

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

### **Briefing: The Ethics of Mitochondrial Donation**

Prepared by the **Progress Educational Trust** and the **British Fertility Society**  
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The **Progress Educational Trust (PET)** and the **British Fertility Society (BFS)** urge you to vote in favour of the **Human Fertilisation and Embryology (Mitochondrial Donation) Regulations 2015**.

- **Who has prepared this briefing?**

The **Progress Educational Trust (PET)** is a registered charity whose Patron is **Baroness Mary Warnock**. **PET** was founded in 1992, as an independent voice informing debate on assisted conception and genetics.

PET has no financial stake in research or clinical practice. The ultimate beneficiaries of all the charity's work are families and individuals threatened by infertility and genetic disease, including people wanting an opportunity to give birth to healthy children.

PET first reported on mitochondrial donation as a hypothetical possibility in its flagship publication **BioNews** in 1999.<sup>1</sup> As research has progressed in recent years, with mitochondrial donation moving from theory to reality, PET has continued to monitor closely the relevant ethical and scientific issues.

The **British Fertility Society (BFS)** is a national multidisciplinary organisation representing professionals practising in the field of reproductive medicine. BFS is committed to promoting good clinical practice and working with patients to provide safe and effective fertility treatment.

Below are answers from PET and BFS to some questions that you may have about the ethics of mitochondrial donation, and that may arise in Parliamentary debate. Detailed references are provided in the '**Endnotes**' at the end of this briefing.

PET and BFS have also issued an accompanying briefing on '**The Science of Mitochondrial Donation**'.

- **Is mitochondrial donation safe?**

Claims about safety often serve as a convenient proxy, for the ethical objections of people who are in fact more fundamentally opposed to mitochondrial donation.

According to prevailing scientific opinion, mitochondrial donation is safe. It employs techniques that have been the subject of 30 years of research in animals, and more than five years of research in human embryos. The safety of mitochondrial donation has been assessed in exhaustive detail, in

expert scientific reviews convened by the Human Fertilisation and Embryology Authority (HFEA) in 2011, 2013 and 2014.<sup>2</sup>

These reviews considered evidence from all areas of science and medicine relevant to mitochondrial donation, including both peer-reviewed literature and unpublished research, and took account of deliberations on this subject in other countries.<sup>3</sup> The experts who conducted the reviews solicited evidence, assessed every theoretical concern that was presented to them, and came to the conclusion that there is no compelling reason to think that mitochondrial donation is unsafe.

Assisted conception techniques that are now well-established – such as IVF, preimplantation genetic diagnosis and intracytoplasmic sperm injection – all involved a degree of uncertainty when they were first performed in humans. The scientific reviews of mitochondrial donation convened by the HFEA exceed, in their thoroughness, any comparable assessment of risk that was made prior to those earlier techniques being used in clinical practice.

All novel treatments raise the question of when and how the treatment can be judged safe to offer to patients. Moving from research into clinical practice always involves some uncertainty. The best that can be done is to reduce risks as much as possible, and then continue to monitor the situation after the treatment has been offered.

In the case of mitochondrial donation, this is exactly what has been done and what will continue to be done. As an additional precaution going forward, the scientific reviews convened by the HFEA have recommended long-term follow-up studies of anyone conceived via mitochondrial donation, and of subsequent generations.<sup>4</sup>

- **How will mitochondrial donation affect future generations? How will it affect the germline?**

Mitochondrial donation will change the mitochondrial germline, with positive consequences for future generations.<sup>5</sup>

Children conceived via mitochondrial donation will inherit healthy mitochondrial DNA from a donor. If these children are female, and if they go on to have children of their own later in life, then *those* children and any generations that follow will *also* inherit the donor's mitochondrial DNA.

In this way, it is hoped that mitochondrial donation will be an effective means of preventing both the occurrence of mitochondrial disease *in*, and the transmission of mitochondrial *between*, successive generations of people.

- **Is mitochondrial donation genetic modification? Is it genetic engineering?**

Mitochondrial donation is neither a form of genetic modification nor a form of genetic engineering.

