Re: Regulations to avoid mitochondrial disease

We are writing on behalf of the bioscience sector and patient groups to assist your committee in its consideration of the Human Fertilisation and Embryology (Mitochondrial Donation) Regulations 2015 (Regulations), which we support. In particular we commend the detailed scrutiny and consultation process which has resulted in informed and clear regulations.

Mitochondrial disease is a devastating and debilitating condition. Many children born with the condition will not make it to adulthood.1 New IVF techniques (mitochondrial donation)2 could allow women who carry mitochondrial disease the reproductive option to choose to have their own genetically related children unaffected by these devastating disorders. We support mitochondrial donation as a reproductive choice to enable families to avoid having children with serious mitochondrial disease.

The relevant Regulation-making powers were included in the Human Fertilisation and Embryology Act 2008 (Act), enabling the Secretary of State to make regulations when appropriate, to allow the Human Fertilisation and Embryology Authority (HFEA) to licence the use of these ground breaking therapies in the clinic. This Act passed through Parliament after extensive debate in both the House of Lords and House of Commons, generating an unprecedented 80 hours of parliamentary time.

The relevant section of the Act was carefully scrutinised and was itself the result of debate where both Houses concluded by an overwhelming margin that Regulation-making powers in this area was appropriate.3

The Regulations are the culmination of seven years of extensive scrutiny;5 there have been independent ethical reviews,6 three separate reviews of the scientific evidence on the

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1 http://www.thelilyfoundation.org.uk/animation/
2 Wellcome Trust, 'Mitochondrial Donation, Q&A': http://www.wellcome.ac.uk/stellent/groups/corporatesite/@policy_communications/documents/web_document/wtp057782.pdf;
3 http://www.publications.parliament.uk/pa/cm200708/cmhansrd/cm081022/debtext/81022-0016.htm#08102255000176
4 http://www.publications.parliament.uk/pa/ld200708/ldhansrd/text/80204-0002.htm#08020422000094
technique’s safety by a specially convened independent panel of experts, and an extensive public consultation, independently validated, which has revealed broad public support.

It is an accepted fact in the clinical and research communities, and should be recognised by the Committee, that it is never possible to answer every question on safety before new procedures are used in people for the first time. However, if medicine is to progress, clinicians must be permitted to use new techniques with informed consent of the patient when they are ethical (including that the potential benefits outweigh the potential risks), and when there is sufficient evidence of safety and effectiveness. An exemplary consultation and review process has revealed that mitochondrial donation has reached this stage.

We therefore welcome the Regulations, and the detailed and informative explanatory memorandum supporting them. As provided in the parent Act, these Regulations allow the statutory regulator, the HFEA, to consider applications for licences permitting the use of these techniques in treatment. The HFEA and its expert committees are highly regarded internationally for their expertise in evaluating whether proposed techniques are sufficiently safe and effective. This will include whether centres that apply for licences have the necessary staff, expertise, skill and equipment to perform the proposed activity. The Regulations, if adopted, simply allow this further review process to begin, and thus ensure that regulatory oversight, itself under Parliamentary control, runs concurrently with scientific progress. This enabling legislation would put the UK on the same footing as the situation in other countries, including the US, where mitochondrial donation is not specifically illegal and regulators are empowered to decide whether treatment should be allowed based on safety and efficacy data.

We recognise, as did the Minister in her evidence to the House of Commons Science and Technology Select Committee, that some people will always object to the techniques on principle, regardless of the scientific evidence about safety. It was never the intention of the Act for Parliament only to permit the HFEA to consider applications after all possible safety studies had been concluded and when the procedure was judged entirely safe. Rather the intention of the Act was to enable the statutory regulator to consider applications when the science and research had progressed to a point where therapeutic uses are possible and to ensure that the HFEA was given the relevant parameters within which to carry out those duties. This is identical to the role of the HFEA in many other areas of clinical practice. Allegations about lack of safety will be matters for the HFEA in any licensing decision; there is no evidence on safety that warrants delaying these Regulations.

We are happy to provide you with additional information on any of the issues noted above and hope that you will agree these Regulations should be considered by the House without further delay.

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5 A detailed timeline of this process is appended in Annex A
7 HFEA, Expert review of scientific methods to avoid mitochondrial disease 2011: http://www.hfea.gov.uk/6372.html
8 HFEA, Expert review of scientific methods to avoid mitochondrial disease 2012: http://www.hfea.gov.uk/9359.html
11 An overview of the key studies reviewed in these deliberations are appended in Annex B
Annex A

Timeline: debating mitochondrial donation regulations since 2000


2005 - The Science and Technology Committee publish the extensive report Human Reproductive Technologies and the Law, supporting further research in this area.

2005 – University of Newcastle obtain license to work with human oocytes.

2008 – Human Fertilisation and Embryology Act passed, allowing researchers to develop techniques to prevent transmission of maternally inherited mitochondrial disease.

April 2010 – Researchers at Newcastle University develop techniques to prevent diseased mitochondria being passed from mother to child.


