perceived social and psychological interests of donors and donor-conceived people in maintaining a relatively small number of siblings/children. It is also there to minimise the possibility of two children from the same donor having a relationship with each other without knowing they are genetically related.
- 3.27.** We proposed that the 10 family limit should also apply to women donating their mitochondria. The reasons for the limit, referred to above, do not apply in the case of mitochondrial donation, but we nevertheless felt that the limit should apply in order to keep the number of offspring from one donor low to mitigate against the impact of one of those donors later being found to have a transmissible disease or condition.
- 3.28.** However, stakeholders argued that the risk of a donor transmitting a disease or condition to the child is very low because mitochondrial donors do not donate their nuclear genetic material and will have undergone genetic screening for pathogenic mitochondrial DNA mutations. This, coupled with the fact that the main reasons for the limit do not apply to mitochondrial donation, means that we propose introducing guidance (paragraph 33.27) that the family limit will not apply to those who only donate their mitochondria and those sperm donor's who's gametes are used to produce embryos with donor eggs in PNT (and are thus not genetically related to the child).

### **Compensating donors**

- 3.29.** Under the [current system of donor compensation](#), clinics can compensate egg donors a fixed sum of up to £750 per cycle of donation and compensate sperm donors a fixed sum of up to £35 per clinic visit. Paragraph 16 in General Directions 0001 (at annex four) will specify that the system for compensating people providing eggs or sperm for mitochondrial donation should be consistent with that of gamete and embryo donation. People donating for the purposes of PNT and/or MST will be required to undergo the same process for providing

their sperm or eggs as egg or sperm donors. For the same reason, the current benefits in kind system for egg and sperm donors should equally apply.

### **Import of eggs or embryos which have undergone mitochondrial donation**

- 3.30.** New mandatory requirements set out in box 33C explain the statutory provisions which prohibit UK clinics from importing eggs or embryos for treatment in the UK which have undergone MST or PNT abroad. Eggs or embryos which been created abroad using either MST or PNT do not fall within the statutory definition of 'permitted' because they will not have been created within the circumstances prescribed by the Regulations.
- 3.31.** A clinic is prohibited by Section 3 of the 1990 Act from using eggs or embryos unless they fall within the definition of permitted. There is no statutory power for the Authority to retrospectively authorise the use of PNT or MST. Consequently, the new guidance reflects the fact that, even if it were lawful to import eggs or embryos created abroad using PNT or MST, there would be little point in doing so because the use of the material in the UK would not be lawful. This has been highlighted in the import and export guidance note.
- 3.32.** In relation to the import of eggs, embryos or sperm for use in treatment involving mitochondrial donation (ie, where PNT or MST using the donor gametes takes place in the UK), the Regulations do not prevent this. However, as with any other import, clinics need to ensure that there is compliance with the requirements for information provision, screening and consent etc., specific to mitochondrial donation.

### **Follow-up of children born following mitochondrial donation**

- 3.33.** Clinics offering mitochondrial donation must have a documented process for monitoring children born following mitochondrial donation, including long-term medical follow-up, where patients have consented. New guidance (at paragraph 33.34) proposes that clinics should explain to patients the benefits of participating in follow-up. The majority of stakeholders agreed that patients should be encouraged to consent to follow-up of children born following mitochondrial donation, but that this should not be mandatory. There is no legal power to mandate follow-up studies.
- 3.34.** Proposed guidance (at 33.33) also states that clinics should establish links with mitochondrial disease clinics to facilitate follow-up. If the patient is not a UK resident, the clinic should decide whether to establish links with either a mitochondrial disease clinic based in the UK or an overseas clinic. Plans for follow-up must be submitted with a clinic's application to vary its licence to perform mitochondrial donation as stated in Direction 0008 (paragraph 7(iiv)) at annex four.
- 3.35.** Proposed guidance (paragraph 33.35) states that if a clinic becomes aware that a child born following mitochondrial donation has been born with a mitochondrial disease, birth defect, or genetic abnormality, or other adverse outcome (such as a miscarriage), the clinic must regard this as an adverse

incident and report this in line with the requirements on adverse incidents set out in [guidance note 27](#). This is to capture information about any abnormalities that may occur as a result of carrying out the MST or PNT treatment.

## Recommendation

- 3.36.** The Authority is asked to approve the proposed approach for clinics running a good quality service, including the:
- Registration process, as set out in General Directions 0005 - Collecting and recording information for the HFEA (at annex four).
  - The proposed approach to obtaining consent set out at paragraphs 3.4-3.9 above, guidance within the new Mitochondrial donation guidance note, paragraphs 33.28-33.32 (at annex three) and the General Directions 0007 - Consent (at annex four).
  - Staff to be involved in mitochondrial donation, as set out in the Mitochondrial donation guidance note, paragraphs 33.1 to 33.11 (at annex three).
  - Provision of counselling and information, as set out in the Mitochondrial donation guidance note, paragraphs 33.12 to 33.22 (at annex three).
  - Mitochondrial donor screening, as set out in the Mitochondrial donation guidance note, 33B Mandatory requirements box and paragraphs 33.23-33.25 (at annex three).
  - Age limit for mitochondrial donors, as set out in the Mitochondrial donation guidance note, paragraph 33.26 (at annex three).
  - The 10 family limit, as set out in the Mitochondrial donation guidance note, paragraph 33.27 (at annex three).
  - Compensating donors, as set out in General Directions 0001 - Gamete and Embryo donation (at annex four).
  - Import of eggs or embryos which have undergone mitochondrial donation, as set out in the Mitochondrial donation guidance note, mandatory requirements set out in box 33C (at annex three).
  - Follow-up of children born following mitochondrial donation, as set out in the Mitochondrial donation guidance note, paragraphs 33.33-33.35 (at annex three).
- 3.37.** The Authority is also asked to consider whether to allow certain non-identifying information about the mitochondrial donor to be accessed by patients and/or parents of children born following mitochondrial donation prior to the child reaching the age of 16. This decision will affect the Mitochondrial donation guidance at paragraphs 33.28-29 (at annex three).

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## 4. What to do after treatment

- 4.1. Following treatment clinics must ensure that they continue to comply with their obligations under this new regulatory framework.

#### **Submitting outcome of treatment**

- 4.2. The same data submission requirements that apply to other treatment outcomes will also apply to mitochondrial donation treatments. This involves informing the HFEA of the outcome of treatment 14 weeks after the treatment cycle completion date and the outcome of any pregnancy where there is foetal pulsation.

#### **Follow-up reporting**

- 4.3. As mentioned above in 3.33, clinics will be required to have in place a documented process for monitoring children born following mitochondrial donation, where patients have consented to follow-up. In addition clinics should submit an annual report on patient uptake of follow-up studies and (non-patient specific) information on the outcomes. These requirements are outlined in General Directions 0005 (at annex four) and the Mitochondrial donation follow-up information sheet that must be submitted for your information (at annex five).

#### **Export of eggs or embryos which have undergone mitochondrial donation**

- 4.4. The Regulations do not prevent post MST or PNT eggs or embryos (created following authorisation by the Authority) from being exported. The Authority's current policy is that within the UK, only clinics licensed to undertake mitochondrial donation are permitted to also use those eggs or embryos in treatment once PNT or MST is completed. [General Directions 0006](#) currently require a receiving clinic abroad to be licensed, authorised, accredited or designated before a UK clinic can export to it (a requirement arising from EU legislation). However, they do not require the clinic abroad to be specifically accredited to do mitochondrial donation nor its embryologists to be accredited to undertake the two processes.
- 4.5. It is therefore possible that post MST or PNT eggs or embryos could be exported to a clinic with little or no experience of treatment involving mitochondrial donation and with overseas clinics there would be no mechanisms in place to follow up any child born following mitochondrial donation treatment. We propose that the Authority agrees, in principle, that clinics should not export post MST or PNT eggs or embryos under general directions.
- 4.6. Pending legal advice, we think that it will be possible to include specific requirements in General Directions 0006 to reflect the need for clinics abroad to have equivalent expertise and mechanisms in place – either by an addition to requirements for general directions or by requiring clinics wishing to export to apply for special directions. If the Authority agrees with this approach, we will amend General Directions 0006 – Imports and exports and invite the Authority to delegate the approval thereof to the sub-group of members that will also be approving the final version of General Directions 0008.

### Record keeping

- 4.7. Additions have been made to the General Directions 0012 to require licensed clinics to retain copies of the 'Mitochondrial donation follow-up information sheets' for a period of at least 30 years from the date on which any gametes or embryos were used in treatment.

### Recommendation

- 4.8. The Authority is asked to approve the proposed approach to what clinics must do following treatment, including follow-up reporting and record-keeping:
- General Directions 0005 - Collecting and recording information for the HFEA on outcome reporting and the 'Other submissions' section (at annex four).
  - General Directions 0012 - Retention of records, at paragraph 1(k) (at annex four).
- 4.9. The Authority is also asked to approve the proposed approach to the export of eggs or embryos following mitochondrial donation at paragraphs 4.4-4.6 of the paper.

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## 5. Consequential amendments to the Code of Practice

- 5.1. Consequential changes following the introduction of the new Regulations have been made to existing guidance in the Code of Practice (see separate document). These changes are not substantial but are required to ensure accuracy across the Code of Practice.

### Recommendation

- 5.2. The Authority is asked to approve the consequential changes following the introduction of mitochondrial donation.

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## 6. Implementation

- 6.1. On the 29 October we will issue a Clinic Focus article and Chair's letter setting out the final processes, systems and guidance for regulating mitochondrial donation. All forms and guidance will be published on the HFEA website.
- 6.2. At the same time we will publish patient information on our website with information for those who may be interested in finding out more about the treatment, the approval process and the first steps that should be taken.





## **Annex 1: Regulating mitochondrial donation: stakeholder feedback report**

## **1. Introduction**

- 1.1. In February 2015 Parliament approved The Human Fertilisation and Embryology (Mitochondrial Donation) Regulations 2015 to permit the use of maternal spindle transfer (MST) and pronuclear transfer (PNT) to avoid serious mitochondrial disease. The regulations will come into force on 29 October 2015.
- 1.2. Since Parliament approved the regulations we have been designing a regulatory system to develop a robust framework for licensing mitochondrial donation. As part of this process we have sought expert stakeholder views on a number of our draft processes and guidance, which were set out in the [‘Regulating mitochondrial donation: seeking expert views. Background document’](#)
- 1.3. This report summarises stakeholder feedback on the:
  - Clinic licensing process and how to demonstrate competency
  - Patient approval process for mitochondrial donation
  - Eligibility criteria for mitochondrial donors
  - Process by which the HFEA will collect information about mitochondrial donation
  - Information patients undergoing mitochondrial donation and mitochondrial donors need
  - Follow-up process for clinics carrying out mitochondrial donation.

## **2. Methodology**

- 2.1. We sought stakeholder views throughout June 2015, on some of the operational aspects of regulation through an online survey and a workshop held in Central London.
- 2.2. The workshop was attended by 30 stakeholders and we received 28 completed responses to the online survey. Both the workshop and the survey attracted contributions from a broad spectrum of stakeholders, including but not limited to staff from HFEA licensed clinics and mitochondrial disease centres, experts in mitochondrial genetics and inheritance, and patient groups and charities.

## **3. The clinic licensing process and how to demonstrate competency**

- 3.1. Before an HFEA-licensed clinic can undertake treatments using mitochondrial donation, they will need to apply to the HFEA to vary their licence to include the ‘express provision’ required by the regulations, which will allow clinics to carry out the techniques. As part of this process the competency of the proposed embryologist to perform mitochondrial donation will need to be assessed.



- 3.2. We asked stakeholders to consider the appropriateness of the proposed approach for assessing the competency of a clinical embryologist to perform mitochondrial donation techniques. The proposal suggested that clinics should submit evidence of the clinical embryologist having experience in performing micro-manipulation on human or animal (eg, mice) eggs or embryos, performing MST and PNT techniques in treatment, training or research and also submission of supporting references of the embryologist's knowledge and experience. In addition stakeholders were asked if they had suggestions for alternative or additional evidence that could demonstrate the competency of a clinical embryologist intending to perform one or both of the recognised techniques

#### **Stakeholder views**

- 3.3. In general stakeholders thought that due to the highly specialised techniques it was essential for a clinical embryologist to have previously carried out PNT and MST on human gametes and embryos (either under a research licence or from overseas experience) before carrying out the technique in clinical treatment.
- 3.4. Encouraging clinics to first obtain a research licence prior to applying to varying a treatment licence was seen as advantageous for the scientific community at large, as this would encourage a greater number of clinics to independently reproduce published data. An opportunity to replicate and adapt previous research was seen as a chance to improve knowledge and methodologies based on published results.
- 3.5. Aside from an embryologist demonstrating an ability to carry out the technique using human embryos, there was a broad consensus of what would evidence competency. A competent practitioner would demonstrate a low carryover of mitochondria from the patient's egg or embryo comparable with published results and obtain good quality blastocysts. However, it is not known how blastocyst quality could be evaluated, some suggested considerations of morphology or gene expression could be taken into account.
- 3.6. Onward monitoring of competency assessments for the clinical embryologist was seen as paramount. Suggestions of monitoring competency included assessing against key performance indicators (KPIs) derived from published literature regarding safety and efficacy as well as advice from practicing/publishing research centres. It was suggested that the competency frameworks should recognise competencies of embryologists who had been trained overseas.
- 3.7. Some stakeholders thought that it would be unnecessary for the HFEA to conduct an onsite inspection for every licence variation, but instead suggested that it would be desirable for the HFEA to conduct an onsite inspection if there is a belief it is necessary (e.g. change in the premises or lab used) on a case by case basis. Others thought onsite inspections were necessary due to the novel nature of PNT and MST.

- 3.8. A few stakeholders highlighted the importance of providing genetic counselling for women undergoing mitochondrial donation treatment. However, there were mixed views on competency requirements for counsellors. Some thought that it is important to have counsellors who are associated with a mitochondrial diagnostic service with considerable experience of genetic counselling, whilst others thought counsellors competent for fertility counselling would have appropriate skills to counsel mitochondrial donation patients. One stakeholder said that: *“Linkage to a mitochondrial diagnostic service with substantial experience of genetic counselling for mitochondrial disease is essential until experience is gained and standard operating procedures fully established and success rates known.”*- Clinical lead of the Oxford mitochondrial genetics service.

### Summary

- Clinical embryologists should have previously carried out PNT and MST on human gametes and embryos before carrying out the technique in clinical treatment. Key performance indicators (KPIs) and performance metrics for clinical embryologists performing mitochondrial donation should be developed.
- Patients should have access to a genetic counselling service to explore their treatment options, including alternative options to MST and PNT. Mixed views on different competency requirements for counsellors seeing people affected by mitochondrial disease.

## 4. The patient approval process for mitochondrial donation

- 4.1. Stakeholders were asked to firstly consider the proposed approach for assessing the particular risk of a patient passing on abnormal mitochondria to their embryos. Secondly stakeholders were asked to consider how we should assess significant risk and seriousness, including whether the draft application form allows for the capture of all the information that would be necessary for the HFEA to make this assessment.

### Stakeholder views

- 4.2. Generally, stakeholders agreed with the proposed approach for assessing the ‘particular’ risk by reference to the presence of mutant mitochondria. Some stakeholders thought the assessment should be ‘stricter’ as women with lower mitochondria load may not be affected. However, others were of the view that women with lower mutant mitochondria load were still at risk of having an affected embryo. One stakeholder said that: *“If a women goes forward for this technique she should have evidence to say her mitochondrial DNA is effected - any level should make her suitable for the technique.”* - The Lily Foundation.
- 4.3. Some stakeholders thought the current process used by the HFEA to peer review applications from clinics wishing to carry out preimplantation genetic diagnosis (PGD) for a new condition, should be used as a model in the assessment of particular risk. Others were concerned that the proposal for each application to be peer reviewed may delay decisions on cases.



Stakeholders thought that the HFEA Statutory Approvals Committee should have some guidance in determining seriousness as this would be important for consistency.

- 4.4. The majority of stakeholders agreed that the proposed process took into account all aspects relevant to the risk of, and seriousness, of the disease as well as mitochondria disease biology. However, a few emphasised that we should be flexible to account for rare or unknown mitochondrial diseases and suggested allowing room for other evidence to be submitted. One stakeholder stated that “...*mutation threshold is much more difficult to assess and may vary between different families. Often family trees are small and thus being precise about the threshold is NOT possible. Even for relatively common mtDNA mutations the threshold causing disease can be challenging with differences between different families. For rarer mutations where there is less information this will be even more challenging*” – Newcastle Fertility Centre.
- 4.5. Stakeholders had mixed views on using published literature to help assess seriousness. Some highlighted that existing literature would be important (both as evidence for the application and to aid putting the patient case into context), but others thought that this would be difficult where the literature on a patient's condition was inadequate. Some had significant reservations about assessing seriousness based on the worst possible symptoms for a given mutation. This is because many mutations have significant variability in their symptoms, with some manifesting very severe symptoms but only rarely. Therefore an application could put down symptoms that are very unlikely to be seen. However, it was pointed out that while these worst case symptoms might be rare it is still possible and would have serious consequences for this resulting child.
- 4.6. Some suggested that assessment of seriousness is subjective and different for each family. Patient views and familial risk should be taken into account through an impact statement of the disease and this should be presented by geneticists with experience in mitochondrial disease. One stakeholder said “*It is important that the patient perspective of choice is also considered following appropriate implications discussions.*”- The British Fertility Society.
- 4.7. A small number of stakeholders expressed a desire to only allow mitochondrial donation treatment to women who had previously undergone unsuccessful preimplantation genetic diagnosis (PGD). Others reasoned that having PGD as a pre-requisite could potentially undermine the very purpose of PNT and MST. One group of stakeholders stated that “*mitochondrial donation has the potential to be used for women whose eggs contain very high levels of, or exclusively, mitochondrial DNA mutation, which are not suitable for PGD. Mitochondrial donation is likely to be a safer option than PGD when levels of mitochondrial DNA mutation are borderline, both for the child born, but particularly for subsequent generations if the child is female.*” - The Association of Medical Research Charities, The Academy of Medical Sciences, Medical Research Council, Wellcome Trust and The Royal Society.



- 4.8. Stakeholders suggested that it may be preferable in some circumstances for PGD to be offered as an option to patients but should not be made a pre-requisite.

### **Summary**

- Stakeholders broadly agreed on the proposed approach to the patient approval process, which will involve take into account all aspects relevant to the risk of, and seriousness, of the disease as well as mitochondria disease biology of assessing particular risk.

## **5. The eligibility criteria for mitochondrial donors**

- 5.1. Mitochondrial donors will provide their eggs in the same way as egg donors for fertility treatment (the same will apply to men who provide sperm for mitochondrial donation). As their eggs will be collected and used to create embryos, the risk of infectious diseases being transmitted is likely to be the same. For this reason we proposed that most of the same requirements for laboratory tests and storage in relation to sperm and egg donors should apply to mitochondrial donors, except for genetic screening and assessment of mitochondrial donors' medical history.
- 5.2. We also examined the extent to which mitochondrial donor recruitment is comparable to egg donor recruitment for fertility treatment. In particular we focused on whether the existing age limit for egg donors (36 and under, unless there are exceptional circumstances) should also apply to mitochondrial donors and if the ten family limit should also apply to mitochondrial donors.
- 5.3. Another specific issue we considered is whether clinics should attempt to match the haplogroup/haplotype of the mitochondria donor with that of the patient undergoing treatment. Some scientists have suggested that if the patient and the mitochondria donor have different mitochondrial haplotypes, there is a theoretical risk that the donor's mitochondria won't be able to 'communicate' properly with the patient's nuclear DNA, which could cause problems in the embryo and resulting child. We asked stakeholders whether consideration should be given to mitochondria haplotype matching in the process of selecting donors and how this might affect the availability of donors.

### **Stakeholder views**

- 5.4. The majority of stakeholders favoured mitochondrial donors being screened in the same way as egg donors with the addition of next generation sequencing of the donors' mitochondrial genome. In addition, some suggested screening the mitochondria DNA from blood or urine samples to detect levels of abnormal mitochondria DNA and determine risk. Some also thought that consideration should be given to heteroplasmy levels of common pathogenic mutations in the blood as they may not always be linked to phenotypes.



- 5.5. There were mixed views on the value of applying the same age limit of 36 for women donating their mitochondria. Stakeholders recognised that mitochondrial mutations accumulate over time and may therefore indirectly affect the quality of eggs; however they acknowledged the lack of evidence in this area. Some thought that the age limit was too restrictive and suggested instead a broader assessment of a donor's reproductive health (for example, their ovarian reserve) could be more useful to determine the eligibility of a mitochondria donor. It was suggested that any age limit should be justified and regularly reviewed in light of any new evidence.
- 5.6. Similarly, stakeholders had mixed views on the proposed approach to applying the ten family limit for gamete donors to women donating their mitochondria. The family limit is based on the perceived social and psychological interests of donors and donor-conceived people in maintaining a relatively small number of siblings/children. It is also to minimise the possibility of two children from the same donor having a relationship with each other without knowing they are genetically related. It could be argued that the reasons for setting the limit at ten do not apply in the same way to children born from mitochondrial donation.
- 5.7. The majority of stakeholders agreed that this rationale for the ten family limit for gamete donors does not apply in the same way for mitochondria donors. One group of stakeholders said that: *“Although mitochondria donors will ostensibly undergo the same process as gamete donors, namely egg retrieval, the purpose and genetic relatedness is very different. Directly transposing provisions from one technology to another may bring unnecessary restrictions, and could also risk that unique considerations for licensing mitochondrial donation could be overlooked”*. - *The Association of Medical Research Charities, The Academy of Medical Sciences, Medical Research Council, Wellcome Trust and The Royal Society*.
- 5.8. Some stakeholders however did agree with the proposed rationale for having a family limit to limit inadvertent disease transmission from a donor who has a previously undetected genetic condition. Others thought it was not relevant for mitochondrial donors as the mitochondrial genome would be screened to detect most diseases. Some stakeholders also suggested that in order to protect the health of donors there should be a limit on the number of egg collection cycles they could undergo.
- 5.9. The majority of stakeholders agreed with the proposed approach of encouraging clinics to keep a watching brief on emerging evidence concerning haplogroup matching and for clinics to consider haplogroup matching were appropriate, as some studies with inbred laboratory animals have shown some mild adverse health effects associated with mitochondrial donation between divergent mtDNA backgrounds. Given the lack of current evidence to support haplotype matching, most thought this should not be a requirement and were concerned that if it was this would add unnecessary delays to treatment, especially for ethnic minority patients who could potentially have more rare haplotypes.



## Summary

- Stakeholders recommended mitochondrial genome sequencing for prospective mitochondria donors. Genetic testing for nuclear based conditions is not necessary and it would only be necessary to take maternal family medical history.
- Stakeholders had mixed views on applying the same age limit and family limit for egg donors to mitochondrial donors. It was agreed that any limit applied needs to be scientifically justified.
- Most stakeholders thought clinics should be responsible for monitoring emerging evidence on haplogroup matching.

