EXPLANATORY MEMORANDUM TO

THE HUMAN FERTILISATION AND EMBRYOLOGY (MITOCHONDRIAL DONATION) REGULATIONS 2015

2015 No. 572

1. This Explanatory Memorandum has been prepared by the Department of Health and is laid before Parliament by Command of Her Majesty.

2. Purpose of the instrument

2.1. This instrument enables mitochondrial donation techniques to be used as part of in-vitro fertilisation (IVF) treatment to prevent the transmission of serious mitochondrial disease from a mother to her child.

3. Matters of special interest to the Joint Committee on Statutory Instruments

3.1. None.

4. Legislative Context

4.1. Section 3(2) of the Human Fertilisation and Embryology Act 1990 ("the 1990 Act") provides that only "permitted" human sperm, eggs or embryos may be placed in a woman. Section 3ZA of the 1990 Act defines permitted embryos and gametes for this purpose, including the requirement that no nuclear or mitochondrial DNA of any cell of those embryos or gametes has been altered. This instrument includes within the definition of a permitted egg or embryo eggs or embryos which, in the circumstances set out in the Regulations, have had specified processes applied to them to prevent the transmission of serious mitochondrial disease. The instrument also makes consequential amendments to provisions of the 1990 Act and the Human Fertilisation and Embryology Act 2008 ("the 2008 Act") to allow for cases involving mitochondrial donation.

5. Territorial Extent and Application

5.1. This instrument applies to the United Kingdom.

6. European Convention on Human Rights

The Parliamentary Under-Secretary of State for Public Health has made the following statement regarding Human Rights:

In my view the provisions of The Human Fertilisation and Embryology (Mitochondrial Donation) Regulations 2015 are compatible with the Convention rights.

7. Policy background

Mitochondrial disease

7.1. Mitochondria are present in almost all human cells and provide the power that cells need to function. Mitochondrial DNA is inherited through the maternal line. Mothers can carry abnormal mitochondria and be at risk of passing on serious disease to their children, even if they themselves show only mild or no symptoms. Mitochondrial disease affects each sufferer differently with a wide range of potential symptoms at varying levels of severity, including poor growth, loss of muscle co-ordination, muscle weakness, visual and hearing problems, learning disabilities, heart, liver and kidney disease. The disease can result in painful, debilitating and disabling suffering, long-term ill-health and a consequent low quality of life. In its most severe form, a child born with the condition is likely to die at an early age. There is no cure for mitochondrial disease and only very limited means of alleviating a patient's symptoms.

7.2. The 2008 Act amended the 1990 Act to insert a regulation-making power to enable techniques, which were under development at that time, to be used in treatment to prevent a child being born with serious mitochondrial disease. In 2010, the Wellcome Trust Centre for Mitochondrial Research at Newcastle University approached the Department of Health and asked to make the Regulations, as it felt its research had progressed to a point that treatment would shortly be ready to introduce. Researchers have recently estimated that 10-20 families per year might be helped initially by mitochondrial donation treatment, rising up to around 80 families, once the techniques are well established.

Mitochondrial donation techniques

7.3. Two techniques were proposed for use to prevent the transmission of serious mitochondrial disease from a mother to her child. Both techniques involve replacing unhealthy mitochondria with healthy donated mitochondria, but do not involve alteration of the nuclear DNA of the patient's egg or embryo:

- **Maternal spindle transfer (MST)**. The "maternal spindle" is the group of maternal chromosomes within an egg, which contain nuclear DNA and are shaped in a spindle. MST involves removing the spindle from the mother's egg before it is fertilised by the father's sperm. The spindle is then placed into a donor egg with healthy mitochondria (from which the donor's spindle, and therefore her nuclear material, has been removed).
- **Pro-nuclear transfer (PNT)**. The pro-nucleus is the nucleus of a sperm or an egg cell during the process of fertilisation after the sperm enters the egg, but before they fuse. PNT involves removing the pro-nuclei (nuclear material) from a newly fertilised egg that has unhealthy mitochondria. The pro-nuclei are then transferred into a donated embryo, with healthy mitochondria, that has had its own, original pro-nuclei removed.