'Genetic modification' and 'genetic engineering' are terms that usually refer to an intervention in the gene sequence *within* a DNA molecule, which is a process that can involve numerous and complex risks. Mitochondrial donation, by contrast, involves moving DNA molecules from one place to another while leaving them completely *intact*. Mitochondrial donation involves *no* intervention in the gene sequence, and therefore involves none of the risks associated with such intervention.<sup>6</sup>

Intact molecules of mitochondrial DNA move from one place to another as a matter of course during sexual reproduction. The difference, with mitochondrial donation, is that the faulty mitochondria of the mother are replaced with the healthy (and intact) mitochondria of the donor. All fathers effectively get to choose the mitochondrial DNA of their children through their choice of partner, whereas mothers do not have this choice and are compelled to pass on their own mitochondria, even if these are defective. Mitochondrial donation gives this choice – already enjoyed by fathers – to those mothers who desperately need it.

Just as the transplantation of tissue or organs to patients is not generally considered to be a form of genetic modification, so it is inaccurate to characterise mitochondrial donation as a form of genetic modification. This is why, when the power to make Regulations was provided for in the Human Fertilisation and Embryology Act 2008, Parliament decided that the Regulations could define as '*a permitted egg*' or '*a permitted embryo*' an egg or embryo that '*has had applied to it in prescribed circumstances a prescribed process designed to prevent the transmission of serious mitochondrial disease*'.<sup>7</sup>

- **Is mitochondrial donation cloning?**

Some critics have characterised mitochondrial donation techniques as a form of 'cloning'. This is scientifically inaccurate.

In biology, cloning refers to a process that creates an identical copy of an organism, with the possibility that the genetically identical original could continue to exist alongside the copy. In mitochondrial donation, a child is conceived using biological material from three people, *none* of whom will be genetically identical to the child (and one of whom, the mitochondrial donor, will not bear any resemblance to the child at all).

Mitochondrial donation is sometimes confused with cloning because it involves techniques that are similar to somatic cell nuclear transfer (SCNT), a procedure used by scientists to clone animals (this is how Dolly the sheep was created). But mitochondrial donation differs from SCNT in several respects – crucially, SCNT results in the creation (*without* fertilisation) of genetic *duplicates*, while mitochondrial donation results in the creation (*with* fertilisation) of a genetically *unique* child.<sup>8</sup>

- **Will mitochondrial donation result in children with three parents?**

Mitochondrial donation will not result in children with three parents. A child conceived via this method will inherit nuclear DNA from two parents in the usual way. The only DNA that the child will inherit from a donor is the donor's *mitochondrial* DNA.

No tradition exists of ascribing parenthood to a person from whom a child inherits only mitochondrial DNA. This is for the very good reason that such a situation has not existed before now. There is no reason to start ascribing parenthood to mitochondrial donors – being a parent involves much more than contributing genes to a child.

Mitochondrial DNA is so different from nuclear DNA – both in its *quantity* (only 0.1% of our genes are mitochondrial) and in its *quality* (mitochondrial DNA does not code for any individually distinguishing characteristics, and mitochondrial DNA sequences are not normally unique to individuals) – that it does not fit into the popular narrative of our DNA being associated closely with our identity.

Conceiving a child via mitochondrial donation involves using biological material from three people – the child's *parents*, plus a mitochondrial *donor*. 'Three-person IVF' is acceptable shorthand for mitochondrial donation, but 'three-parent IVF' is inaccurate.<sup>9</sup>

- **Should mitochondrial donors be anonymous?**

In the Regulations, there is no requirement for a mitochondrial donor and a person conceived via their donation to be identifiable to one another. This makes sense, because mitochondrial donation creates neither observable nor other shared characteristics between these two individuals (except for the fact that both of them will be free of mitochondrial disease).