## 6. The process by which the HFEA will collect information about mitochondrial donation

- 6.1. The HFE Act 1990 (as amended) requires UK licensed clinics to submit information to the HFEA on their patients, donors, treatments and outcomes. These data are collected via electronic forms and are held on the HFEA Register. We collect information on each patient (the woman who is treated), their partner (if there is one), all donors and every licenced treatment and its outcome.
- 6.2. The HFEA will collect different information about mitochondrial donation because the regulations that apply, particularly to disclosure of information, are different. For example, mitochondria donor-conceived people will not be able to access information that could identify the mitochondrial donor. Instead, they will be able to access non-identifying information from HFEA register at the age of 16. Mitochondrial donors will also be able to find out how many children have been born using their eggs, their sex and year of birth.
- 6.3. We asked stakeholders to consider how the HFEA could collect information about mitochondrial donors. We also asked if there should be any differences in the information we require from mitochondrial donors as compared to information requirements from egg donors as well as entitlement to accessing this information. A proposed mitochondrial donor registration form was also considered at the workshop.

### Stakeholder views

- 6.4. Some stakeholders emphasised that only necessary information that will be useful to mitochondrial donor-conceived people should be collected about a donor's family history in accordance to data protection laws. Some thought that following 'standard' donation, parents generally show greater interest in a donor's medical history, whereas the children are more interested in the donor's personal information.
- 6.5. Stakeholders fed back their views on the draft mitochondrial donor registration form. Some thought that the form should have separate sections for medical history relating to their mitochondria and a general medical history section.



Stakeholders also agreed that both the clinic and the donor should complete the form together.

## 7. The information patients undergoing mitochondrial donation and mitochondrial donors need

- 7.1. Before clinics obtain consent we propose that they should i) provide patients with information about the potential risks of mitochondrial donation, the importance of follow-up studies and ii) encourage patients to be open with any resulting children regarding their conception. We propose that donors should be provided with information in accordance to best practice guidelines which apply to sperm and egg donors as well as information regarding unsuspected heritable conditions. This would mean that if a clinic learns, through the birth of an affected child, that a mitochondria donor carries a previously unsuspected mitochondrial disease, the donor should be notified (if they have indicated that they wish to be notified).
- 7.2. We asked stakeholders to explore the extent to which information provided to patients receiving treatment involving mitochondrial donation, and to mitochondrial donors, should mimic or differ that given to those undergoing fertility treatment/gamete donation. We examined what specific information clinics should provide and collect at what stage, and also guidance that should be offered to clinics about how to discuss with parents the best methods of informing children about their origins.

### Stakeholder views

- 7.3. The majority of stakeholders stated that patients should be provided with information on risks of treatment. One stakeholder said that patients should be given *“information about the potential risks of mitochondrial donation, appropriate alternatives, the importance of follow-up studies and encouraging openness with any resulting children”* - Newcastle Fertility Centre
- 7.4. One stakeholder thought it would be logical to ask patients to confirm that they have been advised by experts in mitochondrial disease on the procedure and any associated risks after visiting a clinic. This guidance could be revised after five years if mitochondrial donation proves to be safe and effective in practice.
- 7.5. Stakeholders were in general agreement that it would be reasonable for clinics to provide patients with information to inform their child about circumstances of their conception whilst they are still young. This would be of particular benefit for families participating in routine follow up after they have received treatment involving mitochondrial donation. Stakeholders reasoned that any child who grows up experiencing frequent interactions with healthcare professionals, as part of clinical follow-up and research, would be able to have a greater understanding of their experiences as a child, and in the longer term the child may be more willing to consent to continue participation in follow up as an adult.

- 7.6. In terms of information provided to the mitochondrial donor, some stakeholders emphasised the importance of explaining the legal position of the mitochondrial donor. The information should explain that donors are not identifiable to recipients or to anyone conceived via their donation and donating mitochondria does not make the donor legally or financially responsible for the resulting child.

### **Summary**

- The majority of stakeholders agreed that mitochondrial donors and patients receiving treatment involving mitochondrial donation should be given similar information as those donating/receiving eggs, sperm or embryos for fertility treatment.
- In particular, they should receive information about the risks, any follow up processes and success rates before they give consent to treatment. Some also thought that mitochondrial donors should receive information on their legal status and relationship to donor conceived child.

## **8. The follow-up process for clinics carrying out mitochondrial donation**

- 8.1. The HFEA proposes that clinics should have in place a documented process for monitoring children born following mitochondrial donation, where patients have consented to follow-up. We propose introducing guidance that clinics should encourage their patients to take part in follow-up studies, whilst also acknowledging the rights of patients and their children not to participate in such studies. The topic examined here was how to encourage patients to take part in the clinical follow-up of children born following mitochondrial donation. Proposals included requiring clinics to submit a documented process for monitoring children born following mitochondrial donation (and any future changes to this process) and annual reports to the HFEA.

### **Stakeholder views**

- 8.2. Stakeholders acknowledged that clinical follow up of children born following mitochondrial donation was important and distinct from broader medical or social research that may take place in the future, for example from researchers accessing data from the HEFA Register. There was consensus that patients should be encouraged to consent to follow-up of children born following mitochondrial donation, but consent should be freely given. A small number of stakeholders felt that follow-up should be mandatory and legally binding at least until the donor conceived child is sixteen years old.
- 8.3. Some stakeholders stated that follow-up should be made easy for patients and resulting children to encourage continued participation. The majority of stakeholders thought that children should not feel medicalised by the process. They felt it would be important for children to be told they were born following mitochondrial donation so they can decide whether or not to continue to consent to follow up in adult years.



One stakeholder said that: *“we must be careful not to be overbearing on this subject - the whole reason for this is to have a “normal child” any parent involved will want protect their very wanted child and ensure that they are ok but not to the point where they feel like an experiment - I cannot imagine any family not wanting follow up”* – The Lily Foundation

- 8.4. Stakeholders felt that follow-up, where possible, should be done locally via GPs and Health Visitors and trips to clinics kept to a minimum. They felt it would be essential for GPs and clinics to work together closely. Stakeholders had mixed views on the frequency of check-ups made during follow-up. Some recommended annual assessments of physical health and mental health were appropriate; other stakeholders recommended check-ups at certain ages of the child’s life. One stakeholder highlighted that the NHS already has established facilities and procedures to allow for appropriate follow-up care during and after pregnancy for women who carry certain mitochondrial DNA mutations.
- 8.5. Most stakeholders agreed that clinics should make arrangements with mitochondrial disease centres. One stakeholder said that: *“...whilst there is an emphasis on licenced centres to ensure that appropriate follow up is available this should be provided by specialist paediatric mitochondrial services to an agreed program. The BFS believes this process should be established through specialist services with a consideration to long term follow-up.”* – The British Fertility Society.
- 8.6. Some also highlighted that submitting follow-up plans to the HFEA could help standardise the quality of information collected by clinics and help standardise provision of information.

### Summary

- The majority of stakeholders agreed that patients should be encouraged to consent to follow-up of children born following mitochondrial donation, but that this should not be mandatory.
- Mixed responses on how frequently the check-ups should take place for consenting families.
- Most agreed that clinics should make arrangements with mitochondrial disease centres to carry out follow-up and some stakeholders agreed that these plans should be submitted to the HFEA in an annual update report.



## **Annex 2: Summary of Standing Orders changes**

### 3. The Statutory Approvals Committee

#### Purpose of the committee

- 3.1 The purpose of the Statutory Approvals Committee is to keep under review and to authorise the use of embryo testing; to authorise the use of mitochondrial donation treatment; to issue Special Directions for the import/export of gametes; and to authorise the use of novel processes in licensed activities.

#### Delegated powers and functions of the Statutory Approvals Committee

- 3.2 The Authority delegates to the Statutory Approvals Committee the following powers:

- a) the authorisation of the use of embryo testing for conditions not previously authorised by the Authority (under Schedule 2, paragraph 1ZA(1)(a), (b) and (c) of the Act)
- b) the authorisation of the use of embryo testing to establish whether the tissue of any resulting child would be compatible with that of a sibling that suffers from a serious medical condition (under Schedule 2, paragraph 1ZA(1)(d))
- c) the authorisation of the use of embryo testing to establish whether an embryo is one of those whose creation was brought about by using the gametes of a particular person (under Schedule 2, paragraph 1ZA(1)(e))
- d) the authorisation of the use of maternal spindle transfer (MST) and/or pronuclear transfer (PNT) for a named patient (under The Human Fertilisation and Embryology (Mitochondrial Donation) Regulations 2015)
- e) the issuing of Special Directions for the import/export of gametes or embryos (under section 24 of the Act), and
- f) the authorisation of the use of novel processes in licensed activities.

- 3.3 The functions of the Statutory Approvals Committee shall include:

- a) keeping under review the genetic conditions authorised by the Authority for embryo testing.

#### Membership of the Statutory Approvals Committee

- 3.4 The Statutory Approvals Committee shall consist of no more than six members, which shall include:

- a) a Committee Chair (who shall be a lay Authority member)
- b) a Deputy Committee Chair (who shall be a lay Authority member);



c) up to four other Authority members.

3.5 The Chair of the HFEA shall appoint the members of the Statutory Approvals Committee.

3.6 Members of the Statutory Approvals Committee shall usually be appointed for a term of three years.

### **Meetings of the Statutory Approvals Committee**

3.7 The quorum for a meeting of the Statutory Approvals Committee shall be three including the Committee Chair or Deputy Committee Chair and two other members.

3.8 The Statutory Approvals Committee shall usually meet 12 times per year. At the discretion of the Chair, the committee may meet additionally at short notice (and, if necessary, by telephone- or video-conference) if the Chair considers there is an item (or items) which cannot be delayed until the next meeting.

3.9 No member of the Statutory Approvals Committee present at a meeting shall abstain from voting.

3.10 Decisions of the Statutory Approvals Committee to authorise embryo testing or novel processes, or to issue Special Directions, require a simple majority (and in the event of a tie, the Committee Chair shall have a casting vote).

### **Attendance at meetings of the Statutory Approvals Committee**

3.11 In addition to members of the Statutory Approvals Committee, the following persons shall usually attend its meetings:

a) a legal adviser

b) a specialist adviser

a) the Head of Governance and Licensing

b) the Committee Secretary.

3.12 The Committee Chair may invite such other persons (including employees) as he/she considers appropriate, to attend the meetings of the Statutory Approvals Committee and/or to provide advice to inform the deliberations of the Statutory Approvals Committee.

3.13 The Committee Chair may determine when and whether it is necessary or desirable for any non-members of the committee to withdraw from the meeting to enable the committee to deliberate in private.

**Annex 3: Draft Mitochondrial  
donation Code of Practice  
guidance note**

DRAFT

# 33. Mitochondrial donation

Version 1.0

## On this page:

### Mandatory requirements:

- [Modifications to the Human Fertilisation and Embryology \(HFE\) Act 1990 \(as amended\)](#)
- [Extracts from the Human Fertilisation and Embryology \(Mitochondrial Donation Regulations\) 2015](#)
- [Extracts from licence conditions](#)
- [Directions](#)

### HFEA guidance:

- [Staff to be involved in mitochondrial donation](#)
- [Mitochondrial donation for the avoidance of serious mitochondrial disease](#)
- [Embryo transfer using embryos following mitochondrial donation](#)
- [Genetic consultation and counselling](#)
- [Information for those seeking mitochondrial donation](#)
- [Importance of informing children of their origins](#)
- [Eligibility requirements for mitochondrial donors](#)
- [Information for prospective mitochondrial donors](#)
- [Informing mitochondrial donors about information available to children born from the treatment](#)
- [Consent](#)
- [Import of eggs or embryos which have undergone mitochondrial donation](#)
- [Follow-up arrangements](#)

## Mandatory requirements

### Human Fertilisation and Embryology (HFE) Act 1990 (as amended)

Amended section 31ZA Request for information as to genetic parentage or mitochondrial donors etc

(1) A person who has attained the age of 16 ("the applicant") may by notice to the Authority require the Authority to comply with a request under subsection (2) or (2A).

(2) The applicant may request the Authority to give the applicant notice stating whether or not the information contained in the register shows that a person ("the donor") other than a parent of the applicant would or might, but for the relevant statutory provisions, be the parent of the applicant, and if it does show that—

(a) giving the applicant so much of that information as relates to the donor as the Authority is required by regulations to give (but no other information), or

(b) stating whether or not that information shows that there are other persons of whom the donor is not the parent but would or might, but for the relevant statutory provisions, be the parent and if so—

- (i) the number of those other persons,
- (ii) the sex of each of them, and
- (iii) the year of birth of each of them.

(2A) The applicant may request the Authority to give the applicant notice stating whether or not the information contained in the register shows that a person is the applicant's mitochondrial donor, and if it does show that, giving the applicant the following information contained in the register —

- (a) the screening tests carried out on the mitochondrial donor and information on that donor's personal and family medical history,
- (b) matters contained in any description of the mitochondrial donor as a person which that donor has provided, and
- (c) any additional matter which the mitochondrial donor has provided with the intention that it be made available to a person who requests information under this section,

but not giving any information which may identify the mitochondrial donor or any person who was or may have been born in consequence of treatment services using genetic material from the applicant's mitochondrial donor, by itself or in combination with any other information which is in, or is likely to come into, the possession of the applicant.

(3) The Authority shall comply with a request under subsection (2) if—

- (a) the information contained in the register shows that the applicant is a relevant individual, and
- (b) the applicant has been given a suitable opportunity to receive proper counselling about the implications of compliance with the request.

(3A) The Authority must comply with a request under subsection (2A) if—

- (a) the information contained in the register shows that the applicant is a mitochondrial donor-conceived person, and
- (b) the applicant has been given a suitable opportunity to receive proper counselling about the implications of compliance with the request.

(4) Where a request is made under subsection (2)(a) and the applicant has not attained the age of 18 when the applicant gives notice to the Authority under subsection (1), regulations cannot require the Authority to give the applicant any information which identifies the donor.

(5) Regulations under subsection (2)(a) cannot require the Authority to give any information as to the identity of a person whose gametes have been used or from whom an embryo has been taken if a person to whom a licence applied was provided with the information at a time when the Authority could not have been required to give information of the kind in question.

(6) The Authority need not comply with a request made under subsection (2)(b) by any applicant if it considers that special circumstances exist which increase the likelihood that compliance with the request would enable the applicant—

(a) to identify the donor, in a case where the Authority is not required by regulations under subsection (2)(a) to give the applicant information which identifies the donor, or

(b) to identify any person about whom information is given under subsection (2)(b).

(7) In this section—

“relevant individual” has the same meaning as in section 31;

“the relevant statutory provisions” means sections 27 to 29 of this Act and sections 33 to 47 of the Human Fertilisation and Embryology Act 2008.

(8) In this section and sections 31ZB to 31ZE—

“mitochondrial donor-conceived person” means a person who was or may have been born in consequence of treatment services using—

(a) an egg which is a permitted egg for the purposes of section 3(2) by virtue of regulations under section 3ZA(5), or

(b) an embryo which is a permitted embryo for those purposes by virtue of such regulations;

the “mitochondrial donor” in respect of a person who was or may have been born in consequence of treatment services using such a permitted egg or such a permitted embryo is the person whose mitochondrial DNA (but not nuclear DNA) was used to create that egg or embryo.

#### **Amended section 31ZD Provision to donor of information about resulting children**

(1) This section applies where a person (“the donor”) has consented under Schedule 3 (whether before or after the coming into force of this section) to—

(a) the use of the donor’s gametes, or an embryo the creation of which was brought about using the donor’s gametes, for the purposes of treatment services provided under a licence, or

(b) the use of the donor’s gametes for the purposes of non-medical fertility services provided under a licence.

(2) In subsection (1)—

(a) “treatment services” do not include treatment services provided to the donor, or to the donor and another person together, and

(b) “non-medical fertility services” do not include any services involving partner-donated sperm.

(3) The donor may by notice request the appropriate person to give the donor notice stating—

- (a) the number of persons of whom the donor is not a parent but would or might, but for the relevant statutory provisions, be a parent by virtue of the use of the gametes or embryos to which the consent relates,
- (ab) the number of persons in respect of whom the donor is a mitochondrial donor,
- (b) the sex of each of those persons, and
- (c) the year of birth of each of those persons.
- (4) Subject to subsections (5) to (7), the appropriate person shall notify the donor whether the appropriate person holds the information mentioned in subsection (3) and, if the appropriate person does so, shall comply with the request.
- (5) The appropriate person need not comply with a request under subsection (3) if the appropriate person considers that special circumstances exist which increase the likelihood that compliance with the request would enable the donor to identify the persons falling within paragraphs (a) to (c) of subsection (3).
- (6) In the case of a donor who consented as described in subsection (1)(a), the Authority need not comply with a request made to it under subsection (3) where the person who held the licence referred to in subsection (1)(a) continues to hold a licence under paragraph 1 of Schedule 2, unless the donor has previously made a request under subsection (3) to the person responsible and the person responsible—
- (a) has notified the donor that the information concerned is not held, or
- (b) has failed to comply with the request within a reasonable period.
- (7) In the case of a donor who consented as described in subsection (1)(b), the Authority need not comply with a request made to it under subsection (3) where the person who held the licence referred to in subsection (1)(b) continues to hold a licence under paragraph 1A of Schedule 2, unless the donor has previously made a request under subsection (3) to the person responsible and the person responsible—
- (a) has notified the donor that the information concerned is not held, or
- (b) has failed to comply with the request within a reasonable period.
- (8) In this section “the appropriate person” means—
- (a) in the case of a donor who consented as described in paragraph (a) of subsection (1)—
- (i) where the person who held the licence referred to in that paragraph continues to hold a licence under paragraph 1 of Schedule 2, the person responsible, or
- (ii) the Authority, and
- (b) in the case of a donor who consented as described in paragraph (b) of subsection (1)—
- (i) where the person who held the licence referred to in that paragraph continues to hold a licence under paragraph 1A of Schedule 2, the person responsible, or

(ii) the Authority.

(9) In this section “the relevant statutory provisions” has the same meaning as in section 31ZA.

### **Amended paragraph 4 of Schedule 3**

#### **Variation and withdrawal of consent**

(1) The terms of any consent under this Schedule may from time to time be varied, and the consent may be withdrawn, by notice given by the person who gave the consent to the person keeping the gametes, human cells, embryo or human admixed embryo to which the consent is relevant.

(1A) Sub-paragraph (1B) applies to a case where an egg is used in the process set out in regulation 4 of the Human Fertilisation and Embryology (Mitochondrial Donation) Regulations 2015 (and “egg A” and “egg B” have the same meanings in this paragraph as in that regulation).

(1B) The terms of the consent to that use of egg A or egg B cannot be varied, and such consent cannot be withdrawn, once all the nuclear DNA of egg B which is not polar body nuclear DNA is inserted into egg A.

(2) Subject to sub-paragraphs (3) to (3B), the terms of any consent to the use of any embryo cannot be varied, and such consent cannot be withdrawn, once the embryo has been used—

- (a) in providing treatment services,
- (aa) in training persons in embryo biopsy, embryo storage or other embryological techniques,
- or
- (b) for the purposes of any project of research.

(3) Where the terms of any consent to the use of an embryo (“embryo A”) include consent to the use of an embryo or human admixed embryo whose creation may be brought about in vitro using embryo A, that consent to the use of that subsequent embryo or human admixed embryo cannot be varied or withdrawn once embryo A has been used for one or more of the purposes mentioned in sub-paragraph (2)(a) or (b).

(3A) Sub-paragraph (3B) applies to a case where an embryo is used in the process set out in regulation 7 of the Human Fertilisation and Embryology (Mitochondrial Donation) Regulations 2015 (and “embryo A” and “embryo B” have the same meanings in sub-paragraph (3B) as in that regulation).

(3B) The terms of the consent to that use of embryo A or embryo B cannot be varied, and such consent cannot be withdrawn, once all the nuclear DNA of embryo B which is not polar body nuclear DNA is inserted into embryo A.

(4) Subject to sub-paragraph (5), the terms of any consent to the use of any human admixed embryo cannot be varied, and such consent cannot be withdrawn, once the human admixed embryo has been used for the purposes of any project of research.

(5) Where the terms of any consent to the use of a human admixed embryo (“human admixed embryo A”) include consent to the use of a human admixed embryo or embryo whose creation may be brought about in vitro using human admixed embryo A, that consent to the use of that subsequent human admixed embryo or embryo cannot be varied or withdrawn once human admixed embryo A has been used for the purposes of any project of research.

#### **Definition of the mitochondrial donor eg, for consent and surrogacy purposes**

### **Schedule 3 Amended paragraph 22**

(A1) For the purposes of this Schedule, neither of the following is to be treated as a person whose gametes were used to create an embryo (“embryo E”)—

- (a) where embryo E is a permitted embryo by virtue of regulations under section 3ZA(5), the person whose mitochondrial DNA (not nuclear DNA) was used to bring about the creation of embryo E;
- (b) where embryo E has been created by the fertilisation of an egg which was a permitted egg by virtue of regulations under section 3ZA(5), the person whose mitochondrial DNA (not nuclear DNA) was used to bring about the creation of that permitted egg.

(3B) For the purposes of this Schedule, in a case where an egg is a permitted egg by virtue of regulations under section 3ZA(5) the egg is not to be treated as the egg of the person whose mitochondrial DNA (not nuclear DNA) was used to bring about the creation of that permitted egg.

(1) In this Schedule references to human cells are to human cells which are not—

- (a) cells of the female or male germ line, or
- (b) cells of an embryo.

(2) References in this Schedule to an embryo or a human admixed embryo which was used to bring about the creation of an embryo (“embryo A”) or a human admixed embryo (“human admixed embryo A”) include an embryo or, as the case may be, a human admixed embryo which was used to bring about the creation of—

- (a) an embryo or human admixed embryo which was used to bring about the creation of embryo A or human admixed embryo A, and
- (b) the predecessor of that embryo or human admixed embryo mentioned in paragraph (a), and
- (c) the predecessor of that predecessor, and so on.

(3) Reference in this Schedule to an embryo or a human admixed embryo whose creation may be brought about using an embryo or a human admixed embryo are to be read in accordance with sub-paragraph (2).

(4) Reference in this Schedule (however expressed) to the use of human cells to bring about the creation of an embryo or a human admixed embryo include the use of human cells to alter the embryo or, as the case may be, the human admixed embryo.

(5) References in this Schedule to parental responsibility are—

- (a) in relation to England and Wales, to be read in accordance with the Children Act 1989,
- (b) in relation to Northern Ireland, to be read in accordance with the Children (Northern Ireland) Order 1995, and
- (c) in relation to Scotland, to be read as references to parental responsibilities and parental rights within the meaning of the Children (Scotland) Act 1995.

(6) References in this Schedule to capacity are, in relation to England and Wales, to be read in accordance with the Mental Capacity Act 2005.

(7) References in this Schedule to the age of 18 years are, in relation to Scotland, to be read as references to the age of 16 years.

## **Regulations**

### **Human Fertilisation and Embryology (Mitochondrial Donation) Regulations 2015**

#### **Permitted eggs and permitted embryos**

## Permitted egg

3. An egg ("egg P") is a permitted egg for the purposes of section 3(2)(b)(a) of the Act if—
- (a) egg P results from the application of the process specified in regulation 4 to two eggs, each of which—
    - (i) is a permitted egg as defined in section 3ZA(2)(b) of the Act (not an egg which is a permitted egg by virtue of these regulations), and
    - (ii) was extracted from the ovaries of a different woman;
  - (b) that process has been applied to those eggs in the circumstances specified in regulation 5; and
  - (c) there have been no alterations in the nuclear or mitochondrial DNA of egg P since egg P was created by means of the application of that process.