7.4. In 2011, the Department of Health asked the UK national regulator for fertility services and human embryo research, the Human Fertilisation and Embryology Authority (HFEA), to convene an Expert Panel to review the science in this area, in order to assess the safety and efficacy of the MST and PNT techniques. The Panel has since carried out three such reviews, reporting in April 2011, March 2013 and June 2014. It has found that both MST and PNT techniques would be effective in preventing the transmission of serious mitochondrial disorders between mother and child. The panel has found no evidence to indicate either technique would be unsafe. In its June 2014 report, the Panel was of the view that research has progressed well since its previous two reviews, although it recommended that some further experiments were necessary before clinical treatment should be offered. In October, the HFEA published its *`introductory briefing note'*, which is a lay summary of the Expert Panel's reports and recommendations. This contained a number of useful clarifications in how the Panel's advice is framed to assist in understanding the relative nature of risk and safety. The Chair of the Expert Panel, Dr Andy Greenfield, recently said that:

"*In three years study the expert panel has seen no evidence which suggests that these new mitochondrial replacement therapies are unsafe. The scientific direction of travel is clear; and although we have recommended further experiments before treatment should be offered we understand that good progress on these is being made and we expect them to support the conclusions we have reached to date*."

7.5 In the light of this, the Government wishes to introduce these regulations now to give Parliament the opportunity to consider whether the new techniques are safe enough for use in a treatment setting with robust regulation and licencing. There are families waiting to use these techniques in order to have children free from the risk of serious mitochondrial disease.

Mitochondrial donation and licensing

7.6. Part 2 of the Regulations enable eggs and embryos created following the MST and PNT techniques to be "permitted" for used in treatment subject to certain conditions (regulations 4 and 7). This includes the HFEA having given a determination that there is a particular risk that the eggs or embryos of the woman seeking treatment may have mitochondrial abnormalities caused by mitochondrial DNA. The HFEA must also be satisfied that there is a significant risk that a person with those abnormalities will have or develop serious mitochondrial disease (regulations 5 and 8).

7.7 As part of describing the MST and PNT techniques the Regulations refer to the terms "polar body" and "associated organelles". The Department of Health engaged with a number of scientists about the Regulations and understands that these are well understood scientific terms with a clear meaning. Any attempt to further define these terms would involve referring to more complex scientific processes and terminology, which the Department considered would be less clear.

7.8 Regulation 9 ensures that clinics holding existing treatment licences cannot carry out mitochondrial donation without specific approval to do so

from the HFEA. Applications will be considered on a case by case basis and centres licensed to carry out mitochondrial donation will be subject to the HFEA's regulatory regime.

Access to donor information

7.9 Part 3 of the Regulations applies the 1990 and 2008 Acts with modifications to provide for cases where mitochondrial donation has taken place. Unlike full gamete and embryo donation, no nuclear DNA of a mitochondrial donor is inherited by a child born following donation. The general scientific understanding, as endorsed by the HFEA's Expert Panel and the Nuffield Council on Bioethics, is that the impact of mitochondrial DNA is limited to powering the cells of the body and that it does not have any impact on the physical characteristics and personality traits of any resulting child, which come solely from nuclear DNA. For this reason the Department has decided that *identifying* information about donors, which is available to offspring born as a result of full gamete and embryo donation, should not be available to children resulting from mitochondrial donation.

7.10 However, the Department recognises that mitochondrial donor-conceived people may still have a desire for information about their donor, so regulations 11-15 modify sections 31ZA–1ZE of the 1990 Act to enable access to limited, *non-identifying* information. Provision is also made for a mitochondrial donor to access limited, non-identifying, information about children born from their donation. The Regulations modify the 1990 Act to clarify that mitochondrial donors are not related to any children who were, or might have been, born following treatment services using their donation and therefore no provision is made to allow access to information in connection with entering into a marriage, civil partnership or intimate physical relationship, nor to access information about other children who share the same mitochondrial donor.

7.11 Regulation 19 also makes amendments to limit the application of the Human Fertilisation and Embryology Authority (Disclosure of Donor Information) Regulations 2004 so that they do not apply to information requests under the 1990 Act about mitochondrial donations.