In this respect, mitochondrial donation is more akin to *tissue or organ donation* (where there is no requirement that donors and recipients be identifiable to one another) than it is to sperm, egg or embryo donation (where donors' entitlement to anonymity was removed 10 years ago). This is the case, *despite* the fact that mitochondrial donation involves the same egg retrieval process as is used in egg donation. The purpose and outcome is very different in mitochondrial donation than it is in egg donation.

Fears have been voiced that anonymity will somehow compromise the safety of mitochondrial donation. These fears are misplaced. With sperm and egg donation, there is a (remote) possibility that people conceived via anonymous donation will unknowingly have children with genetic relatives, thereby posing a risk to the health of the children. No analogous risk exists with mitochondria, which are inherited solely from the mother. Furthermore, should children conceived via mitochondrial donation *or* mitochondrial donors ever need to be traced for an as yet unanticipated reason, their details will be kept in the HFEA's secure Register of information.

Finally, it is important to note that as with tissue and organ donation, these Regulations do not preclude women from using mitochondrial donors who are known to (but unrelated to) them, and do not preclude mitochondrial donors from choosing to waive their anonymity. Nor do the Regulations preclude the creation of local systems, to enable the voluntary exchange of information between mitochondrial donors and anyone conceived via their donation (should this be desired).<sup>10</sup>

- **Is permitting mitochondrial donation a slippery slope?**

The 'slippery slope' is a common term, for a process whereby permitting something leads inexorably to permitting a less desirable or more controversial thing. Permitting mitochondrial donation is not the start of a slippery slope. As explained above, mitochondrial donation replaces one set of mitochondrial DNA molecules with another, but it does not modify any genes in those molecules.

There is no inevitable progression from permitting mitochondrial donation to permitting techniques that constitute genetic modification. The techniques that would be required for the latter are very different from those involved in mitochondrial donation, and critically, there is no provision in existing legislation for Regulations that would permit genetic modification. The Human Fertilisation and Embryology Act 2008 states clearly that only '*a prescribed process designed to prevent the transmission of serious mitochondrial disease*' can be permitted by Regulations.

Note also that the Regulations do not, in themselves, permit mitochondrial donation. Rather, they permit the HFEA to *consider applications for licences* to perform mitochondrial donation. The granting of such licences will be at the HFEA's discretion, subject to rigorous criteria and always within the framework of the UK's well-developed system of regulation.

Mitochondrial donation is the *only* way that patients with high levels of faulty mitochondria can have a child who is both genetically related to them, *and* unaffected by mitochondrial disease. Far from being poised on a downhill slippery slope, patients in this predicament – not to mention the doctors, researchers, charities and politicians who seek to help them – have been engaged in a long *uphill* struggle against devastating and fatal disease.

With the support of Parliament, the end of that struggle is finally in sight.

- **Further information**

For further information on scientific questions, see our accompanying briefing on '**The Science of Mitochondrial Donation**'.

For concise overviews of some of the issues surrounding mitochondrial donation, see:

- The Lily Foundation's factsheet at <http://bit.ly/lilymito>
- The Wellcome Trust's factsheet at <http://bit.ly/wellcomemito>