## Permitted egg: process

- 4.—(1) The process referred to in regulation 3(a) consists of the following two steps.
- (2) In step 1—
- (a) either—
    - (i) all the nuclear DNA of an egg ("egg A") is removed, or
    - (ii) all the nuclear DNA of egg A other than polar body nuclear DNA is removed;
  - (b) either—
    - (i) all the nuclear DNA of another egg ("egg B") is removed, or
    - (ii) all the nuclear DNA of egg B other than polar body nuclear DNA is removed.
- (3) In step 2 all the nuclear DNA of egg B which is not polar body nuclear DNA is inserted into egg A.

## Permitted egg: circumstances

5. The circumstances referred to in regulation 3(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.

## Permitted embryo

6. An embryo ("embryo P") is a permitted embryo for the purposes of section 3(2)(a) of the Act if—
- (a) embryo P results from the application of the process specified in regulation 7 to two embryos, each of which—
    - (i) is a permitted embryo as defined in section 3ZA(4) of the Act (not an embryo which is a permitted embryo by virtue of these regulations), and
    - (ii) was created by the fertilisation of a permitted egg as defined in section 3ZA(2) of the Act (not an egg which was a permitted egg by virtue of these regulations) extracted from the ovaries of a different woman;
  - (b) that process has been applied to those embryos in the circumstances specified in regulation 8; and
  - (c) since embryo P was created by means of the application of that process—
    - (i) there have been no alterations in the nuclear or mitochondrial DNA of any cell of embryo P, and
    - (ii) no cell has been added to embryo P other than by the division of embryo P's own cells.

## Permitted embryo: process

- 7.—(1) The process referred to in regulation 6(a) consists of the following two steps.
- (2) In step 1—
- (a) either—
    - (i) all the nuclear DNA of an embryo ("embryo A") is removed, or

- (ii) all the nuclear DNA of embryo A other than polar body nuclear DNA is removed; and
  - (b) either—
    - (i) all the nuclear DNA of another embryo (“embryo B”) is removed, or
    - (ii) all the nuclear DNA of embryo B other than polar body nuclear DNA is removed.
- (3) In step 2 all the nuclear DNA of embryo B which is not polar body nuclear DNA is inserted into embryo A.

Permitted embryo: circumstances

8. The circumstances referred to in regulation 6(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.

## Licence conditions

- T124 a. No clinic may carry out either the process of pronuclear transfer\* (PNT) or maternal spindle transfer\* (MST) or part of either process, unless express provision has been made on the clinic’s licence permitting it to undertake either or both processes.
- b. Neither PNT nor MST may be carried out under third party, satellite or transport agreements.
- c. No clinic may provide treatment using gametes or embryos which have been created using PNT or MST unless express provision has been made on the clinic’s licence permitting the clinic to undertake either or both processes;

\*Wherever reference is made in this licence to PNT or MST or the process of PNT or MST, that is the process defined in Regulation 4 or Regulation 7 of the Human Fertilisation and Embryology (Mitochondrial Donation) Regulations 2015.

- T125 PNT and MST must only be carried out on premises of clinics that are licensed to undertake mitochondrial donation (‘MD’). These processes must not be carried out on the premises of a clinic that is operating under a third party, satellite or transport agreement with a clinic that holds a licence to undertake MD.
- T127 a. No alterations may be made to the nuclear or mitochondrial DNA of an egg created by means of the application of MST.
- b. No alterations may be made to the nuclear or mitochondrial DNA of an embryo created by means of the application of PNT and no cell may be added to an embryo created by means of the application of PNT other than by the division of the embryo’s own cells.
- T128 a. In the case of treatment involving mitochondrial donation the clinic must ensure that it only carries out the process of PNT or MST for a particular, named patient once the Authority has issued a determination that:
- there is a particular risk that any egg extracted from the ovaries of the named woman or any embryo created by the fertilisation of an egg extracted from the ovaries of the named woman may have mitochondrial abnormalities caused by mitochondrial DNA and

- there is a significant risk that a person with those abnormalities will have or develop a serious mitochondrial disease.

T129 Only those embryologists assessed as competent by the Authority to undertake PNT, MST or both, and named on the front of this licence, are permitted to undertake those processes or any part thereof.

## Directions

### 0001 – Gametes and embryo donation

### 0005 – Collecting and recording information for the HFEA

### 0007 - Consent

### 0008 - Information to be submitted to the HFEA as part of the licensing process

## Staff to be involved in mitochondrial donation

- 33.1 A senior clinical geneticist/mitochondrial disease specialist should be involved in deciding whether a particular patient should receive mitochondrial donation treatment.
- 33.2 The centre should ensure that a multidisciplinary team is involved in providing the treatment. The team should include mitochondrial disease specialists, reproductive specialists, embryologists, clinical geneticists, genetic counsellors and molecular geneticists. It should maintain close contact with the primary care physician, the referring clinician, or the mitochondrial disease centre.
- 33.3 Only embryologists who have been assessed as competent by the HFEA and named on the clinic's licence can perform maternal spindle transfer or pronuclear techniques as defined in Regulation 4 and 7 of the Human Fertilisation and Embryology (Mitochondrial Donation) Regulations 2015. An application for an assessment of the competence of an embryologist must be submitted to the HFEA and will be considered by a Licence Committee. When submitting an application to the HFEA for a competency assessment the person responsible and the relevant embryologist should provide:
- evidence of the embryologist's experience of carrying out MST or PNT in treatment, training or research on human eggs or embryos (eg, embryo survival rates, blastocyst development, and rate of carryover of mutant mitochondria, in line with KPIs determined by the HFEA)
  - references to support the embryologist's experience and knowledge, and
  - any other information that may demonstrate competence (such as the embryologist's experience of performing micro-manipulation on human or animal (e.g., mice) eggs or embryos).
- 33.4 The PR should submit an application to the HFEA for an assessment of the competence of each embryologist who intends performing MST or PNT or any part thereof. A PR wishing to make any changes to the authorised embryologists must submit an application to the HFEA for a variation of the clinic's licence accompanied by the relevant evidence of competency for each proposed embryologist.

## Mitochondrial donation for the avoidance of serious mitochondrial disease

### Interpretation of mandatory requirements

33A

Maternal spindle transfer (MST) can only be carried out where the Authority has issued a determination that —

- there is a particular risk that any eggs collected from the patient named in the application form may have mitochondrial abnormalities caused by mitochondrial DNA; and
- there is a significant risk that a person with those abnormalities will have or develop serious mitochondrial disease

Pronuclear transfer (PNT) can only be carried out where the Authority has issued a determination that—

- there is a particular risk that any embryos created with eggs collected from the patient named in the application form may have mitochondrial abnormalities caused by mitochondrial DNA; and
- there is a significant risk that a person with those abnormalities will have or develop serious mitochondrial disease.

Treatment involving mitochondrial donation can only be carried out by a clinic that is licensed to do mitochondrial donation as evidenced by express provision on the clinic's licence permitting it to undertake either PNT, MST or both.

The process of PNT or MST (as defined in Regulation 4 and 7 of the Human Fertilisation and Embryology Authority (Mitochondrial Donation) Regulations 2015) may only be carried out by embryologists who have been assessed by the HFEA as competent to undertake these processes and who are named on the clinic's licence.

PNT and MST may only be carried out on the premises of a clinic licensed to undertake mitochondrial donation and may not be done on third party premises or the premises of any satellite centre.

Clinics that are not licensed to undertake PNT or MST for treatment purposes may not use eggs or embryos created using these techniques in treatment services.

- 33.5 When deciding if it is appropriate to offer MST or PNT in particular cases, the centre should consider the circumstances of those seeking treatment rather than the particular mitochondrial condition.
- 33.6 The centre should discuss with the patient the likely outcomes of the proposed treatment, the nature and potential risks of the treatment, and any other treatment options that may be suitable, such as pre-implantation genetic diagnosis (PGD) or egg donation.

33.7 When deciding if it is appropriate to offer MST or PNT in particular cases, the seriousness of the disease in that case should be discussed between the patient seeking treatment and the clinical team. The level of risk for those seeking treatment and any child that may be born will also be an important factor for the centre to consider and should be discussed with the patient.

33.8 The centre should consider the following factors before deciding whether it is appropriate to offer MST or PNT in particular cases. Having considered these factors, if a decision is taken to offer MST or PNT, the clinic must submit an application for authorisation to the HFEA.

The Authority's assessment of the seriousness will be made, where possible, based on the most severe symptoms that could be expected for a particular patient's case. When submitting an application to the HFEA, the PR must wherever possible, provide supporting evidence detailing:

- a) the patient's medical history
- b) the patient's family medical history of mitochondrial disease
- c) the patient's mutant mtDNA load and threshold associated with symptoms of disease
- d) scientific literature relevant to the mtDNA mutation or disease, and
- e) any additional information which the clinician may consider is relevant to the application, such as a statement from a genetic counsellor.

### Embryo transfer using embryos following mitochondrial donation

33.9 Embryos that have undergone either MST or PNT (or any other technique) should not be transferred with any other embryos that have not undergone the same technique in the same treatment cycle.

33.10 A centre should not perform embryo biopsy (such as for the purpose of preimplantation genetic diagnosis (PGD) or preimplantation genetic screening (PGS)) on embryos that have undergone MST or PNT.

33.11 A centre should use the same sperm provider for both steps of PNT unless there is a good reason for not doing so (i.e. if the mitochondria donor is a close genetic relative of the intended father).

### Genetic consultation and counselling

33.12 The centre should ensure that people seeking treatment have access to mitochondrial specialists, clinical geneticists, genetic counsellors and, where appropriate, infertility counsellors. Patients who have been referred by one clinic to another for the purposes of mitochondrial donation must be offered specific counselling about mitochondrial donation by the clinic licensed to do mitochondrial donation regardless of whether the patient has previously been offered counselling by the referring centre.

33.13 The centre should work closely with the local genetics/mitochondrial disease centre of those seeking treatment.

### Information for those seeking mitochondrial donation

33.14 The centre should ensure that people seeking MST or PNT are given the appropriate information about the treatment. Where a patient has been referred by one clinic to another for the purposes of mitochondrial donation, the clinic licensed to provide

mitochondrial donation must ensure that it provides the patient with appropriate information including:

- a) information about the process, procedures and possible risks involved in mitochondrial donation including the risks for any child that may be born following the mitochondrial donation, and in the IVF treatment
  - b) information about the experience of the centre and embryologist(s) carrying out the techniques.
- 33.15 The centre should also provide information to those seeking treatment to help them make decisions about their treatment, including:
- a) genetic and clinical information about the mitochondrial disease
  - b) the possible impact (if known) of the mitochondrial disease on those affected and their families
  - c) the importance of telling any resulting children of the mitochondrial donation treatment
  - d) information about treatment and social support available, and
  - e) information from a relevant patient support group or the testimony of people living with the condition, if those seeking treatment have no direct experience of it themselves.
- 33.16 If the person seeking treatment has already been given information about the particular mitochondrial disease, for example from a regional mitochondrial disease centre with appropriate expertise, the centre need not provide this information again. However, the centre should ensure that the information which has been provided is accurate, sufficiently detailed and that the patient fully understands the information.
- 33.17 Before providing mitochondrial donation treatment the centre should ensure that those seeking treatment have had sufficient opportunity to fully consider the possible outcomes and risks of these techniques and their implications.
- 33.18 The centre should provide information to people seeking mitochondrial donation treatment about the collection and provision of information, specifically:
- a) information that centres must collect and register with the HFEA about the donors
  - b) what information may be disclosed to people born as a result of the mitochondrial donation and in what circumstances, and
  - c) that person's right to access anonymous information about the mitochondrial donor from the age of 16.
- 33.19 The centre should give people seeking mitochondrial donation treatment information about the screening of people providing mitochondria. This information should include details about:
- a) the sensitivity and suitability of the tests, and
  - b) the possibility that a screened provider of mitochondria may be a carrier of a mitochondrial disease or infection.
- 33.20 The centre should provide information that explains the limitations of procedures and the risks of treatment to anyone seeking mitochondrial donation treatment. The centre should make available appropriate counselling.

Guidance note 20 applies to mitochondrial donation except guidance 20.1, 20.2 d)iii)-v).

### See also:

### Guidance note 20 – Donor assisted conception

### Guidance note 3 - Counselling

#### Importance of informing children of their origins

- 33.21 The centre should tell people who seek mitochondrial donation treatment that it is best for any resulting child to be told about their origin early in childhood.
- 33.22 Centres should inform patients of the potential risk of mitochondrial disease in future generations and the potential ways to avoid this (eg, that any female born following MST or PST that, should she wish to have children of her own, could have her eggs or early embryos analysed by PGD in order to select for embryos free of abnormal mitochondria).

#### Eligibility requirements for mitochondrial donors

#### Licence conditions

- T52 Prior to the use and/or storage of donor gametes and/or embryos created with donor gametes the centre must comply with the selection criteria for donors and the requirements for laboratory tests and storage set out below, namely:
- a. donors must be selected on the basis of their age, health and medical history, provided on a questionnaire and through a personal interview performed by a qualified and trained healthcare professional. This assessment must include relevant factors that may assist in identifying and screening out persons whose donations could present a health risk to others, such as the possibility of transmitting diseases, (such as sexually transmitted infections) or health risks to themselves (eg, superovulation, sedation or the risks associated with the egg collection procedure or the psychological consequences of being a donor).
  - b. the donors must be negative for HIV1 and 2, HCV, HBV and syphilis on a serum or plasma sample tested as follows, namely:
    - HIV 1 and 2: Anti-HIV – 1, 2
    - Hepatitis B: HBsAg and Anti-HBc
    - Hepatitis C: Anti-HCV-Ab
    - Syphilis: see (d) below
  - c. the centre must devise a system of storage which clearly separates:
    - quarantined/unscreened gametes and embryos,
    - gametes and embryos which have tested negative, and
    - gametes and embryos which have tested positive.
  - d. a validated testing algorithm must be applied to exclude the presence of active infection with *Treponema pallidum*. The non-reactive test, specific or non-specific, can allow gametes to be released. When a non-specific test is performed, a reactive result will not prevent procurement or release if a specific *Treponema* confirmatory test is non-reactive. The donor whose specimen test reacted on a *Treponema*-specific test will require a thorough risk assessment to determine eligibility for clinical use
  - e. in addition to the requirements in (b) and (d) above, sperm donors must be negative for chlamydia on a urine sample tested by the nucleic acid amplification technique (NAT)
  - f. This requirement has been removed.

- g. HTLV-1 antibody testing must be performed for donors living in or originating from high-prevalence areas or with sexual partners originating from those areas or where the donor's parents originate from those areas, and
- h. in certain circumstances, additional testing may be required depending on the donor's history and the characteristics of the gametes donated (eg, RhD, Malaria, T.cruzi).
- i. genetic screening for autosomal recessive genes known to be prevalent, according to international scientific evidence, in the donor's ethnic background and an assessment of the risk of transmission of inherited conditions known to be present in the family must be carried out, after consent is obtained. Complete information on the associated risk and on the measures undertaken for its mitigation must be communicated and clearly explained to the recipient.

T126 Donors of gametes for use in PNT and or MST must be screened for pathogenic mitochondrial DNA mutations and an assessment of the risk of transmission of inherited conditions known to be present in the maternal line, must be carried out, after consent is obtained. Complete information on the associated risk and on the measures undertaken for its mitigation must be clearly communicated and explained to the recipient.

### Interpretation of mandatory requirements

**33B**

Sections (a) to (h) of Licence condition T52 on medical and laboratory tests should apply to mitochondrial donors and to men providing sperm used to fertilise eggs of the mitochondrial donor in the process of PNT.

- 33.23 As well as taking their medical and maternal medical history (in line with T52 and T126) the recruiting centre should take details of previous donations. If a prospective donor cannot give a full and accurate maternal family history, the centre should record this fact and take it into account in deciding whether or not to accept their eggs for treatment.
- 33.24 Centres should ensure that they keep up to date with relevant literature and professional guidance, such as on refinements to the techniques, to improve their efficacy in treatment. Centres should also keep up to date with emerging research relevant to mitochondria haplotype matching and consider matching the haplotypes of donors with recipients where possible.
- 33.25 Before accepting a mitochondrial donor, centres should follow the same requirements and guidance as set out in guidance note 11, except guidance 11.2, 11.3, 11.32g,j 11.32 i-l), 11.36, 11.37, 11.38, 11.39, 11.42, 11.46-11.52.
- 33.26 Guidance on the upper age limits for egg and embryo donors does not apply for mitochondrial donors. There is some evidence to suggest that mitochondria in a woman's eggs accumulate damage over time meaning the eggs of older donors may have reduced mitochondrial function. Age should therefore be taken into consideration when determining the suitability of a woman donating her eggs, in conjunction with an assessment of her reproductive health, such as an assessment of ovarian reserve.
- 33.27 The ten family limit guidance for those providing donor gametes (or embryos created using donated gametes) outlined at 11.46, does not apply to:
  - egg donors who have donated their mitochondria only or
  - sperm donors who have donated for pronuclear where they will not be genetically related to the child.

**See also:**

## Guidance note 11 - Donor recruitment, assessment and screening

### Information for prospective mitochondrial donors

33.28 Before any consents or samples are obtained from a prospective mitochondrial donor, the recruiting centre should provide information about:

- a) the screening that will be done, and why it is necessary
- b) the possibility that the screening may reveal unsuspected conditions (eg, mitochondrial related anomalies or HIV infection) and the practical implications
- c) the scope and limitations of the genetic testing that will be done and the implications for the mitochondria donor and their family
- d) the importance of informing the recruiting centre of any medical information that may come to light after donation that may have health implications for any woman who received treatment with their mitochondria or for any child born as a result of such treatment
- e) the procedure used to collect gametes, including any discomfort, pain and risk to the mitochondria donor (eg, from the use of superovulatory drugs)
- f) the legal parenthood of any child born as a result of their mitochondrial donation
- g) what information about the mitochondrial donor must be collected by the centre and held on the HFEA Register
- h) that only non-identifying information will be disclosed when the applicant is aged over 16. No identifying information about the donor will be disclosed.
- i) the possibility that a child born as a result of their mitochondrial donation who is disabled as a result of an inherited condition that the donor knew about, or ought reasonably to have known about, but failed to disclose, may be able to sue the donor for damages, and
- j) the ability of the mitochondrial donor to withdraw consent, procedure for withdrawal of consent for the use of their mitochondria and the point up until which the donor can withdraw consent.

### Informing mitochondrial donors about information available to children born from the treatment

33.29 The centre should inform mitochondrial donors that anyone born as a result of their mitochondrial donation will have access to the following non-identifying information provided by them, from the age of 16:

- a) the screening tests carried out on the mitochondrial donor and information on that donor's personal and family medical history,
- b) matters contained in any description of the mitochondrial donor as a person which that donor has provided, and
- c) any additional matter which the mitochondrial donor has provided with the intention that it be made available to a person who requests information under this section.

### Consent

33.30 The centre should obtain written informed consent from patients and their spouse or partner (if relevant), for mitochondrial donation treatment. Where a patient and their partner have been referred by one centre to another for the purposes of mitochondrial donation, the clinic that will be undertaking the mitochondrial donation must obtain consent specific to the treatment involving mitochondrial donation regardless of what consent the patient and their partner may have provided to the referring centre. This is because the centre doing the mitochondrial treatment will have the necessary experience and expertise in mitochondrial donation and is best placed to provide the relevant information and obtain fully informed consent.

- 33.31 For mitochondrial donors, the centre should obtain the donor's written informed consent to the donation of her eggs or embryos for MST or PNT.
- 33.32 Any prospective women donating their eggs for mitochondrial donation, or men donating sperm for PNT where they will not be genetically related to the child, should be aware that they cannot withdraw or vary their consent once the donated egg or embryo has undergone the process of MST or PNT (ie, the nuclear material has been moved from one egg or embryo to another).
- 33.33 Centres should follow all other requirements and guidance on consent as outlined in guidance note 11 on donor recruitment, assessment and screening and in guidance note 5 on consent to treatment, storage, donation and disclosure of information.

### Import of eggs or embryos which have undergone mitochondrial donation

#### Interpretation of mandatory requirements

**33C**

It is not lawful in the UK to provide treatment using gametes or embryos created abroad following the use of pronuclear transfer or maternal spindle transfer. Schedule 1(f) and 3 (i) of General Direction 0006 provides that the purpose of importing gametes or embryos must be to provide treatment services. However, as treatment using gametes or embryos created abroad following the use of pronuclear transfer or maternal spindle transfer is not lawful, it follows that the import of such gametes or embryos should not take place.

#### See also:

[Guidance note 16 - Imports and exports](#)

#### See also:

[Guidance note 5 - Consent to treatment, storage, donation and disclosure of information](#)

[Guidance note 11 - Donor recruitment, assessment and screening](#)

#### Follow-up arrangements

- 33.33 Centres offering mitochondrial donation should have a documented process setting out how children born from mitochondrial donation will be followed up, where patients have consented to follow-up. These should include long-term medical follow-up of children born as a result. Centres should establish links with mitochondrial disease centres to facilitate follow-up. If the patient is not a UK resident but nevertheless wishes to participate follow-up, the centre and patient should discuss whether the patient wishes to be followed up at a mitochondrial disease centre based in the UK or a relevant centre overseas, in a location more convenient for the patient.
- 33.34 Centres should explain to patients the benefits of participating in follow-up.
- 33.35 If a centre becomes aware that a child born following mitochondrial donation has been born with a mitochondrial disease, birth defect, or genetic abnormality, or if there has been

some other adverse outcome (such as a miscarriage) following treatment involving mitochondrial donation, the centre must regard this as an adverse incident and report this to the HFEA in line with the requirements on adverse incidents set out in guidance note 27. This is to capture information about any abnormalities that may occur as a result of carrying out the MST or PNT treatment, to inform any regulatory or licensing action that the HFEA may wish to take and inform the scientific sector.

**See also:**

**Guidance note 27 – Adverse incidents**

DRAFT

## **Annex 4: Draft general directions, including:**

- 0001 - Gamete and Embryo donation
- 0005 - Collecting and recording information for the HFEA
- 0007 - Consent
- 0008 - Information to be submitted to the HFEA as part of the licensing process
- 0012 - Retention of records

**Ref: 0001**  
**Version: 4**

## **Gamete and embryo donation**

These Directions are:	GENERAL DIRECTIONS
Sections of the Act providing for these Directions:	Sections 12 (1) (d), 12 (1) (e), 12 (1) (g) and 13 (2) (f)
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### **Re-registering an anonymous donor as an identifiable donor**

1. Licensed centres must use form Bv2005/1 to re-register any person who:
  - (a) registered as a donor before 1 April 2005 and/or who donated gametes and/or embryos before that date; and
  - (b) now wishes to be registered as an identifiable donor so that information about him or her may be disclosed to any persons born as a result of the donation.
2. Centres must use Donor Information form Dv2009 to record any additional updating information about a donor who now wishes to be re-registered as an identifiable donor. Licensed centres should ensure that the appropriate box in Part 1 is ticked to indicate that the form “Corrects or changes Details already registered”. This form should be completed in addition to form Bv2005/1.

### **Giving and receiving money or other benefits in respect to any supply of gametes or embryos**

3. Centres must not accept an individual as a donor who is known (or is reasonably suspected) by that centre to have received or to be about to receive money or other benefits not in line with these Directions.
4. Where the person responsible is aware that a person wishes to be treated using gametes obtained from a donor sourced by another agency or intermediary, including introductory agencies and internet websites, the person responsible should take reasonable steps to satisfy himself that the requirements of paragraph 3 have not been breached and must keep a record of the steps taken for this purpose.