Consent and parental orders

7.12 Regulation 16 modifies the consent provisions in Schedule 3 to the 1990 Act to provide that where a person has consented to the use of their egg or embryo in mitochondrial donation such consent cannot be withdrawn once all the nuclear DNA is inserted into the donated egg or embryo. This provides certainty for both the donor and the prospective parents. Further modifications are made by regulation 17 to ensure that for the purposes of the consent provisions in the 1990 Act the resulting egg or embryo is not treated as the egg or embryo of the mitochondrial donor. This ensures that control of the egg or embryo will be with the person/ people who provided the nuclear material for it. Regulation 18 also modifies section 54 of the 2008 Act so that, if mitochondrial donation is used in a surrogacy arrangement, a mitochondrial donor is not able to apply for a parental order in relation to any resulting child on the basis of that donation alone. This reflects the Government's position

that a mitochondrial donor does not have the same status as a full genetic donor.

8. Consultation Outcome

HFEA Public Dialogue & Consultation Exercise

8.1 Between July and December 2012, the HFEA conducted a public dialogue and consultation exercise to ascertain the views of stakeholders and the wider public on the acceptability of allowing mitochondrial donation techniques in clinical practice in the UK[1]. The consultation was wide ranging with a number of strands including workshops and focus groups, as well as an open, web-based, public questionnaire. When the responses to the separate strands of the exercise were taken together, the view was that the techniques should be allowed in treatment, providing their use was carefully regulated.

Nuffield Council on Bioethics Review

8.2 In 2012, the Nuffield Council on Bioethics published `Novel techniques for the prevention of mitochondrial DNA disorders: an ethical review'. The review of the ethical issues raised by these techniques concluded that the techniques would be an ethical treatment option for affected families, provided research shows that treatment is likely to be safe and effective, and families are offered full information and support.

Consultation on draft regulations

8.3. From 27 February to 21 May 2014, the Department of Health consulted on draft regulations that would enable mitochondrial donation techniques to be used in clinical practice[2]. The Department received 1,857 responses. The overwhelming majority of responses (1,541, 83%) did not respond to the consultation questions, they simply expressed a view for or against allowing the use of mitochondrial donation. It was clearly noticeable that responses for and against had been inspired by one of a number of organised campaigns.

8.4. 316 responses (17% of the total response) addressed the consultation questions and the detail of the Regulations. The majority of respondents agreed with the provisions in the draft regulations. On the proposal that only non-identifying information about mitochondrial donors should be made available to any resulting children, respondents were equally divided as to whether this should be non-identifying or identifiable information.

8.5 A full analysis of the consultation responses, *Mitochondrial donation, Government response to the consultation on draft regulation to permit the use of new treatment techniques to prevent the transmission of a serious*

[1] http://www.hfea.gov.uk/6896.html

[2] https://www.gov.uk/government/consultations/serious-mitochondrial-disease-new-techniques-to-prevent-transmission

mitochondrial disease from mother to child is published on the Gov.UK website[3].

9. Guidance

9.1. The HFEA issues guidance for licensed establishments and it is expected that this will cover mitochondrial donation.

10. Impact

10.1. An Impact Assessment is attached to this memorandum and will be published alongside the Explanatory Memorandum on www.legislation.gov.uk.

11. Regulating small businesses

11.1. There are no exceptions for small businesses. As well as an in-depth knowledge of the biology of mitochondrial and DNA disorders, the provision of mitochondrial donation requires that embryologists are highly skilled in egg and embryo manipulation as well as in the provision of IVF treatment services. At this time, only one licensed centre, which is linked to Newcastle University, has the necessary knowledge and skills to provide this service. The number of centres able to offer this service is expected to increase once the clinical use of mitochondrial donation is permitted. At this time, it is unlikely that a small business would have the necessary resources to offer this treatment service.

12. Monitoring and review

12.1. The Department of Health will monitor implementation closely through accountability meetings with the HFEA. This will cover: licence applications, how they have been assessed, inspection and regulation of licensed centres and reports on outcomes, including information on the participation of patients in follow-up research. The HFEA will also be asked to monitor the development of new donation techniques through its horizon scanning mechanism.

13. Contact

Steve Pugh at the Department of Health (Tel: 020 7210 4350 or e-mail: steve.pugh@dh.gsi.gov.uk) can answer any queries regarding the instrument.

[3] Link as at note 3.