June 2012 – Nuffield Council on Bioethics publishes Novel techniques for the prevention of mitochondrial DNA disorders: an ethical review

July 2012 – HFEA runs series of public dialogue events across the UK.

November 2012 – HFEA runs two public discussion events in Manchester and London.

March 2013 – Publication of a letter in The Times supporting changes in legislation. Signed by: Sir John Sulston (Nobel Prize winner), Baroness Deech, Baroness Warnock, Lord Willis of Knaresborough, Lord Winston, Sir Tim Hunt (Nobel Prize winner), Sir John Savill (Chief Executive, MRC) and Sir John Tooke (President, Academy of Medical Sciences).

March 2013 – HFEA publishes report on public consultation and updated scientific review, agreeing advice to Government on ethics and science of mitochondrial donation. Expert panel concludes that the techniques have potential to be used, if safety and efficacy are refined. Consultation reports broad public support for the techniques.

June 2013 – Department of Health (DH) and HFEA state that draft regulations would be issued later in 2013, then taken to further public consultation.

March 2014 – Draft regulations for mitochondrial donation published by DH and public consultation launched for three months.

House of Commons holds an adjournment debate, called by Jacob Rees-Mogg MP. Briefings held by DH in both Houses of Parliament.

April 2014 – Evaluation of HFEA public dialogue and consultation published, concluding the HFEA and Sciencewise collaboration to be a credible and efficacious exercise in public engagement and consultation.

June 2014 – HFEA releases third scientific review of safety and efficacy of mitochondrial donation. It finds no evidence to suggest either technique is unsafe and that both have potential to be used in a specific set of patients with serious mitochondrial disease.

July 2014 – DH publishes Government response to public consultation on draft regulations.

September 2014 – Commons backbench debate on mitochondrial donation, called by Fiona Bruce MP.

October 2014 – HFEA publishes addendum to the 2014 updated scientific review.

Parliamentary Office of Science and Technology holds briefing on Preventing Mitochondrial Disease – debates about mitochondrial replacement.

Commons Science and Technology Select Committee holds evidence session on mitochondrial donation. Findings are shared in letter from Committee Chair Andrew Miller to minister Jane Ellison.

December 2014 – Government publishes regulations on allowing mitochondrial donation.
Mitochondrial donation techniques have been successfully performed in monkeys and mice, leading to the birth of healthy offspring.

Techniques have also been used on human eggs and fertilised human eggs, in both cases leading to the successful development of a bundle of cells, suggesting that they would develop as normal if implanted in the uterus.

Safety is and will always be of paramount importance and the techniques have received unprecedented scrutiny by the Human Fertilisation and Embryology Authority’s specially convened Expert Scientific Review panel. Through three separate reviews, the panel found no evidence to suggest that the techniques are unsafe for clinical use and concluded that both techniques have the potential to be used in patients with mitochondrial disease. Never before has a new reproductive technology been subjected to such thorough investigation before it has been approved.

1983 – Pronuclear transfer (PNT) performed in mice (without mitochondrial abnormalities). PNT-derived embryos developed normally, similar to development of unmanipulated embryos, and resulted in birth of normal offspring. 1

1997 – PNT again successfully performed in mice (lacking mitochondrial abnormalities), demonstrating efficiency and reproducibility of PNT. 2

2005 – PNT successfully performed in mice carrying a mitochondrial DNA (mtDNA) abnormality, preventing transmission of the defect and resulting in the birth of offspring showing no evidence of disease. 3

2005 – Maternal spindle transfer (MST) performed in a wide range of animals as controls in somatic cell nuclear transfer experiments, suggesting it is an efficient technique. 4

2009 – MST successfully performed in mice and leads to the birth of pups with no growth abnormalities or epigenetic defects. 5

2009 – MST successfully performed in non-human primates (rhesus macaques) to prevent transmission of mitochondrial disease and lead to the birth of four healthy offspring. 6

2010 – PNT used in abnormally fertilised human embryos to prevent transmission of mtDNA disease, resulted in the development of blastocysts, which appeared as normal as controls. 7

2013 – The four MST macaque offspring showed normal health after three years with no evidence of abnormalities.

2013 – MST successfully performed in a different subspecies of rhesus macaque with a different mtDNA sequence. No difference in nuclear–mitochondrial genome interactions was noted. 8

2013 – MST performed in activated and normally fertilised human oocytes. Embryos produced from MST-derived normally fertilised oocytes went on to develop normally to the blastocyst stage and produced embryonic stem (ES) cell lines similar to controls, with a euploid karyotype (normal multiple of chromosomes), all of which contained only donor mtDNA. 9

2014 – MST-derived rhesus macaques (born in 2009) continue to show no evidence of abnormalities five years later. 10

On-going – Experiments are being pursued to evaluate the clinical use of these techniques. Progress is encouraging.
References

4. HFEA, April 2011 Scientific review of the safety and efficacy of methods to avoid mitochondrial disease through assisted conception.
13. HFEA June 2014, Scientific review of the safety and efficacy of methods to avoid mitochondrial disease through assisted conception.
14. HFEA June 2014, Scientific review of the safety and efficacy of methods to avoid mitochondrial disease through assisted conception.