5. Centres may compensate sperm donors a fixed sum of up to £35 per clinic visit.
6. Centres may compensate egg donors a fixed sum of up to £750 per cycle of donation. Where a prospective egg donor does not complete the cycle, the centre may compensate the egg donor on a 'per clinic visit' basis.
7. Where a person has stored gametes or embryos for use in their own treatment but then consents to donate them, a centre may compensate the donor for subsequent visits on a 'per clinic visit' basis.
8. Centres may compensate donors an excess amount in cases where expenses (such as for travel, accommodation or childcare) exceed the amounts specified in paragraphs 5 and 6 above. Centres may only provide excess expenses which:
  - (a) are reasonable;
  - (b) do not include loss of earnings;
  - (c) have been incurred by the donor in connection with the donation of gametes provided to that centre; and
  - (d) have been incurred by the donor solely within the United Kingdom.
9. Donors who are not permanent residents of the UK should be compensated in the same way as UK donors without an excess for overseas travel expenses. Centres must not directly or indirectly pay the overseas travel of a non-UK donor.

### Recording excess expenses for donors

10. Where centres compensate donors an excess amount, as specified in paragraph 8 above, the centre must keep:
  - (a) a record of the actual excess expenses incurred by the donor;
  - (b) a record of the amount reimbursed to the donor; and
  - (c) the receipts produced by the donor, and/or the steps taken by the person responsible to satisfy themselves that the excess expenses claimed by the donor have in fact been incurred.
11. The records referred to in paragraph 10 must be made available to the Centre's Inspector or provided directly to the Human Fertilisation and Embryology Authority, on request.

### **Giving and receiving money or other benefits in respect to any import of gametes or embryos from outside the UK**

12. When considering whether to import gametes donated overseas, the centre should ensure the donor has not received compensation which exceeds:
  - (a) reasonable expenses incurred by the donor in connection with the donation of gametes provided to that centre; and
  - (b) loss of earnings (but not for other costs or inconveniences) incurred by the donor up to a daily maximum of £61.28 but with an overall limit of £250 for each course or cycle of donation (local currency equivalent).
13. When receiving donated gametes from overseas, the centre must keep a record (provided by the overseas centre) of:
  - (a) the actual expenses incurred by the donor;
  - (b) the amount reimbursed to the donor; and
  - (c) the receipts produced by the donor, and/or the steps taken by the person responsible to satisfy themselves that the excess expenses claimed by the donor have in fact been incurred.

### **Supply of gametes or embryos from one establishment to another**

14. Licensed centres that supply gametes or embryos to other licensed centres may only be given money or other benefits by the receiving centre for reimbursement of the reasonable expenses incurred in the supply of the gametes or embryos.

### **Benefits in kind**

15. Gamete donors may receive licensed services, such as treatment, storage, or access to licensed services, in return for supplying gametes for donation. Egg donors who receive a benefit should be provided with that benefit in the course of the donation cycle unless there is a medical reason why they cannot be.

### **Mitochondrial donation**

16. Centres may compensate those providing gametes for use in mitochondrial donation in line with paragraphs 3 to 15 above.

### **Definitions**

17. The terms listed in these Directions are explained below:

- (a) “clinic visit” means an appointment a donor attends in connection with the donation, including where the sperm sample is produced at home. This may include, but is not limited to, consultation visits, blood collection, counselling sessions and sperm sample collection.
- (b) “cycle of egg donation” means the period from the first consultation until the donor’s recuperation is complete.

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Ref: 0005  
Version: 4

**Collecting and recording  
information for the Human  
Fertilisation Embryology Authority**

These Directions are:	GENERAL DIRECTIONS
Sections of the Act providing for these Directions:	Section 12 (1) (d) and (g)
These Directions come into force on:	1 October 2009
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1. All licensed centres undertaking licensed treatments, with the exception of IUI and GIFT using partner sperm, must use the Authority's Electronic Data Interchange (EDI) to submit records relating to such activities to the Authority.
2. All licensed centres must use the following EDI forms to submit their records to the Authority:

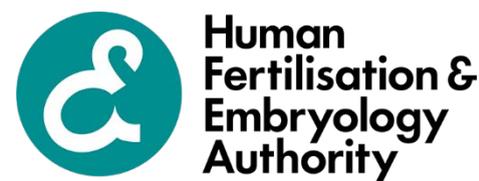
Type of form	Purpose of form
Patient registration	To provide details of the patient receiving fertility treatment.
Partner registration	To provide details of the partner of the patient receiving fertility treatment.

Donor information	<p>To provide identifiable details of a donor and the reasons why they are donating</p> <p>Licensed centres must use Donor Information form D v. 2012 to record information relating to donors and ensure that sections 1 to 20 are completed for each donor.</p> <p>Sections 21 to 27 of the Donor Information form (pages 3 &amp; 4) must be submitted to the HFEA in paper format with the donor code and the centre's code referenced.</p> <p>Intended parents supplying gametes in a surrogacy arrangement are to be registered with the IP prefix to their donor code. When registering an intended parent as a donor, pages 3 &amp; 4 of the donor form are not required by the HFEA.</p>
Donor re-registration (also known as a B form)	This form enables a previously anonymous donor to register as identifiable on the HFEA Register
Intention to treat	To inform the HFEA when a cycle in which eggs are to be collected has started
IVF treatment & embryo creation and use	To inform the HFEA about the circumstances surrounding egg collection, embryo creation and /or transfer
Donor insemination treatment	To inform the HFEA when a patient has been inseminated with donor sperm
Early pregnancy outcome	To inform the HFEA of the early outcome of a treatment
Pregnancy outcome	To inform the HFEA of the outcome of any early outcome recording 'fetal pulsation seen'
Donor sperm procurement	To inform the HFEA about the quantity of sperm donated by each donor

Embryo and gamete movement - in	To inform the HFEA about the number of embryos, eggs and ampoules, straws or vials of donor sperm transferred from another UK centre or imported from outside the UK
Embryo and gamete movement - out	To inform the HFEA of the number of embryos, eggs and ampoules, straws or vials of donor sperm removed from storage at a centre and the reason for the removal
Consent Variation	To inform the HFEA of a patient's or partner's variation of their preferences set out in the 'Consent to the disclosure of identifying information form' (CD form); to inform the HFEA of the initial completion of the CD form by a patient or partner registered for treatment prior to 1 October 2009; to inform the HFEA of preferences regarding the disclosure of information about children born as a consequence of treatment

3. All licensed centres must submit the relevant EDI forms to the Authority within the following timescales:

<b>Category of information</b>	<b>Timescale for records to be submitted to the Authority</b>
Patient registration details	10 working days after the patient has confirmed intention to undergo treatment
Partner registration details	10 working days after the patient has confirmed intention to undergo treatment
Intention to treat	3 <b>calendar</b> days after last menstrual period or stimulatory drugs being administered to/taken by a patient with the intention to perform IVF treatment



Donor information	10 working days after confirmation of sperm being released for use by the clinic, the harvesting of oocytes or in the case of imports, receipt of the imported eggs, sperm or embryos
IVF treatment & embryo creation and use	10 working days after the treatment cycle completion date
Donor insemination treatment	10 working days after the last insemination of the cycle
Early pregnancy outcome	8 weeks after the treatment cycle completion date
Pregnancy outcome	14 weeks after the predicted outcome date
Embryo and gamete movement - in	Within 10 working days of gametes or embryos coming into storage
Embryo and gamete movement - out	Within 10 working days of gametes or embryos being removed from storage
Consent variation	10 working days after the patient has completed the CD form

4. All licensed centres must ensure that EDI forms submitted to the Authority are completed according to the guidance issued by the Authority (the most recent versions of which are available, alongside the forms, on the HFEA website). Where an error is identified, centres must correct the error within 2 calendar months.
5. Any licensed centre wishing to amend records that it has previously submitted to the Authority must do so via EDI on a “correcting form”. This must be the same as the original form supplied to the Authority, but must be clearly marked as a correcting form, and must reference the number of the original form that is to be corrected.
6. Licensed centres must notify the HFEA within 10 working days of any change to the patient or partner consent decision in relation to disclosure of HFEA Register information for research purposes. To do so, for patients registered after 1 October 2009 the centre must amend previously submitted Patient registration or Partner registration forms via EDI on a “correcting form”. This must be the same as the original form supplied to the Authority, but must be clearly marked as a correcting form, and must reference the number of the original form that is to be corrected. For patients registered before 1 October 2009 the centre must submit a Consent Variation form.
7. Where a licensed centre has submitted duplicate forms, that clinic must submit a deletion request to the Authority via the EDI system, clearly referencing the form to be deleted and stating the reasons for the request.



8. When a Person Responsible is satisfied with the accuracy of the data for their licensed centre, they must sign off this data. To do this, the Person Responsible must sign and date a hard copy of the draft 'Choose a Clinic' entry and return it to the Authority no later than 5pm on the date notified to the centres by the Authority (the sign-off deadline). The draft entry can be returned by post, fax or by email with a scanned image of the signed document.
9. Persons Responsible must ensure that, before they sign off their data, they are satisfied that:
  - a) the number of treatment cycles (both generic IVF and DI) completed within the reporting period is 100% accurate;
  - (b) all early outcome forms relating to cycles in a) above and all outcome forms relating to clinical pregnancies in a) above have been submitted to the Authority and have been filled in accurately; and
  - (c) all registration forms relating to patients undergoing treatment received in a) above have been submitted to the Authority and have been filled in accurately.

### Other Submissions

10. All licensed centres undertaking Intra Uterine Insemination (IUI) or Gamete Intra-Fallopian Transfer (GIFT) with partner sperm must submit an annual return to the Authority no later than 28 February in each calendar year. The annual return must be in the format set out. Guidance is available on the HFEA website at <http://www.hfea.gov.uk/2508.html>
11. All licensed centres undertaking maternal spindle transfer (MST) and/or pronuclear transfer (PNT) must use the following paper or EDI forms to submit their records to the Authority within the following timescales:

<b>Type of form</b>	<b>Purpose of form</b>	<b>Mechanism and timescales for submission</b>
Patient Registration	To provide identifying information about the female patient having treatment.	To be submitted via EDI 10 working days after the patient has confirmed intention to undergo treatment.
Partner Registration	To provide identifying information about the partner (sperm provider) of the patient.	To be submitted via EDI 10 working days after the patient has confirmed intention to undergo treatment.
Mitochondrial donor registration	To provide identifying information about the mitochondrial donor. This is required even if the mitochondrial donor is also registered as a patient or egg donor.	To be submitted in paper* form 10 working days after the patient has confirmed intention to undergo treatment.
Pronuclear ONLY Sperm Donor Registration	To provide identifiable details of a donor whose sperm will ONLY be used in pronuclear transfer mitochondrial donation treatment for fertilisation of the mitochondrial donor's eggs. NB. This form is not required if the individual is already registered as a sperm donor or is the partner of the woman being treated.	To be submitted in paper* form 10 working days after confirmation of sperm being released for use by the clinic, the harvesting of oocytes or in the case of imports, receipt of the imported eggs, sperm or embryos.
Intention to treat	To inform the HFEA when a cycle in which eggs are to be collected has started	To be submitted via EDI 3 <b>calendar</b> days after the last menstrual period or stimulatory drugs being administered to/taken by a patient with the intention to perform IVF treatment.
IVF egg donation /storage	To inform the HFEA about the egg donation by the mitochondrial donor. The number of eggs donated for mitochondrial donation are to be recorded in the comments section of the form.	To be submitted via EDI 10 working days after the treatment cycle completion date.



Mitochondrial donation treatment	To inform the HFEA of a treatment cycle involving mitochondrial donation	To be submitted using a paper* form 10 working days after the treatment cycle completion date.
Early pregnancy outcome	To inform the HFEA of the early outcome of a treatment	To be submitted via EDI 8 weeks after the treatment cycle completion date.
Pregnancy outcome	To inform the HFEA of the outcome of any early outcome recording 'fetal pulsation seen'	To be submitted via EDI 14 weeks after the predicted outcome date.

\*All paper forms submitted should be sent by recorded delivery addressed to the HFEA's Register Information Team.

12. All licensed centres must ensure that paper forms submitted to the Authority are completed according to the guidance issued by the Authority (the most recent versions of which are available, alongside the forms, on the HFEA website). Where an error is identified, centres must correct the error within 2 calendar months.
13. All licensed centres undertaking maternal spindle transfer and/or pronuclear transfer must complete and submit to the Authority a copy of the 'Mitochondrial donation follow-up information sheet', available on the HFEA website, no later than 29 October each year. Licensed centres holding these records must be able to produce copies upon request from an HFEA member or employee.

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**Ref: 0007****Version: 6****Consent**

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1. Licensed centres must record any consent of a person whose consent is required under:
  - (a) Schedule 3 and Section 33B of the Human Fertilisation and Embryology Act 1990 as amended; and
  - (b) Sections 37 (1) and 44 (1) of Part 2 of the Human Fertilisation and Embryology Act 2008
 in the appropriate form listed in the Schedule to these Directions.
2. Where the storage period of a person's gametes or embryos has been extended, in accordance with the Human Fertilisation and Embryology (Statutory Storage Period for Embryos and Gametes) Regulations 2009, the PR of the licensed centres at which those gametes or embryos are stored must maintain a record of evidence that the conditions for extended storage of those gametes or embryos have been fulfilled.
3. Licensed centres must maintain a record of any withdrawal of consent by a person who has previously given a consent required under Schedule 3 to the Human Fertilisation and Embryology Act 1990, as amended, or under sections 37 (1) or 44 (1) of Part 2 of the Human Fertilisation and Embryology Act 2008. This consent should be recorded in the WC form, or in the case of surrogacy, the SWC form, as listed in the Schedule to these Directions.
4. Licensed centres holding any of the records referred to in these Directions must be able to produce a copy of those records (either electronically or as a hard copy) upon request from an HFEA member or employee.
5. From 1 May 2010, anyone receiving treatment at a licensed centre must complete a 'Consent to the disclosure of identifying information form' (CD Form)

if they have not already done so, regardless of when they first registered for treatment.

<b>Version control</b>	
Directions name:	Consent
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## Schedule

### Storage

- GS Your consent to the storage of your eggs or sperm  
 LGS Your consent to extending the storage of your eggs or sperm beyond 10 years  
 ES Your consent to extending the storage of your embryos beyond 10 years

### Donation

- MD Your consent to donating your sperm  
 WD Your consent to donating your eggs  
 ED Your consent to donating embryos

### Treatment

- WT Women's consent to treatment and storage form (IVF and ICSI)  
 MT Men's consent to treatment and storage form (IVF and ICSI)  
 MGI Your consent to the use of your sperm in artificial insemination  
 WGI Your consent to the use of your eggs in GIFT

### Surrogacy

- MSG Men's consent to the use and storage of sperm or embryos for surrogacy  
 WSG Women's consent to the use and storage of eggs or embryos for surrogacy  
 SPP Your consent to being the legal parent in surrogacy  
 SWP Your consent (as a surrogate) nominating an intended parent to be the legal parent

### Mitochondrial donation

- WMT Women's consent to mitochondrial donation treatment and storage form  
 MMT Men's consent to mitochondrial donation treatment and storage form  
 WDM Your consent to mitochondrial donation  
 MD - including PNT Your consent to donating sperm, including for use in pronuclear transfer  
 MD - PNT only Your consent to donating sperm for mitochondrial donation (for pronuclear transfer only)

### Disclosure of information

- CD Your consent to disclosing identifying information

## Parenthood

- WP Your consent to your partner being the legal parent
- PP Your consent to being the legal parent

## Withdrawal or stating lack of consent

- WC Withdrawing your consent
- SWC Surrogacy - withdrawing your consent
- LC Stating your spouse or civil partner's lack of consent

DRAFT

Ref: 0008

Version: 4

**Information to be submitted to the  
Human Fertilisation and  
Embryology Authority as part of  
the licensing process**

These Directions are:	GENERAL DIRECTIONS
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**General requirement relating to all applications to the Authority**

1. Applications to the Authority relating to categories A-M must be made by completing and submitting the relevant on-line application, together with relevant supporting information detailed below, via the 'electronic portal' located on the Authority's website ([www.hfea.gov.uk](http://www.hfea.gov.uk)). An application fee (details of current fees payable are available on the Authority's website) must also be submitted.
2. Failure to submit a fully completed application form, pay the application fee or provide all the necessary information set out below will, in normal circumstances, result in the application not being considered until such times as these requirements have been satisfied.
3. Persons Responsible for centres which are licensed by the Authority to carry out licensed activities (treatment, storage, non-medical fertility services or research) must at all times have available the information set out in iv-xiv of paragraph 4 of this Direction and submit this information to the Authority when requested no later than 10 working days after the date of any written request.

**Information to be supplied with applications**

**A. Applications for a new (initial) treatment, storage and non-medical fertility services licence**

4. An application for a new licence authorising:
  - (a) activities in the course of providing treatment services; and/or

- (b) the storage of gametes, embryos or human admixed embryos; or
- (c) activities in the course of providing non-medical fertility services,

must be accompanied by the information specified below:

- i. where the proposed Person Responsible is not the applicant, a written confirmation from the proposed Person Responsible that the application is made with his or her consent;
- ii. a current CV of the proposed Person Responsible listing academic and professional qualifications; work experience and registration details with the relevant professional body;
- iii. a current CV of the proposed Licence Holder listing academic and professional qualifications; work experience and registration details with the relevant professional body;
- iv. the Person Responsible Entry Programme (“PREP”) certificate number confirming satisfactory completion of the PREP by the proposed Person Responsible;
- v. a floor plan of the premises to be referenced on the licence;
- vi. a suite of information documents to be provided to patients undergoing treatment at the centre once licensed;
- vii. a completed self-assessment questionnaire submitted via the electronic portal;
- viii. a copy of the centre’s organisational chart clearly defining accountability and reporting relationships for named individuals;
- ix. evidence that staff are registered with a professional or statutory body and are appropriately qualified and trained in techniques relevant to their work, or are in a programme of supervised training;
- x. a copy of the centre’s induction and training programme that ensures that staff have adequate knowledge of the scientific and ethical principles, together with the regulatory context, relevant to their work;
- xi. evidence that a robust quality management system is in place;
- xii. a statement that all the equipment and processes to be used in activities authorised by a licence, and in other activities carried out in the course of providing treatment services that do not require a licence, have been validated;
- xiii. a detailed list of the quality indicators, a schedule of the audit programme and the reporting arrangements established for all activities authorised by a licence, and other activities carried out in the course of providing treatment services that do not require a licence; and
- xiv. a copy of the centre’s multiple birth minimisation strategy (where applicable).

**B. Applications to renew a treatment, storage or non-medical fertility services licence**

5. An application for the renewal of a licence authorising:
- (a) activities in the course of providing treatment services; and/or
  - (b) the storage of gametes, embryos or human admixed embryos; or
  - (c) activities in the course of providing non-medical fertility services,

must be accompanied by the information specified below:

- i. where the Person Responsible is not the applicant, a written confirmation from the Person Responsible that the application is made with his or her consent;
- ii. a completed self-assessment questionnaire; and
- iii. a suite of information documents to be provided to patients undergoing treatment at the centre (if different to those submitted with the original or previous renewal application).

**C. Applications to vary the activities authorised by a current treatment, storage or non-medical services licence**

6. An application to vary the activities authorised by a current licence in the course of providing treatment services or non-medical fertility services must be accompanied by the information specified below:

- i. copies of information provided to patients relating to the new activity;
- ii. evidence that the process(es) and, where applicable, the equipment used in carrying out the new activity have been validated; and
- iii. a schedule of the quality indicators, and reporting arrangements, established for this activity.

7. An application to vary a licence to authorise mitochondrial donation through maternal spindle transfer (MST) or pronuclear transfer (PNT) must be accompanied by the information specified below:

- i. copies of information provided to patients and donors relating to treatment involving mitochondrial donation;
- ii. information to demonstrate the competence of the embryologist(s) proposed to conduct the technique(s) being applied for, as follows:

- a) a CV and references of the embryologist(s), to support their experience and knowledge
  - b) key performance indicator data relating to the proposed embryologist's/embryologists' experience in carrying out the technique(s) on human eggs or embryos as follows:
    - i) whether they have carried out the techniques in treatment, training or research
    - ii) embryo survival rates (which must exceed [insert kpi 1])
    - iii) blastocyst development rates (which must exceed [insert kpi 2])
    - iv) rate of carryover of mtDNA (which must not exceed [insert kpi 3])
  - c) any other information that may demonstrate competence (such as their experience of performing micro-manipulation on human or animal (eg, mice) eggs or embryos)
- iii. evidence that the equipment, and process(es) where applicable, used in carrying out the new technique(s) has been validated;
  - iv. a schedule of the quality indicators, and reporting arrangements, established for the new treatments;
  - v. procedures for the follow-up of children born as result of mitochondrial donation, including the arrangements the centre has in place with a mitochondrial disease expert centre.

An application to add or vary the name of the embryologist(s) practicing MST or PNT need only include section 7ii)(a-c).

#### **D. Application to carry out a licensed activity using a 'novel' process**

- 8. Where centres want to carry out a licensed activity using a process that has not been authorised by the Authority, an application must be accompanied by the information specified below:
  - i. copies of information provided to patients relating to the new activity;
  - ii. evidence that the process and, where applicable, the equipment used in carrying out the new activity have been validated; and
  - iii. a schedule of the quality indicators, and reporting arrangements, established for this process.

#### **E. Applications for a new (initial) research licence**

9. An application for a new licence authorising activities for a research project must be accompanied by the information specified below:
  - i. where the proposed Person Responsible is not the applicant, a written confirmation from the proposed Person Responsible that the application is made with his or her consent;
  - ii. the PR Entry Programme (“PREP”) certificate number confirming satisfactory completion of the PREP (for Person Responsible appointed after 1 October 2009);
  - iii. a floor plan of the premises to be specified on the licence;
  - iv. copies of all information provided to patients and/or donors relating to the proposed research project;
  - v. copies of the consent forms to be used to authorise the use of gametes, embryos or human cells in the research project;
  - vi. evidence of ethics approval of the research project from a properly constituted research ethics committee; and
  - vii. a completed self-assessment questionnaire.
  
10. For applications for a new licence authorising activities in connection with the derivation from embryos of stem cells that are intended for human application, the following additional information must be submitted with the application:
  - i. evidence that the proposed Person Responsible possesses a diploma, certificate or other evidence of formal qualifications in the field of medical or biological sciences, awarded on completion of a university course of study, or other course of study recognised in the United Kingdom as equivalent and has at least two years’ practical experience which is directly relevant to the activity to be authorised by the licence; and
  - ii. evidence that the centre has, or is obtaining, a licence from the Human Tissue Authority.

#### **F. Applications to renew a research licence**

11. An application for the renewal of a licence authorising activities for a research project must be accompanied by the information specified below:
  - i. a completed self-assessment questionnaire;
  - ii. evidence of ethics approval of the research project from a properly constituted research ethics committee;

- iii. copies of all information provided to patients and/or donors relating to the proposed research project (if different to those submitted with the original or previous renewal application); and
  - iv. copies of the consent forms to be used to authorise use of gametes, embryos or human cells in the research project (if different to those submitted with the original or previous renewal application).
12. For applications to renew a licence authorising activities in connection with the derivation from embryos of stem cells that are intended for human application, the following additional information must be submitted with the application:
- i. evidence that the centre has a licence from the Human Tissue Authority.