## • Endnotes

1. See 'Dolly not a perfect clone', *BioNews*, 1999 – [http://www.bionews.org.uk/page\\_10488.asp](http://www.bionews.org.uk/page_10488.asp)
2. See the three scientific reviews:
  - *First Scientific Review of the Safety and Efficacy of Methods to Avoid Mitochondrial Disease through Assisted Conception* – [http://www.hfea.gov.uk/docs/2011-04-18\\_Mitochondria\\_review\\_-\\_final\\_report.PDF](http://www.hfea.gov.uk/docs/2011-04-18_Mitochondria_review_-_final_report.PDF)
  - *Second Scientific Review of the Safety and Efficacy of Methods to Avoid Mitochondrial Disease through Assisted Conception* – [http://www.hfea.gov.uk/docs/Mito-Annex\\_VIII-science\\_review\\_update.pdf](http://www.hfea.gov.uk/docs/Mito-Annex_VIII-science_review_update.pdf)
  - *Third Scientific Review of the Safety and Efficacy of Methods to Avoid Mitochondrial Disease through Assisted Conception* – [http://www.hfea.gov.uk/docs/Third\\_Mitochondrial\\_replacement\\_scientific\\_review.pdf](http://www.hfea.gov.uk/docs/Third_Mitochondrial_replacement_scientific_review.pdf)
3. For example, the 59th Meeting of the Cellular, Tissue, and Gene Therapies Advisory Committee of the US Food and Drug Administration is discussed on p10-11 of the *Third Scientific Review of the Safety and Efficacy of Methods to Avoid Mitochondrial Disease through Assisted Conception* – [http://www.hfea.gov.uk/docs/Third\\_Mitochondrial\\_replacement\\_scientific\\_review.pdf](http://www.hfea.gov.uk/docs/Third_Mitochondrial_replacement_scientific_review.pdf)
4. As discussed on p26 and p33 of the *Third Scientific Review of the Safety and Efficacy of Methods to Avoid Mitochondrial Disease through Assisted Conception* – [http://www.hfea.gov.uk/docs/Third\\_Mitochondrial\\_replacement\\_scientific\\_review.pdf](http://www.hfea.gov.uk/docs/Third_Mitochondrial_replacement_scientific_review.pdf)  
  
Follow-up was also addressed in detail at an evidence session held by the House of Commons Science and Technology Select Committee on 22 October 2014. See p12-13, p16-18, p21 and p24-26 of the transcript – <http://data.parliament.uk/writtenevidence/committeeevidence.svc/evidencedocument/science-and-technology-committee/mitochondrial-donation/oral/14822.pdf>
5. The HFEA reports on the public's (generally positive) understanding of how mitochondrial donation will affect the germline, on p16 of its 2013 document *Mitochondria Replacement Consultation: Advice to Government* – [http://www.hfea.gov.uk/docs/Mitochondria\\_replacement\\_consultation\\_-\\_advice\\_for\\_Government.pdf](http://www.hfea.gov.uk/docs/Mitochondria_replacement_consultation_-_advice_for_Government.pdf)
6. The Government explains why it does not consider mitochondrial donation to constitute genetic modification on p15 of its 2014 document *Mitochondrial Donation: Government Response to the Consultation on Draft Regulations to Permit the Use of New Treatment Techniques to Prevent the Transmission of a Serious Mitochondrial Disease from Mother to Child* – [https://www.gov.uk/government/uploads/system/uploads/attachment\\_data/file/332881/Consultation\\_response.pdf](https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/332881/Consultation_response.pdf)
7. Human Fertilisation and Embryology Act 2008, Section 3(5) – <http://www.legislation.gov.uk/ukpga/2008/22/section/3>

8. See p17 of the *Third Scientific Review of the Safety and Efficacy of Methods to Avoid Mitochondrial Disease through Assisted Conception* –  
[http://www.hfea.gov.uk/docs/Third\\_Mitochondrial\\_replacement\\_scientific\\_review.pdf](http://www.hfea.gov.uk/docs/Third_Mitochondrial_replacement_scientific_review.pdf)
  
9. The Government explains why it does not consider mitochondrial donation to be genetic modification on p15 of its 2014 document *Mitochondrial Donation: Government Response to the Consultation on Draft Regulations to Permit the Use of New Treatment Techniques to Prevent the Transmission of a Serious Mitochondrial Disease from Mother to Child* –  
[https://www.gov.uk/government/uploads/system/uploads/attachment\\_data/file/332881/Consultation\\_response.pdf](https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/332881/Consultation_response.pdf)
  
10. The establishing of such systems is recommended by the HFEA on p5 of its 2013 document *Mitochondria Replacement Consultation: Advice to Government* –  
[http://www.hfea.gov.uk/docs/Mitochondria\\_replacement\\_consultation\\_-\\_advice\\_for\\_Government.pdf](http://www.hfea.gov.uk/docs/Mitochondria_replacement_consultation_-_advice_for_Government.pdf)