**G. Applications to vary a research licence to vary the purposes for which the research is licensed**

13. An application to vary a research licence to vary the purposes for which the current research is licensed must be accompanied by the information specified below:
- i. evidence of ethics approval of the research project from a properly constituted research ethics committee;
  - ii. copies of all information provided to patients and/or donors relating to the proposed research project (if different to those submitted with the original or previous renewal application); and
  - iii. copies of the consent forms to be used to authorise use of gametes, embryos or human cells in the research project (if different to those submitted with the original or previous renewal application).

**H. Applications to vary a licence to either relocate to new premises or change existing premises**

14. An application to vary a licence to either relocate to new premises not authorised by a current licence for the conduct of licensed activities (treatment, storage, research and non-medical fertility services) or to alter premises authorised by a current licence for the conduct of licensed activities (treatment, storage, research and non-medical fertility services) must be accompanied by the information specified below:

- i. where the Person Responsible is not the applicant, a written confirmation from the Person Responsible that the application is made with his or her consent;
- ii. a floor plan of the premises to be referenced on the licence, and;
- iii. confirmation that any re-commissioned equipment has been tested and validated.

#### **I. Applications to change the Person Responsible or the Licence Holder**

15. An application to change the Person Responsible or the Licence Holder of a licence authorising licensed activities (treatment, storage, research and non-medical fertility services) must be accompanied by the information specified below:
  - i. a current CV of the proposed Person Responsible listing academic and professional qualifications; work experience and registration details with the relevant professional body;
  - ii. a current CV of the proposed Licence Holder listing academic and professional qualifications; work experience and registration details with the relevant professional body; and
  - iii. the PR Entry Programme (“PREP”) certificate number confirming satisfactory completion of the PREP (applications for a change of PR only).

#### **J. Applications to authorise pre-implantation genetic diagnosis**

16. An application to authorise pre-implantation genetic diagnosis (PGD) for a condition which has not previously been authorised by the Authority is subject to an application as per paragraph 1.

#### **K. Applications to authorise human leukocyte antigen tissue typing**

17. An application to authorise human leukocyte antigen (HLA) tissue typing, in isolation or in conjunction with PGD must be accompanied by the information specified below:
  - i. a copy of a signed letter of support from a clinician responsible for the care of the sibling child providing information on the:
    - (a) degree of suffering associated with the disease of the affected sibling,
    - (b) speed of degeneration in progressive disorders,

- (c) prognosis for the affected sibling in relation to all treatment options available,
- (d) availability of alternative sources of tissue for the treatment of the affected sibling, now and in the future, and
- (e) availability of effective therapy for the affected sibling now and in the future.

**L. Applications to authorise mitochondrial donation for a specific patient**

18. Applications for authorisation of mitochondrial donation for a specific patient must be made by completing the relevant application and submitting this to the HFEA.

**M. Applications for Special Directions to export gametes or embryos**

19. An application for a Special Direction to export gametes or embryos must be accompanied by the information specified below:
- i. a letter from the intended export destination centre/clinic confirming that it is willing to accept the gametes or embryos for the purpose specified in the application form.

**Notifying the Authority of information relating to licensed activities**

20. Persons Responsible must notify the Authority, through the electronic portal located on the Authority's website, of all processes undertaken in the licensed centre in carrying out a licensed activity.

**Additional information to be submitted to the Authority as part of on-going compliance**

21. Persons Responsible for centres licensed by the Authority must complete and submit to the Authority the self-assessment questionnaire (SAQ) published on the Authority's website no later than six weeks prior to the date on which the Authority has confirmed it will carry out an inspection visit. Before submitting the SAQ, Persons Responsible must confirm that the information they have provided on that document is true and accurate.
22. Where a member of the Authority's Compliance Department requests the Person Responsible to submit a further SAQ in addition to that required by paragraph 21 above, the Person Responsible must submit this to the

Authority no later than 15 working days after the date of the written request.

23. Where a member of the Authority's Compliance Department requests the Person Responsible to submit a further PREP, the Person Responsible must submit this to the Authority no later than 21 working days after the date of the written request.

<b>Version control</b>	
Directions name:	Information to be submitted to the Human Fertilisation and Embryology Authority as part of the licensing process
Reference number:	0008
Date version 1 came into force:	1 October 2009
Date version 2 comes into force:	1 October 2011
Chair's letter reference:	CH(11)06
Date version 4 comes into force:	29 October 2015
Chair's letter reference:	CH(15) 02

**Ref: 0012****Version: 3****Retention of records**

These Directions are:	GENERAL DIRECTIONS
Sections of the Act providing for these Directions:	Section 13(4), 14(2), 15(3) and 24(1)
These Directions come into force on:	1 October 2009
These Directions remain in force:	Until revoked
This version issued on:	29 October 2015

1. Subject to paragraph 2, licensed centres must retain a record of the following information for a period of at least 30 years from the date on which any gametes or embryos were used in treatment or, if not so used, the date on which any gametes or embryos were removed from storage:
  - (a) patient or donor identifying information (first name; surname; date of birth; age and sex);
  - (b) how, and by whom, the patient or donor has been reliably identified, where necessary;
  - (c) the services provided to the patient or donor;
  - (d) the medical history of the patient or donor;
  - (e) the outcome of the welfare of the child assessment, where appropriate;
  - (f) all consent forms and any specific instructions relating to the use and/or disposal of gametes and embryos;
  - (g) all clinical data (including administration of medicine and the results of any tests carried out) necessary for traceability;
  - (h) all laboratory data necessary for traceability, including records relating to any taking of an embryo from a woman or other acquisition of an embryo; the use and storage of any gametes or embryos; any testing of an embryo; consumables, drug treatments, equipment and environment (including servicing, cleaning, testing and monitoring); what equipment was used (and by whom) and staff training;
  - (i) any child born as a result of treatment provided to the patient; and

- (j) all other information necessary for traceability;
  - (k) copies of the 'Mitochondrial donation follow-up information sheets',
2. The record of information specified in paragraph 1 must be kept for a period of at least 50 years from the date on which information about the treatment was first recorded if:
    - (a) a patient has undergone treatment (other than basic partner treatment) at a licensed centre; and
    - (b) the Person Responsible for that licensed centre is unable to confirm whether or not that patient has given birth to a child as a result of the treatment undertaken at that centre.
  3. Licensed centres must retain a record of any information not specified in paragraph 1, which relates to the safety and quality of gametes and embryos, for a period of at least 10 years after the use of gametes or embryos in treatment or, if not so used, the date on which any gametes or embryos were removed from storage.
  4. The Person Responsible for a research project must retain a record of the following information for a period of at least 3 years from the date the final report of any research project is submitted to the Authority:
    - (a) the total number of embryos or human admixed embryos created, used or disposed of during the research project;
    - (b) the results of the research project; and
    - (c) the conclusions drawn from the research project.
  5. Where a research project involves the derivation of stem cells for human application, a record of the information specified in paragraph 4 and relevant information specified in paragraph 1 must be retained for a period of at least 30 years from the date the final report of any research project is submitted to the Authority.
  6. Centres licensed by the Authority to undertake preimplantation genetic diagnosis (PGD) must, in respect of each case of PGD, retain information in the patient records which fully details the reasons why the Person Responsible considered PGD to be appropriate in that particular case, in line with guidance in the Code of Practice (at 10.5, 10.6). This information shall include an explanation of why the Person Responsible

considered there to be a particular risk that the embryo tested may have a gene, chromosome or mitochondrion abnormality.

<b>Version control</b>	
Directions name:	Retention of records
Reference number:	0012
Date version 1 issued:	1 October 2009
Date version 2 issued:	6 April 2010
Chair's letter reference:	CH(10)03
Date version 3 issued:	29 October 2015
Chair's letter reference:	CH(15)02

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## **Annex 5: Draft forms and guidance, including:**

- [Licence variation form](#)
- [Mitochondrial donation follow-up information sheet](#)
- [Patient application form](#)
- [Clinical expert review form](#)
- [Decision trees for the Statutory Approvals Committee](#)
- [Mitochondrial donation: explanatory note for Statutory Approvals Committee](#)
- [Consent forms](#)



## Variation of HFEA treatment and storage licence to allow mitochondrial donation

### 1. Introduction

Please use this form to apply to vary a licence to allow mitochondrial donation through either maternal spindle transfer and/or pronuclear transfer.

To make changes to the embryology staff you only need to complete section 8.

Once complete submit to your inspector.

### 2. Centre contact information

Person responsible
Centre name
Centre number

### 3. Corporate information

Are there any changes being made to the corporate status of the centre?

Is the centre a NHS facility or a private operation?  NHS  Private  Both

### 4. Registration

Are any changes being made to the registration status of the centre?

Will the centre be registered with a regulator other than the HFEA?



**5. Licensed activities**

Please tick which additional authorised processes you are applying to add to your licence:

- Maternal spindle transfer (under the authorised activities of ‘processing gametes’ and ‘creation of embryos’).
- Pronuclear transfer (under the authorised activities of ‘processing embryos’ and ‘creation of embryos’)

**6. Reason**

Please provide reasons for the change in licensed treatments and the expected volume of any additional services.

**7. Processes**

Please provide details of any critical new equipment that will be used or processes that will be revalidated as a result of the variation

**8. Key staff**

Please list key staff responsible for the new treatment activities. Note, only an embryologist who has been assessed by the Authority as competent to undertake pronuclear transfer, maternal spindle transfer or both is permitted to undertake those processes or any part thereof.

Name	Role	Professional body registration (HCPC, GMC, NMC etc)



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## 11. Attachments

- An index of all documents in the quality manual revised as a result of the variation of licensed activities
- All patient information revised as a result of the variation of licensed activities
- A functional organisational chart, if changed as a result of the variation of licensed activities
- The procedures for the follow-up of children born as result of mitochondrial donation, including the arrangements in place with a mitochondrial disease expert centre.

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## 12. Declarations

I consent to the HFEA processing the data that I have provided on this form and any supporting documentation submitted with it, for the purposes of considering my application; statistical analysis; and quality control.

I further consent to the HFEA sharing my data with any other body with whom there is an agreement to undertake inspections or other regulatory functions on behalf of, or in conjunction with, the HFEA.

I understand that my data will be stored securely by the HFEA and saved in accordance with the HFEA's published retention and disposal schedule.

I further understand that the HFEA will not disclose my data to any third parties except as specified above, or as permitted or required by law, and in particular by the requirements of the Data Protection Act 1998 and the Freedom of Information Act 2000.

Persons submitting this application should note that by Section 18(2) of the Human Fertilisation and Embryology Act 1990 (as amended) the Authority may revoke a licence if it is satisfied that any information given for the purposes of application for the grant of licence was in any material respect false or misleading. They should also note that under Section 41(3) provision of false or misleading information, knowingly or in a reckless manner is a criminal offence.

The information provided on this form is to the best of my knowledge true and accurate

Check the box to confirm acceptance of the above statement I consent to the HFEA processing the data that I have provided on this form and any supporting documentation submitted with it, for the purposes of considering my application; statistical analysis; and quality control.

I further consent to the HFEA sharing my data with any other body with whom there is an agreement to undertake inspections or other regulatory functions on behalf of, or in conjunction with, the HFEA.

I understand that my data will be stored securely by the HFEA and saved in accordance with the HFEA's published retention and disposal schedule.



I further understand that the HFEA will not disclose my data to any third parties except as specified above, or as permitted or required by law, and in particular by the requirements of the Data Protection Act 1998 and the Freedom of Information Act 2000.

Persons submitting this application should note that by Section 18(2) of the Human Fertilisation and Embryology Act 1990 (as amended) the Authority may revoke a licence if it is satisfied that any information given for the purposes of application for the grant of licence was in any material respect false or misleading. They should also note that under Section 41(3) provision of false or misleading information, knowingly or in a reckless manner is a criminal offence.

**The information provided on this form is to the best of my knowledge true and accurate**

Check the box to confirm acceptance of the above statement

**Admin use only**

Form received from
Reference number
Submitted date

DRAFT

## Mitochondrial donation follow-up information sheet

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Centre name(s)

Centre number(s)

### How many patients have received treatment at your centre involving maternal spindle transfer or pronuclear transfer?

#### Number of patients

Current year, ending 28 October:

Previous years beginning 29  
October 2015 (cumulative):

### How many of these patients consented to being followed-up after their treatment?

#### Number of patients

Current year, ending 28 October:

Previous years beginning 29  
October 2015 (cumulative):

### As far as you are aware how many of these patients attended follow-up appointments (relevant to the outcome of their mitochondrial donation treatment)?

#### Number of patients

Current year, ending 28 October:

Previous years beginning 29  
October 2015 (cumulative):

**For these patients was treatment successful in avoiding the inheritance of mitochondrial disease (eg, if known what is the outcome of early tests on the child eg, mutant load)?**

Please provide in a non-identifying format.

**Current year, ending 28 October:**

<b>Patient No</b>	<b>Successful outcome? (Y/N)</b>
1	
2	
3	
4	
5	
6	

**Previous years beginning 29 October 2015 (cumulative):**

<b>Patient No</b>	<b>Successful outcome? (Y/N)</b>
1	
2	
3	
4	
5	
6	

### Detail any birth abnormalities

[Note: If a centre becomes aware that a child born following mitochondrial donation has been born with a mitochondrial disease, birth defect, or genetic abnormality, or other adverse outcome (such as a miscarriage), the centre must regard this as an adverse incident and report this in line with the requirements on adverse incidents set out in guidance note 27 of the Authority's Code of Practice]

#### Current year, ending 28 October:

Patient No	Successful outcome? (Y/N)
1	
2	
3	
4	
5	
6	

#### Previous years beginning 29 October 2015 (cumulative):

Patient No	Successful outcome? (Y/N)
1	
2	
3	
4	
5	
6	

**Any other outcome information the centre is able to provide in a non-identifying format**

**Current year, ending 28 October:**

<b>Patient No</b>	<b>Successful outcome? (Y/N)</b>
1	
2	
3	
4	
5	
6	

**Previous years beginning 29 October 2015 (cumulative):**

<b>Patient No</b>	<b>Successful outcome? (Y/N)</b>
1	
2	
3	
4	
5	
6	



## Mitochondrial donation: new case application form

### 1. Introduction

Please use this form if you wish to carry out a mitochondrial donation technique to treat a patient not previously authorised by the HFEA.

Before you begin your application please make sure the following statements are true:

- You hold a licence to carry out the mitochondrial donation technique (PNT and/or MST) intended for use in the treatment of this patient.
- You have identified a pathogenic mutation in the mtDNA of the patient
- You have evidence that the patient has a significant risk of having a child who will have or go on to develop serious mitochondrial disease.

It is important that the language used in this application is clear and as far as possible, understandable to non-specialists.

All abbreviations should be explained.

The application form has been designed to ensure that applying centres provide all of the information required to enable the Authority's Statutory Approvals Committee to make its decision. If the form is completed incorrectly or does not provide sufficient information it could delay the decision-making process.

The Committee is aware that not all pieces of evidence asked for will be relevant to every case.

An independent assessment of the application may also be sought from clinical experts and may inform the Statutory Approvals Committee's decision-making process

The guidance has been developed for centres licensed to carry out maternal spindle transfer (MST) and/or pronuclear transfer (PNT) that wish to apply for approval perform mitochondrial donation on a new patient. Please refer to this as you fill in the application form. These applications are all considered on a case-by-case basis.

### 2. Current centre information

Person responsible
Centre name
Centre number

### 3. Regulatory requirements

Is this application from a centre licensed to carry out maternal spindle transfer (MST) and/or pronuclear transfer (PNT)?



Only centres licensed to carry out mitochondrial donation (MST and/or PNT) are permitted to make an application. Please state whether or not the application is from an assisted reproduction clinic, licensed by the HFEA.

MST  PNT  No

Which technique is intended for the treatment of this patient?

MST  PNT

Has all the diagnostic genetic testing taken place in an accredited laboratory?

Genetic testing should only be carried out by an accredited laboratory.

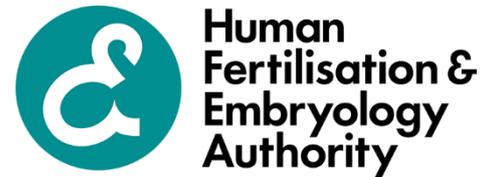
If not, please provide an explanation as to why the genetic testing will not be carried out in an accredited laboratory.

Yes  No

**As the Person Responsible I confirm that the purpose of the application is to treat a patient with an mtDNA mutation, and there is a significant risk of this resulting in a serious mitochondrial disease in their children.**

Please confirm that the reason you want to carry out mitochondrial donation is for the statutory purposes.

Please tick the box to confirm acceptance of the above statement:  Confirmed



#### 4. Patient details

Surname
Forename
Patient number

I wish to apply for authorisation for this patient/case  Yes

#### 5. Genetic cause

Has a pathogenic genetic alteration to the mtDNA been identified in the female patient?

Only patients for whom a pathogenic mtDNA genetic alteration has been identified are considered to be at particular risk of passing on abnormal mtDNA to their children.

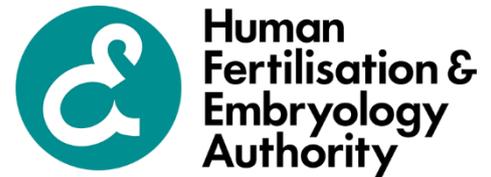
Yes  No

Please give a description of this genetic alteration, i.e. point mutation deletion, rearrangement.

Please describe the pathogenic genetic alteration present in the patient's mtDNA, e.g. T8993G in ATP synthase subunit 6 (MTAPT6)

Please list any OMIM numbers associated with this mitochondrial disease

If applicable also provide the OMIM (On Line Mendelian Inheritance in Man System) number for this mitochondrial disease. This is indicated by a hash (#) for phenotypes and a plus sign (+) for the description of a gene of known sequence and a phenotype.



## 6. Seriousness and significant risk: general information

In this section of the form we would like you provide information based on scientific literature, which is **not patient specific**, about the disease(s) caused by this genetic change and about the relationship between mutant mitochondrial load and disease manifestation.

When considering the seriousness of a condition, the **Statutory Approvals Committee** will consider non-case specific evidence from the scientific literature, which you will provide in this section, as well as the case-specific information given in section 5. The Committee will take the following factors into account. Please provide as much information as possible under each of these sections.

Please include references.

Where information about the disease(s) or genetic abnormality listed above is available please provide:

Please provide a summary of the genetic condition and, if applicable, all the types of the condition in non-technical / lay language in no more than 200 words. This should include a description of how the condition affects a person, if known, how mutant mitochondrial load correlates to clinical symptoms and, if applicable, whether any treatments for the condition are available.

### Lay summary



Please describe the range of symptoms which an individual with this mitochondrial disease might have, indicating the worst possible outcomes.

**Symptoms of the disease**

At what age will the symptoms of the condition start to develop. Is the condition apparent at birth or does it manifest later in life? If so, at what stage, for example, childhood, early adulthood, later?

**Age symptoms are likely to develop**



In this section, please include evidence about the effect the condition has on the quality of life on a child/adult (this might include the speed of degeneration in progressive disorders together with the extent of any physical and / or intellectual impairment).

### **Effect on quality of life**

If there is any evidence from the scientific literature to indicate the effect of mutant mtDNA load on the severity of disease, please include this information here. How does the mutant mtDNA load correlate to clinical symptoms? What is the mutant mtDNA load above which clinical symptoms become manifest? Are there any studies indicating how high the mutant mitochondrial loads were in women that have had children affected by mitochondrial disease? What is the lowest mutant mitochondrial load in a woman that has had a child affected by serious mitochondrial disease?

### **Threshold level of mutant mitochondria necessary to cause symptoms**



Please list any treatment options available. How invasive is the treatment or likely treatment?

#### Available treatments

## 7. Significant risk and seriousness: patient information

It is important that you explain to the patient why they are being asked to provide the information on their own medical history and that of their family. Explain to the patient that this information will be disclosed to the HFEA to assist in the Statutory Approval Committee's decision making process and that all information will be treated in a confidential fashion by those to whom it is disclosed.

In this section please provide evidence that is **specific to the patient** named in this application.

The Committee may only authorise mitochondrial donation if it is satisfied that there is a significant risk that a person with the abnormality will have or will develop a serious physical or mental disability, a serious illness or another serious medical condition.

Please explain why you think the patient's child, if conceived naturally, is at significant risk of having or developing a mitochondrial disease causing a serious physical or mental disability; a serious illness; or another serious medical condition.

When considering risk and seriousness, the **Statutory Approvals Committee** will take the following factors into account. Please provide as much information as possible under each of these sections.

Is there a significant risk that a child born without mitochondrial donation will have or go on to develop a serious mitochondrial disease?

Yes       No



What's the patient's medical history? How does it provide evidence of risk and seriousness? You may wish to consider the following questions:

- Does the patient have any symptoms? If so, how severe are they?
- 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?
- Has the patient previously been treated with preimplantation genetic diagnosis (PGD) to avoid transmission of mitochondrial disease? Was the PGD 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?

**Please provide information on the patient's medical history**

A large, empty rectangular area with a light beige background, intended for the applicant to provide detailed information on the patient's medical history.



Has the patient's mutant mtDNA load been assessed? How does it provide evidence of risk and seriousness? You may wish to address the following questions:

- Is the patient is homoplasmic or heteroplasmic for the mutation?
- What is the patient's mutant mtDNA load and in which tissues?
- Have patients with similar mutant mtDNA loads have had children affected by serious mitochondrial disease?
- How the patient's mutant mitochondrial load compares to the threshold level for clinical manifestation, if known.

**Please provide information on the patient's mutant mtDNA load**



What's the patient's family history? How does it provide evidence of risk and seriousness?

You may wish to consider the following questions:

- 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? For each affected family member, how serious was their disease: 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?
- For each family member, 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.

A family pedigree may also be useful.

Note: Please ensure that you either have consent before providing disclosure of family medical history that is capable of identifying an individual or take measures to ensure that confidentiality is not breached, such as by anonymising the family tree.

**Please provide information on the patient's family history**



If there is any additional information you feel provides evidence of risk and seriousness, please include it here. For example you may wish to include a statement from the patient's genetic counsellor, outlining the impact that mitochondrial disease has had on them and why they feel mitochondrial donation is the most appropriate treatment for them.

**Please provide any additional information to support this**

## 8. Declarations

I consent to the HFEA processing the data that I have provided on this form and any supporting documentation submitted with it, for the purposes of considering my application; statistical analysis; and quality control.

I further consent to the HFEA sharing this data with any other body with whom there is an agreement to undertake inspections or other regulatory functions on behalf of, or in conjunction with, the HFEA.

I understand that this data will be stored securely by the HFEA and saved in accordance with the HFEA's published retention and disposal schedule.

I further understand that the HFEA will not disclose this data to any third parties except as specified above, or as permitted or required by law, and in particular by the requirements of the Data Protection Act 1998 and the Freedom of Information Act 2000.

Persons submitting this application should note that by Section 18(2) of the Human Fertilisation and Embryology Act 1990 (as amended) the Authority may revoke a licence if it is satisfied that any information given for the purposes of application for the grant of licence was in any material respect false or misleading. They should also note that under Section 41(3) provision of false or misleading information, knowingly or in a reckless manner is a criminal offence.

The information provided on this form is to the best of my knowledge true and accurate

Please tick the box to confirm the declaration. This must be completed by the person responsible of the licensed centre applying for the treatment. The form should then be submitted to the HFEA by recorded delivery.

Check the box to confirm acceptance of the above statement

## Mitochondrial donation: clinical expert review form

### 1. Introduction

The law in the United Kingdom permits the use of the mitochondrial donation techniques, pronuclear transfer (PNT) and maternal spindle transfer (MST), to prevent the transmission of serious mitochondrial diseases caused by mutations to the mtDNA.

However, the use of mitochondrial donation is only permissible if a patient meets certain criteria and this must be assessed on a case by case basis. The responsibility for deciding whether the necessary requirements have been met rests with the Human Fertilisation and Embryology Authority (HFEA) and in particular its Statutory Approvals Committee.

The purpose of this form is to enable clinical experts, who may be called upon to act as an independent source of advice, to inform the Statutory Approvals Committee's decision-making process.

When deciding whether to authorise mitochondrial donation for a particular patient the committee must be satisfied that the patient's embryos are at risk of inheriting abnormal mitochondria caused by mutations to the mtDNA and that the patient's child, if conceived without the use of mitochondrial donation, would be at significant risk of having or developing a serious mitochondrial disease.

The committee considers the particular circumstances for each individual application and makes an assessment based on a range of sources of evidence, including the patient's medical history, family history, patient mutant mtDNA load, as well as more general information about the mitochondrial disease/genetic alteration from the scientific literature.

To aid the committee in considering whether to authorise mitochondrial donation for a particular case the HFEA would like your opinion on how serious the mitochondrial disease is, based on your own knowledge and from the scientific literature. We would also like to know whether you feel the patient-specific information provided in the application is sufficiently detailed to enable the committee to make an assessment of the likely risk of transmission of a serious mitochondrial disease from patient to child.

In providing your opinion we would ask you to outline the range of symptoms associated with the mitochondrial disease/genetic alteration, highlighting the most severe clinical outcomes.

The HFEA does not expect you to be expert in the particular mitochondrial disease but instead it would value your opinion as a clinician/clinical geneticist with experience of mitochondrial disease.

### 2. Seriousness: general information

When considering the seriousness of a condition, the Statutory Approvals Committee will frame its discussion by taking into account information from the scientific literature (which is **not** case specific) on these factors, in addition to evidence specific to the patient.

Please provide as much information as possible under each heading based on evidence from the scientific literature and your experience of mitochondrial disease pathology.



Please include references.

2.1 When are symptoms likely to develop?

- |  |  |                                     |
|--|--|-------------------------------------|
| <input type="checkbox"/> At birth      | <input type="checkbox"/> Infancy         | <input type="checkbox"/> Childhood  |
| <input type="checkbox"/> Teenage years | <input type="checkbox"/> Early adulthood | <input type="checkbox"/> Middle age |
| <input type="checkbox"/> Later life    |  |                                     |

2.2 What symptoms would an individual with this mitochondrial disease/caused by this alteration to the mitochondrial DNA (mtDNA) have?

Please describe the range of symptoms, highlighting the worst possible outcomes.

A large, empty, light beige rectangular box intended for the user to provide a detailed description of symptoms and outcomes.



2.3 What effect does this mitochondrial disease/genetic alteration to the mtDNA have on the quality of life of an affected individual?

Please include the rate of any degenerative aspect and the extent of any physical and/or intellectual impairment.

[Empty response area for question 2.3]

2.4 Is there a treatment currently available that modifies the underlying disease process?

Yes  No

If yes, please describe

Please list any treatment options available. How invasive is the treatment?

[Empty response area for question 2.4]

### 3. Risk: general information

When considering how significant the risk would be to a patient's child if conceived without the use of mitochondrial donation, the Statutory Approvals Committee will take into account information from the scientific literature (which is **not** case specific) on the effect of mutant mitochondrial load on the clinical presentation of disease.

3.1 Is there any evidence from the scientific literature to indicate the effect of mutant mtDNA load on the severity of disease?

Yes  No

3.2 If so, how does the mutant mtDNA load correlate to clinical symptoms and what is the mutant mtDNA load above which clinical symptoms are likely to manifest?

### 4. Seriousness and risk: patient information

The committee may only authorise mitochondrial donation if it is satisfied that there is a significant risk that a person with the abnormality will have or develop serious mitochondrial disease.

4.1. Please review the information provided by the applying clinic in Section 5 of 6 of the 'Mitochondrial donation – New case application form'. Is sufficient information provided to make an assessment of the significance of the risk?

Yes  No



In Section 5 of the 'Mitochondrial donation – New case application form', the applying clinic has been asked to provide information specific to the patient, that suggests there is a significant risk that a child born without mitochondrial donation will have or go on to develop a serious mitochondrial disease.

In making its decision on whether to authorise mitochondrial donation, the Statutory Approvals Committee will rely heavily on this evidence.

We understand that it will not be possible for applicants to provide every piece of evidence for each individual patient's case; however we would like to know whether, in your expert opinion, the evidence provided is sufficiently complete to make an assessment of significant risk and seriousness.

Note: we do not require your assessment of the risk or seriousness, only of the level of information provided.

4.2. If no, what additional information should be provided?

A large, empty rectangular box with a light beige background, intended for providing additional information in response to question 4.2.



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5. Any other comments

---

6. Personal details of clinical expert

Name
Position held/area of work

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Signature

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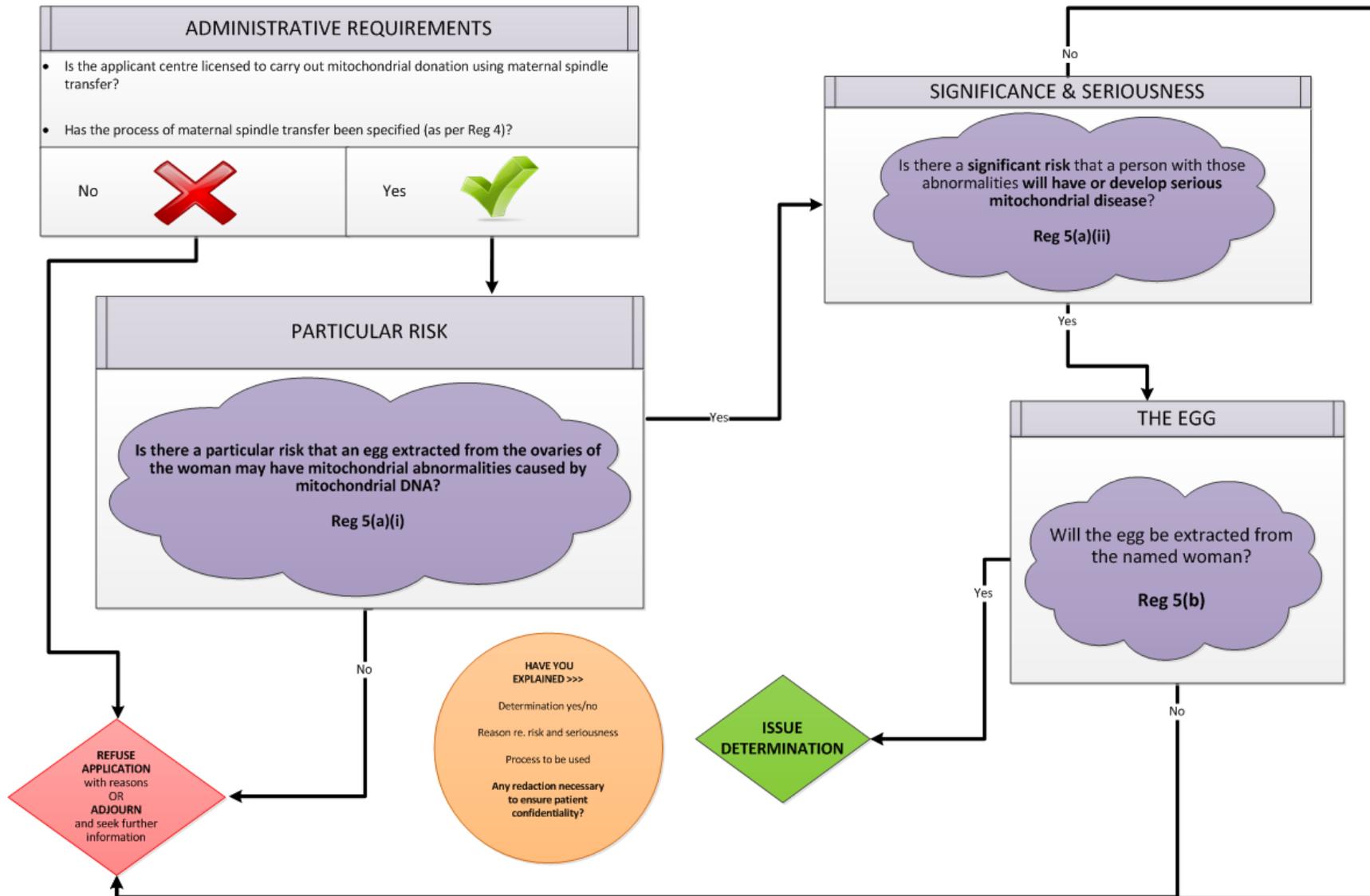
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Date

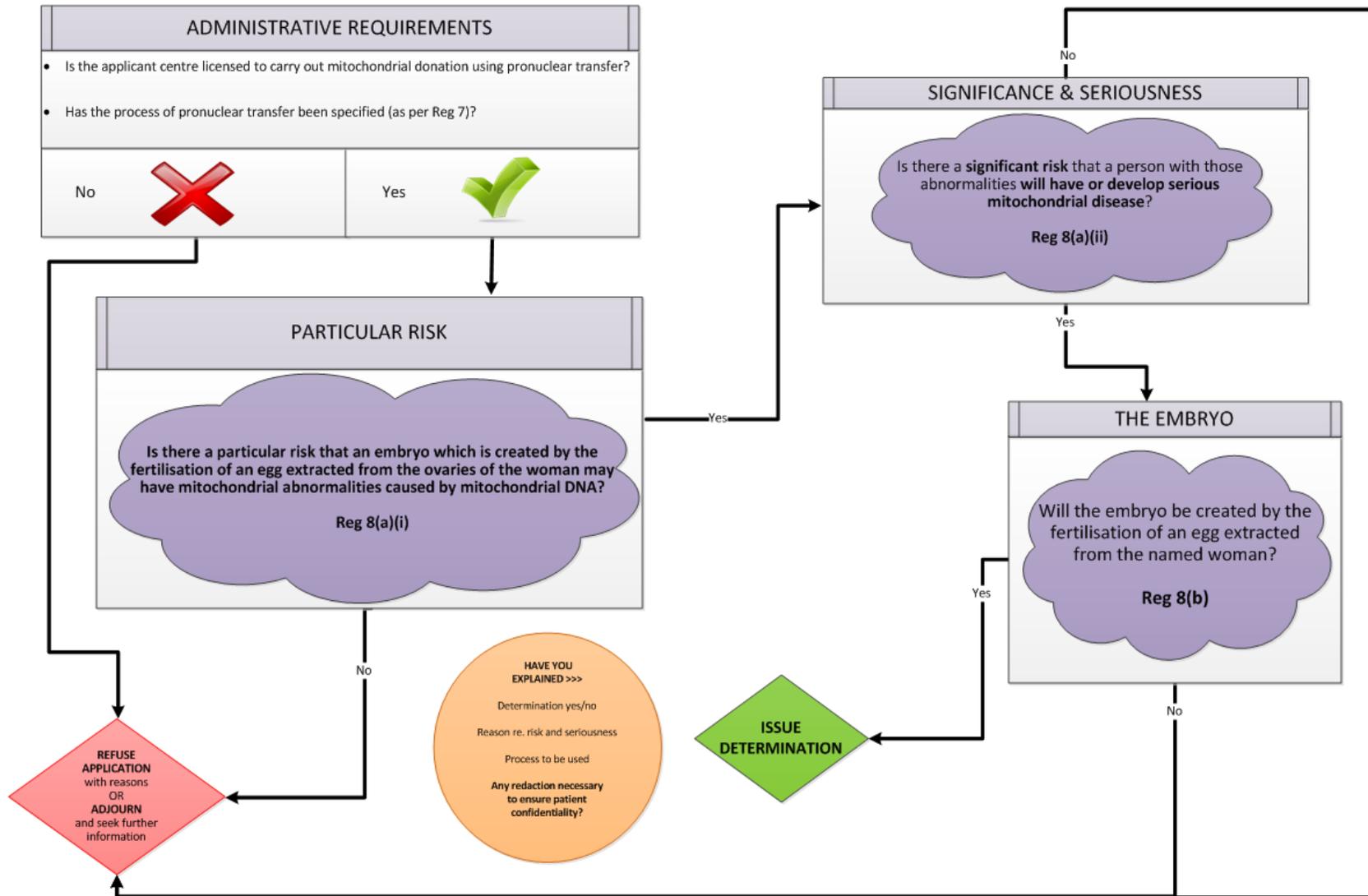
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# Statutory Approvals Committee decision tree

## MITOCHONDRIAL DONATION: MATERNAL SPINDLE TRANSFER



# MITOCHONDRIAL DONATION: PRONUCLEAR TRANSFER



# Mitochondrial donation: explanatory note for Statutory Approvals Committee

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## 1. Overview

- 1.1. 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 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 [DD Month].
  - 1.3. This explanatory note is effective for the Statutory Approvals Committee from [DD Month].
- 

## 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.
- 

## 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.

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## 4. Particular risk

- 4.1. When considering whether or not there is a particular risk that an 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.

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## 7. Significant risk and seriousness: patient information

7.1. 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.

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

7.3. 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 diagnosis (PGD) to avoid transmission of mitochondrial disease? Was the PGD 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 PGD 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.
  - Likewise a patient who has had a successful PGD cycle in which embryos were found to have mutant mitochondrial loads sufficiently high to cause a serious mitochondrial disease may be at significant risk of transmitting a serious mitochondrial disease to any children conceived in the absence of mitochondrial donation.
- 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? For each affected family member, how serious was their disease: 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 each family member, 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.

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## 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.

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## 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.

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## Annex A: Regulations

### 5. Permitted egg: circumstances

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

- a) The Authority has issued a determination that
  - 1. 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
  - 2. 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,
  - 3. and
  - ii. there is a significant risk that a person with those abnormalities will have or develop serious mitochondrial disease,
  - 4. and
- b) Embryo B was created by the fertilisation of an egg extracted from the ovaries of the woman so named.

## Mitochondrial donation: women's consent to treatment and storage

WMT

### About this form

This form is produced by the Human Fertilisation and Embryology Authority (HFEA), the UK's independent regulator of fertility treatment and human embryo research. For more information about us, visit [www.hfea.gov.uk](http://www.hfea.gov.uk).

### Who should fill in this form?

Fill in this form if you are a woman having mitochondrial donation treatment to avoid passing on an inheritable mitochondrial disease to your child, using embryos created outside the body (in vitro) with your eggs. This may be by in vitro fertilisation (IVF) or intracytoplasmic sperm injection (ICSI).

### What are mitochondria?

Mitochondria are present in almost all human cells, including your eggs. They generate the majority of a cell's energy supply which power every part of our body. Mitochondria carry just a few genes. These genes are involved in energy production. For any cell to function, the mitochondrial genes need to work properly. Mitochondria with gene abnormalities can cause severe medical disorders known as mitochondrial disease.

### What does mitochondrial donation involve?

Your eggs or embryos together with donated eggs, or embryos created outside the body with donor eggs will be used in technique(s) based on IVF, so you can avoid passing on an inheritable mitochondrial disease to your child. The IVF-based techniques used to achieve this are called maternal spindle transfer (MST) and pronuclear transfer (PNT). On this form you can consent to MST, PNT or both.

For clinic use only (optional)

HFEA centre reference

Other relevant forms

Date embryos were placed in storage

Date embryos can remain in storage until

Before filling out this form please speak to your clinic about which technique will be used in your treatment.

### What are the MST and PNT techniques?

MST and PNT are both techniques of mitochondrial donation allowing eggs or embryos to be created containing your nuclear genetic material (the genes which make you who you are) and donated mitochondria.

In MST, your nuclear genetic material will be removed from your eggs and transferred into donated eggs once their nuclear genetic material has been removed. The eggs containing your nuclear genetic material and the donor's mitochondria will be fertilised with your partner's (or a donor's) sperm to create embryos.

In PNT, your eggs will be fertilised with your partner's (or a donor's) sperm to create embryos. The nuclear genetic material within each embryo (which contains your genetic material) will then be transferred into embryos created using donated eggs and sperm from the sperm provider, from which the nuclear genetic material has been removed.

In both MST and PNT, the resulting embryos containing your and your partner's (or a sperm donor's) genetic material and the donor mitochondria will be transferred to your womb and hopefully implant and develop into a baby. You and the sperm provider, not the egg donor, will be the genetic parents of the child.

If you're unsure of anything, please ask your clinic for more information.

## What do I need to know before filling in this form?

You should be certain that your clinic has given you all the relevant information you need to make fully informed decisions. This includes:

- information about:
  - the different options set out in this form
  - the implications of giving your consent
  - the consequences of withdrawing this consent, and
  - how and when you can make changes to, or withdraw, your consent
- an opportunity to have counselling.

If you are unsure, or think that you have not been given all of this information, please speak to your clinic.

There is a declaration at the end of this form which you must sign to confirm you have received this information before filling in this form. If you haven't your consent may be invalid. If you are unable to complete this form because of physical illness, injury or disability you may direct someone else to complete and sign it for you.

## Why do I have to fill in this form?

By law (the Human Fertilisation and Embryology Act 1990 (as amended)), you need to give your written consent if you want your eggs, or embryos created outside the body (in vitro) with your eggs, to be used or stored (which includes mitochondrial donation).

If following MST or PNT your eggs or embryos are going to be stored, you must consent to this and state in writing how long you consent to them remaining in storage.

Once your nuclear genetic material has been transferred into the donor eggs or embryos, you (and the sperm provider) will determine what happens to them, including how long they will be stored for.

The eggs and embryos that have had your nuclear material removed will be discarded.

You are also legally required to record what you would like to happen to your eggs and embryos if you were to die or lose the ability to decide for yourself (become mentally incapacitated). While this is perhaps not something you have considered, your clinic needs to know this so that they only allow your eggs and embryos to be used according to your wishes.

If you are unsure of anything in relation to this, please ask your clinic.

## Why are there questions about using my eggs for training purposes?

There may be some eggs or embryos left after treatment, which you do not wish to use (eg, because you do not want future treatment or the eggs and embryos are not viable for treatment).

This form allows you to consent to donate eggs or embryos (containing your nuclear genetic material) for training purposes, allowing healthcare professionals to learn about, and practice, the techniques involved in IVF-based treatments.

## What if I want to donate my eggs and/or embryos?

Unused eggs and embryos can also be donated for research purposes, helping to increase knowledge about diseases and serious illnesses and potentially develop new treatments. If you would like to donate any eggs or embryos (containing your nuclear genetic material) to research, speak to your clinic who will provide you with any relevant consent form(s).

When filling in this form, make sure you sign the declaration on every page to confirm that you have read the page and fully agree with the consent and information given.

When you have completed the form you may request a copy of it from your clinic.

Patient number

Version 1, 29 October 2015

## 1. About you

First name(s)

Surname

Date of birth

NHS/CHI/HCN number (please circle)

## 2. About your partner

Your partner's first name(s)

Your partner's surname

Your partner's date of birth

Your partner's NHS/CHI/HCN number

## 3. About your treatment

### 3.1. Do you consent to your eggs undergoing MST and embryos created from eggs following MST being used in your treatment?

This process will involve:

- your eggs undergoing the MST process (this means that your nuclear genetic material will be removed from your eggs and transferred into a 'new' egg containing donor mitochondria but no donor nuclear genetic material. The egg containing your mitochondria will be discarded.),
- the eggs, following the MST process (containing your nuclear genetic material and donor mitochondria), being used to create embryos outside of the body, and
- those embryos being used in your treatment (embryo transfer).

 Yes       No

### 3.2. Do you consent to your eggs being used to create embryos outside of the body which will undergo PNT and be used in your treatment? This process will involve:

- your eggs being used to create embryos outside the body (those embryos will contain your and the sperm provider's nuclear genetic material),
- those embryos (containing your nuclear genetic material) undergoing the PNT process (this means that genetic material will be removed from your embryo and transferred into a 'new' embryo containing donor mitochondria but no donor nuclear genetic material. The embryonic material containing your mitochondria will be discarded), and
- those embryos (containing your nuclear genetic material and donor mitochondria), used in your treatment (embryo transfer).

 Yes       No

Page declaration signature

Date

Patient number

Version 1, 29 October 2015

## 4. Storing eggs and embryos

You may wish to store any eggs and/or embryos before or after they have undergone MST or PNT so they can be used in future treatment.

To be stored, eggs or embryos are frozen or 'vitrified'. When considering how long to store for, you may want to think about how far in the future you might want/be able to use your stored eggs and embryos and the costs of storing – ask your clinic if you are unsure.

The law permits you to store for any period up to 10 years but in cases where you or your partner are prematurely infertile, or likely to become prematurely infertile, you may store for longer, up to 55 years.

Please note that any arrangements you need to make regarding the practicalities of storage with your clinic or funding body are separate from this consent. For example, your clinic may only continue to store your eggs and/or embryos for the period you have specified in this form if you, or your funding provider, continue to pay the storage fees.

**4.1.** Do you consent to your eggs (containing your nuclear genetic material and donated mitochondria, or your nuclear genetic material and mitochondria) being stored?

Yes  No

**4.2.** For how long do you consent to these eggs being stored? **Only complete this section if you answered yes to section 4.1.**

10 years

55 years

A specific period (up to 55 years). Specify number of years

**4.3.** Do you consent to embryos (containing your nuclear genetic material and donated mitochondria, or your nuclear genetic material and mitochondria) being stored? **Please note that embryos can only be stored if the sperm provider (whose nuclear genetic material is being used) has also given his consent.**

Yes  No

**4.4.** For how long do you consent to these embryos being stored? **Only complete this section if you answered yes to section 4.3.**

10 years

55 years

A specific period (up to 55 years). Specify number of years

Page declaration signature

Date

Patient number

Version 1, 29 October 2015

- 4.5.** Please note here if you would like to specify different storage period for eggs or embryos before or after they have undergone MST or PNT, or if you want to restrict your consent to only eggs or embryos at a certain stage (ie, pre or post MST or PNT). Your consent to store eggs or embryos prior to the MST or PNT process is not needed on this form if you have already completed the GS or WT form.

The consent period will start from the date of storage. Remember you can always change the time period you consent to by completing this form again and specifying the new total time period you would like your eggs and embryos to be stored for. For example, if you consented to five years' storage on the original form and wish to consent for a further five years (10 years in total), you should complete another copy of this form but tick the box for 10 years. This second form would supersede the first form you completed.

## 5. Using eggs and embryos in training

- 5.1.** Do you consent to eggs surplus to your treatment being used for training purposes?

Yes  No

- 5.2.** Do you consent to embryos (already created outside the body containing your nuclear genetic material) surplus to your treatment being used for training purposes? **Please note that embryos can only be used if the sperm provider (whose nuclear genetic material is being used) has also given his consent.**

Yes  No

## 6. In the event of your death or mental incapacity

As part of your consent, you also need to decide what you would like to happen to your eggs, or embryos containing your nuclear genetic material, if you die or lose the ability to decide for yourself (become mentally incapacitated). Please note your eggs or embryos may only be used within the storage period you consented to above. If you do not give your consent in the section below, your eggs or embryos must be allowed to perish in the event of your death or mental incapacity and cannot be used for treatment.

- 6.1.** Do you consent to eggs being used for training purposes?

If you die

If you become mentally incapacitated

Yes  No  Yes  No

- 6.2.** Do you consent to embryos (already created outside the body containing your nuclear genetic material) being used for training purposes? Please note that embryos can only be used if the sperm provider (whose nuclear genetic material is being used) has also given his consent.

If you die

If you become mentally incapacitated

Yes  No  Yes  No

Page declaration signature

Date

Patient number

Version 1, 29 October 2015

If you are storing eggs or embryos following MST or PNT you may wish for them to be used in someone else's treatment if you die or become mentally incapacitated, please speak to your clinic for more information.

Depending on your circumstances, you will need to complete one of the following:

- 'Your consent to donating your eggs' (WD form),
- 'Your consent to donating embryos' (ED form), or
- 'Women's consent to the use and storage of eggs or embryos for surrogacy' (WSG form).

## 7. Declaration

Please sign and date the declaration

- I declare that I am the person named in section one of this form.
- I declare that:
  - before I completed this form, I was given information about the different options set out in this form, and I was given an opportunity to have counselling
  - the implications of giving my consent, and the consequences of withdrawing this consent, have been fully explained to me, and
  - I understand that I can make changes to, or withdraw, my consent at any point until the time of embryo transfer, use of eggs or embryos in training, or the eggs or embryos have been allowed to perish.
- I declare that the information I have given on this form is correct and complete.
- I understand that information on this form may be processed and shared for the purposes of, and in connection with, the conduct of licensable activities under the Human Fertilisation and Embryology Act 1990 (as amended) in accordance with the provisions of that act.

Your signature

Date

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### If signing at the direction of the person consenting

If you have completed this form at the direction of the person consenting (because she is unable to sign for herself due to physical illness, injury or disability), you must sign and date below. There must also be a witness confirming that the person consenting is present when you sign the form.

I declare that the person named in section one of this form is present at the time of signing this form and I am signing it in accordance with her direction.

Representative's name

Representative's signature

--	--

Relationship to person consenting

Date

--	--

Witness's name

Witness's signature

--	--

Date

--

## Mitochondrial donation: men's consent to treatment and storage

MMT

### About this form

This form is produced by the Human Fertilisation and Embryology Authority (HFEA), the UK's independent regulator of fertility treatment and human embryo research. For more information about us, visit [www.hfea.gov.uk](http://www.hfea.gov.uk).

### Who should fill in this form?

Fill in this form if you are a man and your partner is having mitochondrial donation treatment using embryos created outside the body (in vitro) with your sperm. This may be by in vitro fertilisation (IVF) or intracytoplasmic sperm injection (ICSI).

### What are mitochondria?

Mitochondria are present in almost all human cells, including your partner's eggs. They generate the majority of a cell's energy supply which power every part of our body. Mitochondria carry just a few genes. These genes are involved in energy production. For any cell to function, the mitochondrial genes need to work properly. Mitochondria with gene abnormalities can cause severe medical disorders known as mitochondrial disease.

### What does mitochondrial donation involve?

Your sperm will be used to create embryos with donated eggs and/or your partner's eggs, by IVF or ICSI, so your partner can avoid passing on an inheritable mitochondrial disease to your child. The IVF-based techniques used to achieve this are called maternal spindle transfer (MST) and pronuclear transfer (PNT). On this form you can consent to MST, PNT or both. Before filling out this form please speak to your clinic about which technique will be used in your partner's treatment.

### What are the MST and PNT techniques?

MST and PNT are both techniques of mitochondrial donation allowing embryos to be created for you containing your and your partner's nuclear genetic material (the genes which make you who you are) and donated mitochondria.

In MST, the nuclear genetic material will be removed from your partner's eggs and transferred into donated eggs with mitochondria which have had the donor's nuclear genetic material removed. Your sperm will then be used with these eggs to create embryos containing your and your partner's nuclear genetic material and donated mitochondria.

In PNT, your sperm may be used for two stages: -

**Stage one** – your sperm will be used to create embryos with your partner's eggs. The nuclear genetic material will be removed and transferred into embryos created in stage two. Once the nuclear genetic material has been removed the embryonic material created in stage one will be discarded.

**Stage two** – either your sperm or donor sperm (for example, if you are genetically related to the egg donor) will be used to create embryos with donated eggs. The nuclear genetic material will be removed, discarded, and replaced with the nuclear genetic material removed from the embryos created in stage one, above.

Following both MST and PNT, the embryos containing your and your partner's genetic material and the donor's mitochondria will be transferred to your partner's womb and hopefully implant and develop into a baby. You

For clinic use only (optional)

HFEA centre reference

Other relevant forms

Date embryos were placed in storage

Date embryos can remain in storage until

Patient number

Version 1, 29 October 2015

and your partner, not the donor, will be the **What do I need to know before filling in this form?**

You should be certain that your clinic has given you all the relevant information you need to make fully informed decisions. This includes:

- information about:
  - the different options set out in this form
  - the implications of giving your consent
  - the consequences of withdrawing this consent, and
  - how and when you can make changes to, or withdraw, your consent
- an opportunity to have counselling.

If you are unsure, or think that you have not been given all of this information, please speak to your clinic. There is a declaration at the end of this form which you must sign to confirm you have received this information before filling in this form. If you haven't your consent may be invalid.

If you are unable to complete this form because of physical illness, injury or disability you may direct someone else to complete and sign it for you.

### Why do I have to fill in this form?

By law (the Human Fertilisation and Embryology Act 1990 (as amended)), you need to give your written consent if you want your sperm, and embryos created using your sperm, to be used or stored. If your sperm or embryos following MST or PNT are going to be stored, you must consent to this and state in writing how long you consent to them remaining in storage.

In MST once eggs containing your partner's nuclear genetic material have been fertilised with your sperm to create embryos, you (and your partner) will determine what happens to them, including how long they will be stored for.

In PNT embryos will be created from donated eggs and your (or donor) sperm. The nuclear genetic material will be removed from those embryos and replaced with the nuclear genetic material from embryos created with your sperm and your partner's eggs.

genetic parents of the child.

Once PNT takes place you (and your partner) will determine what happens to them, including how long they will be stored for. The embryos that have had their nuclear genetic material removed will be discarded.

You are also legally required to record what you would like to happen to your sperm and embryos if you were to die or lose the ability to decide for yourself (become mentally incapacitated). While this is perhaps not something you have considered, your clinic needs to know this so that they only allow your sperm and embryos to be used according to your wishes.

If you are unsure of anything in relation to this, please ask your clinic.

### Why are there questions about using my sperm and embryos for training?

There may be some sperm or embryos left after treatment, which you do not wish to use (eg, because you do not want future treatment or the sperm and embryos are not viable for treatment).

This form allows you to consent to donate sperm or embryos (containing your nuclear genetic material) for training purposes, allowing healthcare professionals to learn about, and practice, the techniques involved in IVF-based treatments.

### What if I want to donate my sperm/embryos?

Unused sperm and embryos can also be donated for research purposes, helping to increase knowledge about diseases and serious illnesses and potentially develop new treatments. If you would like to donate any sperm or embryos (containing your nuclear genetic material) to research, speak to your clinic who will provide you with any relevant consent form(s).

**When filling in this form, make sure you sign the declaration on every page to confirm that you have read the page and fully agree with the consent and information given.**

**When you have completed the form you may request a copy of it from your clinic.**

Patient number

Version 1, 29 October 2015

## 1. About you

First name(s)

Surname

Date of birth

NHS/CHI/HCN number (please circle)

## 2. About your partner

Your partner's first name(s)

Your partner's surname

Your partner's date of birth

Your partner's NHS/CHI/HCN number

## 3. About your treatment

**3.1.** Do you consent to your sperm being used to create embryos outside of the body with eggs that have undergone MST for use in your partner's treatment?

This process will involve:

- eggs undergoing the MST process (this means that your partner's nuclear genetic material will be removed from her eggs and transferred into a 'new' egg containing donor mitochondria but no donor nuclear genetic material),
- your sperm being used to create embryos (containing your and your partner's nuclear genetic material and donor mitochondria) with the eggs that have undergone MST, and
- those embryos being used for your partner's treatment (embryo transfer).

Yes  No

### PNT - stage one

**3.2.** Do you consent to your sperm being used to create embryos outside of the body with your partner's eggs (eg, through IVF or ICSI, then PNT) for use in your partner's treatment?

This process will involve:

- your sperm being used to create embryos with your partner's eggs,
- the embryos undergoing the PNT process (this means that your and your partner's nuclear genetic material will be removed and transferred into the embryos created in stage two. Once your nuclear genetic material has been removed from the embryos, the embryonic material will be discarded), and
- the embryos (containing your and your partners nuclear genetic material and donor mitochondria) to be used in your partner's treatment (embryo transfer).

Yes  No

Page declaration signature

Date

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**PNT - stage two**

- 3.3.** Do you consent to your sperm being used to create embryos outside of the body with donor eggs and for those embryos to undergo the PNT process? **Do not complete this section if donor sperm is used for this stage (eg, if you are genetically related to the egg donor).**

This process will involve:

- your sperm being used to create embryos with donated eggs outside the body
- the embryos undergoing the PNT process (this means that your and the donor's nuclear genetic material will be removed, discarded, and replaced with your and your partner's nuclear genetic material from the embryos created in stage one), and
- those embryos (containing your and your partner's nuclear genetic material and donor mitochondria) to be used in your partner's treatment (embryo transfer).

Yes       No

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#### 4. Storing sperm and embryos

You may wish to store any sperm and/or embryos before or after MST or PNT so they can be used in future treatment.

To be stored, sperm or embryos are frozen or 'vitrified'. When considering how long to store for, you may want to think about how far in the future you might want/be able to use your stored sperm and embryos and the costs of storing – ask your clinic if you are unsure. The law permits you to store for any period up to 10 years but in cases where you or your partner are prematurely infertile, or likely to become prematurely infertile, you may store for longer, up to 55 years.

Please note that any arrangements you need to make regarding the practicalities of storage with your clinic or funding body are separate from this consent. For example, your clinic may only continue to store your sperm and/or embryos for the period you have specified in this form if you, or your funding provider, continue to pay the storage fees.

- 4.1.** Do you consent to your sperm being stored?

Yes       No

- 4.2.** For how long do you consent to your sperm being stored? **Only complete this section if you answered yes to section 4.1.**

10 years       55 years

A specific period (up to 55 years). Specify number of years:

- 4.3.** Do you consent to embryos (containing your and your partner's or donor's nuclear genetic material and your partner's or donor's mitochondria) being stored?

Yes       No

Page declaration signature

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**4.4.** For how long do you consent to your embryos being stored? **Only complete this section if you answered yes to section 4.3.**

10 years     55 years

A specific period (up to 55 years). Specify number of years:

**4.5.** Please note here if you would like to specify different storage period for embryos before or after they have undergone PNT, or if you want to restrict your consent to only embryos at a certain stage (ie, pre or post PNT). Your consent to store sperm, or embryos prior to the PNT process, is not needed on this form if you have already completed the GS or MT form.

The consent period will start from the date of storage. Remember you can always change the time period you consent to by completing this form again and specifying the new total time period you would like your sperm and embryos to be stored for. For example, if you consented to five years' storage on the original form and wish to consent for a further five years (10 years in total), you should complete another copy of this form but tick the box for 10 years. This second form would supersede the first form you completed.

## 5. Using sperm and embryos in training

**5.1.** Do you consent to sperm surplus to your treatment being used for training purposes?

Yes     No

**5.2.** Do you consent to embryos (already created outside the body which contain your nuclear genetic material) surplus to your treatment being used for training purposes? **Please note that embryos can only be used if the female provider of the genetic material has also given her consent.**

Yes     No

## 6. In the event of your death or mental incapacity

As part of your consent, you also need to decide what you would like to happen to your sperm, or embryos containing your nuclear genetic material, if you die or lose the ability to decide for yourself (become mentally incapacitated). Please note that if you would like your partner to use your sperm or embryos in the event of your death or mental incapacity, your partner should be named on this form. Your embryos may only be used within the storage period you consented to above. If you do not give your consent in the below section, your sperm or embryos must be allowed to perish in the event of your death or mental incapacity and cannot be used for treatment.

**6.1.** Do you consent to your sperm being used to create embryos outside the body for your partner's treatment? **Please note that the egg provider also has to give her consent for embryos to be created.**

If you die     Yes     No      If you become mentally incapacitated     Yes     No

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**6.2.** Do you consent to embryos (already created outside the body which contain your nuclear genetic material) being used for your partner's treatment? **Please note that embryos can only be used if the female provider of the genetic material has also given her consent.**

If you die  Yes  No      If you become mentally incapacitated  Yes  No

**6.3.** Do you consent to your sperm being used for training purposes?

If you die  Yes  No      If you become mentally incapacitated  Yes  No

**6.4.** Do you consent to embryos (already created outside the body which contain your nuclear genetic material) being used for training purposes? **Please note that embryos can only be used if the female provider of the genetic material has also given her consent.**

If you die  Yes  No      If you become mentally incapacitated  Yes  No

If you are storing sperm or embryos following MST or PNT (containing your genetic material and donor mitochondria) you may wish for them to be used in someone else's treatment if you die or become mentally incapacitated, please speak to your clinic for more information. Depending on your circumstances, you will need to complete one of the following:

- 'Your consent to donating your sperm' (MD form)
- 'Your consent to donating embryos' (ED form), or
- 'Men's consent to the use and storage of sperm or embryos for surrogacy' (MSG form).

### Consent to birth registration

Complete this part of section six if you consented to your sperm, or embryos created outside the body which contain your nuclear genetic material, being used in your partner's treatment after your death. If you have given your consent to your sperm or embryos (to be created outside the body which contain your nuclear genetic material) being used after your death, you may also wish to consent to being registered as the legal father of any child that is born as a result of your partner's treatment.

**6.5.** Do you consent to being registered as the legal father of any child born as a result of your partner's treatment after your death?

By ticking yes, you consent to the following:

- I consent to my name, place of birth and occupation being entered on the register of births as the legal father of any child born from my partner's treatment. This register is kept under the Births and Deaths Registration Act 1953, or the Births and Deaths Registration (Northern Ireland) Order 1976, or the Registration of Births, Deaths and Marriages (Scotland) Act 1965.
- I also consent to information about my or my partner's treatment being disclosed to my partner and one of the following registrars:
  - the Registrar General for England and Wales
  - the Registrar General for Scotland
  - the Registrar for Northern Ireland.

Please note that being recorded in the register of births as the legal father of a child born from your partner's treatment does not transfer any inheritance or other legal rights to the child.

Yes       No

Page declaration signature

Date

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## 7. Declaration

Please sign and date the declaration

- I declare that I am the person named in section one of this form.
- I declare that:
  - before I completed this form, I was given information about the different options set out in this form, and I was given an opportunity to have counselling
  - the implications of giving my consent, and the consequences of withdrawing this consent, have been fully explained to me, and
  - I understand that I can make changes to, or withdraw, my consent at any point until the time of embryo transfer, use of sperm or embryos in training, or the sperm or embryos have been allowed to perish.
- I declare that the information I have given on this form is correct and complete.
- I understand that information on this form may be processed and shared for the purposes of, and in connection with, the conduct of licensable activities under the Human Fertilisation and Embryology Act 1990 (as amended) in accordance with the provisions of that act.

Your signature

Date

### If signing at the direction of the person consenting

If you have completed this form at the direction of the person consenting (because he is unable to sign for himself due to physical illness, injury or disability), you must sign and date below. There must also be a witness confirming that the person consenting is present when you sign the form.

I declare that the person named in section one of this form is present at the time of signing this form and I am signing it in accordance with his direction.

Representative's name

Representative's signature

Relationship to person consenting

Date

Witness's name

Witness's signature

Date

## Mitochondrial donation: your consent

## WDM

### About this form

This form is produced by the Human Fertilisation and Embryology Authority (HFEA), the UK's independent regulator of fertility treatment and human embryo research. For more information about us, visit [www.hfea.gov.uk](http://www.hfea.gov.uk).

### Who should fill in this form?

Fill in this form if you are a woman donating eggs and/or embryos created with your eggs for use in other women's mitochondrial donation treatment so that she can avoid passing on an inheritable mitochondrial disease to her child.

### What are mitochondria?

Mitochondria are present in almost all human cells, including your eggs. They generate the majority of a cell's energy supply which power every part of our body. Mitochondria carry just a few genes. These genes are involved in energy production. For any cell to function, the mitochondrial genes need to work properly. Mitochondria with gene abnormalities can cause severe medical disorders known as mitochondrial disease.

### What does mitochondrial donation involve?

You will be donating eggs (containing your mitochondria) to other women who have mitochondria containing gene abnormalities, for use in IVF-based treatment so that they can avoid passing on an inheritable mitochondrial disease to their child. The IVF-based techniques used to achieve this are called maternal spindle transfer (MST) and pronuclear transfer (PNT). On this form you can consent to MST, PNT or both.

### What are the MST and PNT techniques?

In MST, your nuclear genetic material (the genes which make us who we are) will be removed from your eggs and replaced with the nuclear genetic material from the intended mother's egg. The nuclear genetic material removed from your eggs will be discarded.

Following MST, the eggs containing your mitochondria will be fertilised with the intended father's (or a donor's) sperm to create embryos which will be used in the intended mother's treatment.

This means that the intended mother, not you, will be the genetic parent of any child that is born.

In PNT, your eggs will be fertilised with the intended father's (or a donor's) sperm to create embryos. The nuclear genetic material within these embryos will then be removed and discarded. It will be replaced with the nuclear genetic material removed from embryos created using the intended mother's eggs and father's (or donor's) sperm. This means that they, not you, will be the genetic parents of the child.

If you're unsure of anything, please ask your clinic for more information.

### What do I need to know before filling in this form?

Before you fill in this form, you should have completed the 'Mitochondrial donor registration form'.

You should also be certain that your clinic has given you all the relevant information you need to make fully informed decisions. This includes:

- information about:
  - the different options set out in this form
  - the implications of giving your consent

For clinic use only (optional)

HFEA centre reference

Other relevant forms

Date eggs were placed in storage

Date eggs can remain in storage until

- the consequences of withdrawing this consent, and
- how and when you can make changes to, or withdraw, your consent
- an opportunity to have counselling.

If you are unsure, or think that you have not been given all of this information, please speak to your clinic. There is a declaration at the end of this form which you must sign to confirm you have received this information before filling in this form. If you haven't your consent may be invalid.

If you are unable to complete this form because of physical illness, injury or disability you may direct someone else to complete and sign it for you.

### Why do I have to fill in this form?

By law (the Human Fertilisation and Embryology Act 1990 (as amended)), you need to give your written consent if you want your eggs, or embryos created outside the body (in vitro) with your eggs, to be used or stored.

If your eggs or embryos containing your nuclear genetic material are going to be stored, you must consent to this and state in writing how long you consent to them remaining in storage. Once your nuclear genetic material has been removed and replaced with that of the intended mother and sperm provider, they will determine what happens to them, including how long they will be stored for.

### Why are there questions about using my eggs and embryos for training purposes?

There may be some eggs or embryos left after treatment, eg, because they weren't viable for treatment. This form allows you to consent to donate eggs or embryos (before your nuclear genetic material is removed) for training purposes, allowing healthcare professionals to learn about, and practice, the techniques involved in IVF treatment.

### What if I want to donate my eggs for other purposes?

If you also wish to donate your eggs for regular egg donation (where your eggs are donated to someone to help them conceive rather than

avoid passing on a mitochondrial disease), you must complete the 'Your consent to donating your eggs' (WD form). If you have entered into an egg sharing agreement, you must complete the 'Women's consent to treatment and storage form (IVF and ICSI)' (WT form).

Eggs can also be donated for research purposes, helping to increase knowledge about diseases and serious illnesses and potentially developing new treatments. If you would like to donate any eggs or embryos (before your nuclear genetic material is removed) to research, speak to your clinic who will provide you with the relevant consent form(s).

### What if I want to withdraw my consent?

You can withdraw your consent at any point up until your genetic material is removed from your eggs, or in PNT, the embryos are created with your eggs. After this point you will no longer have any rights over the eggs or embryos and cannot withdraw consent to its use in treatment, storage or training.

### What happens to my eggs or embryos if I die?

By consenting to mitochondrial donation, you are also agreeing to your eggs or embryos (before your nuclear genetic material is removed) being used and stored if you were to die or lose the ability to decide for yourself (become mentally incapacitated). If you do not want your eggs or embryos to be used for the purposes outlined in this form if this were to happen, you can state this as a restriction (at section 2.3).

Please note that the clinic can only act on these wishes if they are informed about your death or mental incapacity. If you're unsure of anything in relation to this, please ask your clinic.

When filling in this form, make sure you sign the declaration on every page to confirm that you have read the page and fully agree with the consent and information given. When you have completed the form you may request a copy of it from your clinic.

Donor number

Version 1, 29 October 2015

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## 1. About you

First name(s)

Surname

Date of birth

NHS/CHI/HCN number (please circle)

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## 2. About your mitochondrial donation

**2.1.** Do you consent to your eggs undergoing MST and for embryos created from eggs following MST being used for the treatment of others?

This process will involve:

- your eggs undergoing the MST process (this means that your nuclear genetic material will be removed from your eggs and replaced with the intended mother's nuclear genetic material. Your nuclear genetic material will be discarded),
- the eggs, following MST (containing your mitochondria and the intended mother's nuclear genetic material) being used to create embryos outside of the body, and
- those embryos being used in the intended mother's treatment (embryo transfer).

Yes       No

**2.2.** Do you consent to your eggs being used to create embryos outside of the body which will undergo PNT and be used in the treatment of others?

This process will involve:

- your eggs being used to create embryos outside of the body (those embryos will contain your and the sperm provider's nuclear genetic material),
- the embryos undergoing the PNT process (this means that your nuclear genetic material will be removed from the embryo, discarded, and replaced with the intended mother's and sperm provider's nuclear genetic material), and
- those embryos (containing your mitochondria and the intended mother's and sperm provider's nuclear genetic material) being used in the intended mother's treatment (embryo transfer).

Yes       No

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Date

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**2.3.** Do you have any restrictions you would like to apply to questions 2.1 and 2.2 above?

You may want to put restrictions on who your eggs, or in PNT, embryos created with your eggs, can be used by (eg, a specified named recipient). Another example may be that you do not wish for your eggs or embryos to be used in the event of your death or mental incapacity. If so, please state it here. Please note that you can only place restrictions on eggs or embryos that still contain your nuclear genetic material (ie, before they have undergone the MST or PNT process).

Yes - specify your restrictions below then continue to section 3.

No - go to section 3.

**3. Using eggs and embryos in training****3.1.** Do you consent to your eggs (containing your nuclear genetic material) being used for training purposes?

Yes  No

**(For PNT only)**

**3.2.** Do you consent to your embryos (containing your nuclear genetic material) already created outside the body with your eggs being used for training purposes?

Yes  No

**4. Storing eggs and embryos**

If your eggs or embryos are going to be stored before MST or PNT (eg, before your nuclear genetic material is removed), you must consent to this and state in writing how long you consent to them remaining in storage.

The law permits you to store for any period up to 10 years but in some cases where you, your partner, or the person to whom your eggs and embryos have been allocated, is prematurely infertile, or likely to become prematurely infertile, you may store for longer, up to 55 years.

A medical practitioner will need to certify in writing that the medical criteria for premature infertility have been met for storage to continue for more than 10 years. When the criteria have been met, the storage period will be extended by 10 years from the date the criteria are met.

The storage period can then be extended by further 10 year periods (up to a maximum of 55 years) at any time within each extended storage period if it is shown that the criteria continue to be met. For more information about this, please ask your clinic.

**Once your nuclear genetic material has been removed from your eggs or embryos, the intended mother and sperm provider (together with the clinic) will determine how long the eggs or embryos will be stored for.**

**4.1.** Do you consent to your eggs (containing your nuclear genetic material) being stored?

Yes  No

Page declaration signature

Date

Donor number

Version 1, 29 October 2015

**4.2.** For how long do you consent to eggs (containing your nuclear genetic material) being stored? Only complete this section if you answered yes to section 4.1. **Please talk to your clinic if you're unsure of how long to store for.**

10 years     55 years

A specific period (up to 55 years). Specify number of years

### PNT only

**4.3.** Do you consent to embryos (containing your nuclear genetic material) being stored?

Yes     No

**4.4.** For how long do you consent to embryos (containing your nuclear genetic material) being stored? **Only complete this section if you answered yes to question 4.3. Please talk to your clinic if you're unsure of how long to store for.**

10 years     55 years

A specific period (up to 55 years). Specify number of years

The consent period will start from the date of storage. Remember you can always change the time period you consent to by completing this form again and specifying the new total time period you would like your eggs and embryos to be stored for. For example, if you consented to five years' storage on the original form and wish to consent for a further five years (10 years in total), you should complete another copy of this form but tick the box for 10 years. This second form would supersede the first form you completed.

## 5. Declaration

Please sign and date the declaration

- I declare that I am the person named in section one of this form.
- I declare that:
  - before I completed this form, I was given information about the different options set out in this form, and I was given an opportunity to have counselling
  - the implications of giving my consent, and the consequences of withdrawing this consent, have been fully explained to me, and
  - I understand that I can make changes to, or withdraw, my consent at any point until the nuclear genetic material has been removed from my eggs, or in PNT, embryos created with my eggs.
- I declare that the information I have given on this form is correct and complete.
- I understand that information on this form may be processed and shared for the purposes of, and in connection with, the conduct of licensable activities under the Human Fertilisation and Embryology Act 1990 (as amended) in accordance with the provisions of that act.

Your signature

Date

Donor number

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**If signing at the direction of the person consenting**

If you have completed this form at the direction of the person consenting (because she is unable to sign for herself due to physical illness, injury or disability), you must sign and date below. There must also be a witness confirming that the person consenting is present when you sign the form.

I declare that the person named in section one of this form is present at the time of signing this form and I am signing it in accordance with her direction.

Representative's name

Representative's signature

Relationship to person consenting

Date

Witness's name

Witness's signature

Date

DRAFT

## Mitochondrial donation: consent to sperm donation (PNT only)

### About this form

This form is produced by the Human Fertilisation and Embryology Authority (HFEA), the UK's independent regulator of fertility treatment and human embryo research. For more information about us, visit [www.hfea.gov.uk](http://www.hfea.gov.uk).

### Who should fill in this form?

If you are a man donating sperm and/or embryos created with your sperm for the treatment of others – specifically for use in mitochondrial donation treatment so that women can avoid passing on inheritable mitochondrial disease to their children.

### What are mitochondria?

Mitochondria are present in almost all human cells, including in a woman's eggs. They generate the majority of a cell's energy supply which power every part of our body. Mitochondria carry just a few genes. These genes are involved in energy production. For any cell to function, the mitochondrial genes need to work properly. Mitochondria with gene abnormalities can cause severe medical disorders known as mitochondrial disease.

### What does mitochondrial donation involve?

Your sperm will be used to create embryos with donated eggs and/or the intended mother's eggs, by IVF or ICSI, so the intended mother can avoid passing on an inheritable mitochondrial disease to her child. The IVF-based technique used to achieve this is called pronuclear transfer (PNT).

### What is the PNT technique?

PNT is a technique of mitochondrial donation.

It allows embryos to be created for women who have mitochondrial gene abnormalities containing their nuclear genetic material (the

genes which make us who we are) and donated mitochondria.

There are two stages to the technique. A woman may need to use donor sperm for both stages of the technique (eg, if she does not have a partner who can provide sperm for her treatment), or may only need donor sperm for the second stage of PNT (eg, if the intended father is genetically related to the egg donor providing the mitochondria).

On this form you can consent to donate your sperm for both stages of the technique or for the second stage only:

**Stage one** – your sperm will be used to create embryos with the intended mother's eggs. Both your nuclear genetic material will be removed and transferred into embryos created in stage two below. Once your and the intended mother's nuclear genetic material is removed the embryonic material created in stage one will be discarded. If you donate sperm for this stage you will be genetically related to the child. You will not have any financial or legal obligations to the child. Your identifying information will be passed on to any child born as a result of your donation upon request after they have reached 18 years old. For more information, see [www.hfea.gov.uk/egg-and-sperm-donors.html](http://www.hfea.gov.uk/egg-and-sperm-donors.html).

**Stage two** – your sperm will be used to create embryos with donor eggs. The genetic material will be removed, discarded, and replaced with the nuclear genetic material from the intended mother and sperm provider from the embryos created in stage one, above. If you only donate sperm for this stage you will not be genetically related to the child. No information that could identify you will be released to any child born following the mitochondrial donation treatment.

For clinic use only (optional)

HFEA centre reference

Other relevant forms

Date sperm were placed in storage

Date sperm can remain in storage until

## What do I need to know before filling in this form?

Before you fill in this form, you should have completed the 'Donor information form' if you are providing sperm for both stages of the technique and going to be genetically related to the child, or the 'Mitochondrial donation:

PNT only sperm donor registration form' if you are providing sperm for stage two only and not going to be genetically related to the child.

You should also be certain that your clinic has given you all the relevant information you need to make fully informed decisions.

This includes:

- information about:
  - the different options set out in this form
  - the implications of giving your consent
  - the consequences of withdrawing this consent, and
  - how and when you can make changes to, or withdraw, your consent
- an opportunity to have counselling.

If you are unsure, or think that you have not been given all of this information, please speak to your clinic. There is a declaration at the end of this form which you must sign to confirm you have received this information before filling in this form. If you haven't your consent may be invalid. If you are unable to complete this form because of physical illness, injury or disability you may direct someone else to complete and sign it for you.

## Why do I have to fill in this form?

By law (the Human Fertilisation and Embryology Act 1990 (as amended)), you need to give your written consent if you want your sperm, or embryos created outside the body (in vitro) with your sperm, to be used or stored.

If your sperm or embryos containing your nuclear genetic material are going to be stored, you must consent to this and state in writing how long you consent to them remaining in storage. If you donate sperm for stage two only, once your nuclear genetic material has been removed and replaced with that of the intended parents, they will determine what happens to them, including how long they will be stored for.

You can make changes to or withdraw your consent to embryos created with your sperm in stage one at any point until the embryos have been transferred, used in training, or have been allowed to perish. For embryos created in stage two with your sperm, you can withdraw your consent at any point up until the nuclear genetic material has been removed from the embryos.

## Why are there questions about using my sperm for training purposes?

There may be some sperm or embryos left after treatment, eg, because they weren't viable for treatment. This form allows you to consent to donate sperm or embryos (before your nuclear genetic material is removed) for training purposes, allowing healthcare professionals to learn about, and practice, the techniques involved in IVF treatment.

## What if I want to donate my sperm for other purposes?

If you also wish to donate your sperm for use in fertility treatment which does not involve PNT you must complete a separate form 'Your consent to donating your sperm' (MD form).

Sperm can also be donated for research purposes, helping to increase knowledge about diseases and serious illnesses and potentially develop new treatments. If you would like to donate any sperm or embryos to research, speak to your clinic who will provide you with the relevant consent form(s).

## What happens to my sperm or embryos if I die?

By consenting to the use of your sperm in PNT, you are also agreeing to your sperm or embryos being used and stored if you were to die or lose the ability to decide for yourself (become mentally incapacitated). If you do not want your sperm or embryos to be used for the purposes outlined in this form if this were to happen, you can state this as a restriction (at section 2.4). Please note that the clinic can only act on these wishes if they are informed about your death or mental incapacity. If you're unsure of anything in relation to this, please ask your clinic.

When filling in this form, make sure you sign the declaration on every page to confirm that you have read the page and fully agree with the consent and information given. When you have completed the form you may request a copy of it from your clinic.

Donor number

Version 1, 29 October 2015

## 1. About you

First name(s)

Surname

Date of birth

NHS/CHI/HCN number (please circle)

## 2. About your sperm donation

### PNT - stage one

- 2.1.** Do you consent to your sperm being used to create embryos outside of the body (eg, through IVF or ICSI, then PNT) and for those embryos to be used for the treatment of others? **Do not complete this section if you are only providing sperm for stage two of PNT.**

This process will involve:

- your sperm being used to create embryos with the intended mother's eggs outside the body,
- the embryos undergoing the PNT process (this means that both your and the intended mother's nuclear genetic material will be removed and inserted into the embryos created in stage two). Once the nuclear genetic material has been removed from the embryos, the embryonic material will be discarded), and
- the embryos (containing your and the intended mother's nuclear genetic material and donor mitochondria) to be used in the treatment of others (embryo transfer).

Yes       No

### PNT - stage two

- 2.2.** Do you consent to your sperm being used to create embryos outside of the body with donor eggs and for those embryos to undergo the PNT process?

This process will involve:

- your sperm being used to create embryos with donated eggs outside the body, and
- the embryos undergoing the PNT process (this means your and the egg donor's nuclear genetic material will be removed and discarded).

Yes       No

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**2.3.** How many families may have children using your donated sperm? **Do not complete this section if you are only providing sperm for stage two of PNT.**

The maximum number is 10 families. This is to minimise the possibility of two children from the same donor having a relationship with each other without knowing they are genetically related.

It is also based on the perceived interests of donor-conceived people and their parents in maintaining a relatively small number of siblings. Consenting to 10 families will help the greatest number of families and maximise the potential of your donation. You should think about how many families you are comfortable donating to and the long-term implications of donation.

families may have children using my donated sperm.

**2.4.** Do you have any restrictions that you would like to apply to questions 2.1 and 2.2 above?

You may want to put restrictions on who can use embryos created with your sperm (eg, a specified named recipient). Another example may be that you do not wish for your embryos to be used in the event of your death or mental capacity. If so, please state it here. Please note that you can only place restrictions on embryos that still contain your nuclear genetic material (ie, before they have undergone the PNT process).

Yes - specify your restrictions below then continue to section 3.

No - go to section 3.

### 3. Using sperm and embryos in training

**3.1.** Do you consent to your sperm being used for training purposes?

Yes  No

**3.2.** Do you consent to your embryos (already created outside the body with your nuclear genetic material) being used for training purposes?

**Please note that embryos can only be used if the female provider of the nuclear genetic material has also given her consent.**

Yes  No

### 4. Storing sperm and embryos

**Please note that sperm donated for the treatment of others needs to be stored.**

**4.1.** Do you consent to your sperm being stored?

Yes  No

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**4.2.** Do you consent to embryos (containing your nuclear genetic material) being stored?

**Please note that embryos can only be stored if the female provider of the nuclear genetic material has also given her consent.**

Yes  No

**If you have answered no to both 4.1 and 4.2, sign the page declaration on this page then go to section five. If you have answered yes to 4.1 or 4.2, or both, then continue below.**

### Sperm and embryo storage periods

In this section you must state how long you consent to your sperm and/or embryos containing your nuclear genetic material being stored for. You may want to think about how far in the future you want others to use your stored sperm and embryos – ask your clinic if you are unsure.

The law permits you to store for any period up to 10 years but in some cases where you, your partner, or the person to whom your sperm and embryos have been allocated, is prematurely infertile, or likely to become prematurely infertile, you may store for longer, up to 55 years.

A medical practitioner will need to certify in writing that the medical criteria for premature infertility have been met for storage to continue for more than 10 years. When the criteria have been met, the storage period will be extended by 10 years from the date the criteria are met.

The storage period can then be extended by further 10 year periods (up to a maximum of 55 years) at any time within each extended storage period if it is shown that the criteria continue to be met. For more information about this, please ask your clinic.

**Once your sperm or embryos have been allocated to someone else’s treatment, the patient (together with the clinic) will determine how long the sperm and embryos are stored for within the boundaries of what you have consented to in this form. If you are only providing sperm for stage two of the PNT process, once your nuclear genetic material is removed the intended mother and sperm provider will determine how long the embryos will be stored for.**

**4.3.** For how long do you consent to your sperm, being stored? **Only complete this section if you answered yes to section 4.1. Please talk to your clinic if you’re unsure of how long to store for.**

10 years  55 years

A specific period (up to 55 years). Specify number of years

**4.4.** For how long do you consent to embryos being stored? **Only complete this section if you answered yes to question 4.2. Please talk to your clinic if you’re unsure of how long to store for.**

10 years  55 years

A specific period (up to 55 years). Specify number of years

The consent period will start from the date of storage. Remember you can always change the time period you consent to by completing this form again and specifying the new total time period you would like your sperm and embryos to be stored for.

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For example, if you consented to five years' storage on the original form and wish to consent for a further five years (10 years in total), you would complete another copy of this form but tick the box for 10 years. This second form would supersede the first form you completed.

## 5. Declaration

Please sign and date the declaration

- I declare that I am the person named in section one of this form.
- I declare that:
  - before I completed this form, I was given information about the different options set out in this form, and I was given an opportunity to have counselling
  - the implications of giving my consent, and the consequences of withdrawing this consent, have been fully explained to me, and
  - I understand that if my sperm is used to create embryos with the intended mother's eggs (stage one of the PNT process) I can make changes to or withdraw my consent at any point until the embryos have been transferred, used in training, or have been allowed to perish.
  - I understand that if my sperm is used only to create embryos with the donor's eggs (stage two of the PNT process), I can make changes to, or withdraw, my consent at any point until my genetic material has been removed.
- I declare that the information I have given on this form is correct and complete.
- I understand that information on this form may be processed and shared for the purposes of, and in connection with, the conduct of licensable activities under the Human Fertilisation and Embryology Act 1990 (as amended) in accordance with the provisions of that act.

Your signature

Date

### If signing at the direction of the person consenting

If you have completed this form at the direction of the person consenting (because he is unable to sign for himself due to physical illness, injury or disability), you must sign and date below. There must also be a witness confirming that the person consenting is present when you sign the form.

I declare that the person named in section one of this form is present at the time of signing this form and I am signing it in accordance with his direction

Representative's name

Representative's signature

Relationship to person consenting

Date

Witness's name

Witness's signature

Date

## Consent to donating your sperm (including for use in pronuclear transfer)

MD (including PNT)

### About this form

This form is produced by the Human Fertilisation and Embryology Authority (HFEA), the UK's independent regulator of fertility treatment and human embryo research. For more information about us, visit [www.hfea.gov.uk](http://www.hfea.gov.uk).

### Who should fill in this form?

Fill in this form if you are a man donating sperm for the treatment of others (by artificial insemination or IVF) or for training purposes (to allow healthcare professionals to learn about, and practice, the techniques involved in fertility treatment).

In some cases the IVF process may also involve the use of a technique called pronuclear transfer (PNT) which can be used to allow women to avoid passing on an inheritable mitochondrial disease to her child.

Mitochondria are present in almost all human cells, including in a woman's eggs. They generate the majority of a cell's energy supply which power every part of our body.

Mitochondria carry just a few genes. These genes are involved in energy production. For any cell to function, the mitochondrial genes need to work properly. Mitochondria with gene abnormalities can cause severe medical disorders known as mitochondrial disease.

### What is the PNT technique?

PNT is a technique of mitochondrial donation allowing embryos to be created for women who have mitochondrial gene abnormalities containing their nuclear genetic material (the genes which make us who we are) and donated mitochondria.

There are two stages to the technique. A woman may need to use donor sperm for both stages of the technique (eg, if she does not have a partner who can provide sperm for her treatment), or may only need donor sperm for the second stage of PNT (eg, if the intended father is genetically related to the egg donor providing the normal mitochondrial).

**Stage one** - your sperm will be used to create embryos with the intended mother's eggs. Both your nuclear genetic material will be removed and transferred into embryos created in stage two below. Once you and the intended mother's nuclear genetic material is removed the embryonic material created in stage one will be discarded.

**Stage two** - your sperm will also be used to create embryos with donor eggs. The genetic material will be removed, discarded, and replaced with the nuclear genetic material from the intended mother and your sperm from the embryos created in stage one, above. These new embryos will be used in the treatment of others (embryo transfer).

If your sperm is used for both stages of the PNT process you will be genetically related to the child in the same way as if your sperm is used for IVF.

### What do I need to know before filling in this form?

Before you fill in this form, you should complete the 'Donor information form'.

You should also be certain that your clinic has given you all the relevant information you need to make fully informed decisions. This includes:

- information about:
  - the different options set out in this form

For clinic use only (optional)

HFEA centre reference

Other relevant forms

Date sperm were placed in storage

Date sperm can remain in storage until

- the implications of giving your consent
- the consequences of withdrawing this consent, and
- how you can make changes to, or withdraw your consent.
- an opportunity to have counselling.

If you are unsure, or think that you have not been given all of this information, please speak to your clinic. There is a declaration at the end of this form which you must sign to confirm you have received this information before filling in this form. If you haven't your consent may be invalid.

If you are unable to complete this form because of physical illness, injury or disability you may direct someone else to complete and sign it for you.

### Why do I have to fill in this form?

By law (the Human Fertilisation and Embryology Act 1990 (as amended)), you need to give your written consent if you want your sperm, or embryos created outside the body (in vitro) with your sperm, to be used or stored (for example, for in vitro fertilisation (IVF) treatment).

If you are storing your sperm or embryos, you must also state in writing how long you consent to them remaining in storage.

### What if I want to donate my sperm for research?

Sperm can also be donated for research purposes, helping to increase knowledge about diseases and serious illnesses and potentially develop new treatments. This form only allows you to consent to donate sperm for the treatment of others or for training purposes.

Your clinic can give you more information about donating for research and provide you with the relevant consent form(s).

### What happens to my sperm or embryos if I die?

By consenting to donate your sperm or embryos, you are also agreeing to them being used and stored if you were to die or lose the ability to decide for yourself (become mentally incapacitated). If you do not want your sperm or embryos to be used for the purposes outlined in this form if this were to happen, you can state this as a restriction (at section 2.5 of this form). You may also state here that you only want your sperm or embryos to be donated in the event of your death.

Please note that the clinic can only act on these wishes if they are informed about your death or mental incapacity.

When filling in this form, make sure you sign the declaration on every page to confirm that you have read the page and fully agree with the consent and information given.

When you have completed the form you may request a copy of it from your clinic.

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## 1. About you

First name(s)

Surname

Date of birth

NHS/CHI/HCN number (please circle)



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## 2. About your sperm donation

- 2.1.** Do you consent to your sperm being used for the treatment of others, without the creation of embryos outside the body, ie, using artificial insemination?

Examples of artificial insemination include intrauterine insemination (IUI) or gamete intra-fallopian transfer (GIFT), a technique which a small number of clinics use.

Yes       No

- 2.2.** Do you consent to your sperm being used to create embryos outside the body (eg, through IVF treatment) and for these embryos to be used for the treatment of others?

Yes       No

- 2.3.** Do you consent to your sperm being used to create embryos outside the body (eg, through IVF treatment), for those embryos to undergo the PNT process (both stages 1 and 2 outlined above) and for resulting embryos (containing your nuclear genetic material) to be used for the treatment of others?

Yes       No

- 2.4.** How many families may have children using your donated sperm?

The maximum number is 10 families. This is to minimise the possibility of two children from the same donor having a relationship with each other without knowing they are genetically related. It is also based on the perceived interests of donor-conceived people and their parents in maintaining a relatively small number of siblings. Consenting to 10 families will help the greatest number of families and maximise the potential of your donation. You should think about how many families you are comfortable donating to and the long-term implications of donation.

families may have children using my donated sperm.

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**2.5.** Do you have any restrictions that you would like to apply to any of your answers to 2.1, 2.2, and 2.3 above? You may want to put restrictions on who your sperm or embryos are used by, eg, a specified named recipient.

Yes - specify your restrictions below then continue to section 3.

No - go to section 3.

### 3. Using sperm and embryos in training

**3.1.** Do you consent to your sperm being used for training purposes?

Yes  No

**3.2.** Do you consent to your embryos (already created outside the body with your sperm) being used for training purposes?

Yes  No

### 4. Storing sperm and embryos

Please note that sperm donated for the treatment of others needs to be stored.

**4.1.** Do you consent to your sperm being stored?

Yes  No

**4.2.** Do you consent to embryos (created outside the body with your sperm) being stored? Only complete this section if you answered yes to section 2.2 or 2.3. Please note that embryos can only be stored if the egg provider has also given her consent.

Yes  No

**If you have answered no to both 4.1 and 4.2, sign the page declaration on this page and then go to section five.**

**If you have answered yes to 4.1 or 4.2, or both, then continue below.**

#### Sperm and embryo storage periods

In this section you must state how long you consent to your sperm and/or embryos being stored for. You may want to think about how far in the future you want others to use your stored sperm and embryos – ask your clinic if you are unsure.

The law permits you to store for any period up to 10 years but in some cases where you, your partner, or the person to whom your sperm and embryos have been allocated, is prematurely infertile, or likely to become prematurely infertile, you may store for longer, up to 55 years.

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The storage period can then be extended by further 10 year periods (up to a maximum of 55 years) at any time within each extended storage period if it is shown that the criteria continue to be met. For more information about this, please ask your clinic.

**Once your sperm or embryos have been allocated to someone else's treatment, the patient (together with the clinic) will determine how long the sperm and embryos are stored for within the boundaries of what you have consented to in this form.**

**4.3.** For how long do you consent to your sperm being stored? **Only complete this section if you answered yes to 4.1.**

10 years     55 years

A specific period (up to 55 years). Specify number of years

**4.4.** For how long do you consent to embryos (created with your sperm) being stored? **Only complete this section if you answered yes to section 4.2. Please note that the egg provider also has to give her consent to storage.**

10 years     55 years

A specific period (up to 55 years). Specify number of years

The consent period will start from the date of storage. Remember you can always change the time period you consent to by completing this form again and specifying the new total time period you would like your sperm and embryos to be stored for.

For example, if you consented to five years' storage on the original form and wish to consent for a further five years (10 years in total), you would complete another copy of this form but tick the box for 10 years. This second form would supersede the first form you completed.

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## 5. Declaration

Please sign and date the declaration

- I declare that I am the person named in section one of this form.
- I declare that:
  - before I completed this form, I was given information about the different options set out in this form, and I was given an opportunity to have counselling
  - the implications of giving my consent, and the consequences of withdrawing this consent, have been fully explained to me, and
  - I understand that I can make changes to, or withdraw, my consent at any point until the sperm or embryos have been transferred, used in training, or have been allowed to perish.
- I declare that the information I have given on this form is correct and complete.
- I understand that information on this form may be processed and shared for the purposes of, and in connection with, the conduct of licensable activities under the Human Fertilisation and Embryology Act 1990 (as amended) in accordance with the provisions of that act.

Your signature

Date

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If you have completed this form at the direction of the person consenting (because he is unable to sign for himself due to physical illness, injury or disability), you must sign and date below. There must also be a witness confirming that the person consenting is present when you sign the form.

I declare that the person named in section one of this form is present at the time of signing this form and I am signing it in accordance with his direction

Representative's name

Representative's signature

Relationship to person consenting

Date

Witness's name

Witness's signature

Date