Mitochondrial Donation

A 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

Response Form

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Question 1: Regulation 2 defines the removal or insertion of nuclear DNA involved in mitochondrial donation. Do you agree with this definition?

Your Comments:

Neither MST nor PNT involve the 'replacement' or 'donation' of mitochondria. Both processes require a **transfer of the nucleus** of an unfertilised or fertilised egg to another fertilised or unfertilised egg - it is not the mitochondria itself that is transferred from one egg to another. As such, the procedures would be more accurately described as 'nuclear donation' or 'chromosomal transplantation' - not mitochondrial 'replacement'.

The ethical and safety concerns surrounding MST and PNT are such that neither procedure should be permitted in the UK (please see our answers to Questions 3 and 9).

Question 2: Regulations 4 (eggs) and 7 (embryos) only allow mitochondrial donation where all the nuclear DNA is transferred from an egg or embryo to another egg or embryo from which all the nuclear DNA has been removed. Do you agree with this description and restriction?

Your Comments:

As mentioned above, neither MST nor PNT involve the 'donation' or 'replacement' of mitochondria. Both processes require a **transfer of the nucleus** of an unfertilised or fertilised egg to another fertilised or unfertilised egg - it is not the mitochondria itself that is transferred from one egg to another. The procedures would be more accurately described as 'nuclear donation' or 'chromosomal transplantation' - not mitochondrial 'replacement'.

Question 3: Regulations 5 (eggs) and 7 (embryos) require that, in order to agree that mitochondrial donation can go ahead, the HFEA must decide if there is both a particular risk that the egg or embryo of the patient has a mitochondrial abnormality and a significant risk that a person with the particular mitochondrial abnormality will have or develop a serious physical or mental disability, a serious illness or other serious medical condition. Do you agree that the HFEA should have this role?

Your Comments:

Given that many scientists and bioethicists have warned of the serious health risks posed by MST and PNT, including the risk of defects more serious than mitochondrial disease itself, we question how the HFEA can assess whether the risk of developing a 'serious' mitochondrial disorder would be greater than the grave risks posed by the process of mitochondrial donation itself? Our concerns are heightened further by the fact that no definitions of the terms 'significant risk' and 'serious physical disability/illness' have been

provided, therefore enabling a range of conflicting, subjective interpretations to be made.

The US Food and Drug Administration (FDA), which discussed the issue in February, re-iterated the strong international consensus that there was not enough preclinical data in animals or in humans on how the procedure could be performed safely, with members echoing the concerns of many that the proposed interventions would "not treat patients, but instead create new ones."

As such, we strongly disagree with the Government's assertion that "research on mitochondrial donation has advanced to a point where it would be suitable for clinical use" (Regulatory Triage Assessment, page 36). It has not been established that mitochondrial donation is sufficiently safe for clinical trials, and the HFEA itself has recommended that further research be undertaken before proceeding with PNT or MST. **The Government should have waited for the conclusion of these further tests before publishing the Draft Regulations.**

The findings of the macaque report, which formed the basis of the HFEA's recommendations to the Government, do not provide conclusive evidence as to long-term risks of mitochondrial donation since none of the macaques used had been monitored beyond the age of three: "Studies in humans have only tracked health through to the blastocyst stage and in macaques to three years of age. The results from mice and invertebrates suggest that many deleterious effects of MR would not be revealed until adulthood.' *Klaus Reinhardt, Damian K. Dowling, Edward H. Morrow 'Mitochondrial Replacement, Evolution, and the Clinic'*).

We would highlight that the consequences of previous experimentations with heritable germ line modification warn of the serious risks associated with mitochondrial gene replacement: (*see Bredenoord, A., Braude, P., 2011. Ethics of mitochondrial gene replacement: from bench to bedside. Br. Med. J. 342, 87–89.*). We note the adverse consequences for children born as a result of ooplasmic transfer (a similar technique used in the US to help infertile women), which led to the FDA imposing a ban on the technique in 2001.

Additional questions remain to be answered about other potential risks of mitochondrial donation, including the loss of genetic material during transfer; the transfer of small amounts of mtDNA from the affected egg to the donor egg; and a mismatch between foreign mtDNA and nuclear DNA. Widespread concerns have been raised, in particular, about the potential adverse effects of disrupting nuclear-mitochondrial interactions, including the production of 'unhealthy mitochondria and compromised cell function' *(See: St. John, J. C., R. E. Lloyd, et al. (2004). The consequences of nuclear transfer for mammalian foetal development and offspring survival. A mitochondrial DNA perspective. Reproduction 127(6): 631-41. The potential risks of abnormal transmission of mtDNA through assisted reproductive technologies. Reprod Biomed Online 8(1): 34-44).*

It would appear that the purpose of the regulations is to enable a very small number of mothers who discover that they carry genes for mitochondrial disease, to have a child to whom they are genetically linked. This desire, though understandable, does not justify

submitting a child to the enormous health risks involved in the proposed procedure, including the danger of conditions more serious that mitochondrial disorder. Any unintended, adverse consequences, which proponents cannot predict, will be irreversible and pass from generation to generation. Significant investment in this area would be better used in research aimed at treating those who are living with a mitochondrial disease.

Question 4: Do you agree with the principle that centres should not be permitted to undertake mitochondrial donation without first obtaining authorisation to do so from the HFEA ?

Your Comments:

The ethical and safety concerns surrounding MST and PNT are such that neither procedure should be permitted in the UK (please see our answers to Questions 3 and 9).

Question 5: Do you agree that people donating eggs and embryos for the purposes of mitochondrial donation should *not* have the same status as those donating eggs and embryos for use in fertility treatment but rather regarded more like organ or tissue donors?

Your Comments:

We re-iterate that the ethical and safety concerns surrounding MST and PNT are such that neither procedure should be permitted (please see our answers to Questions 3 and 9).

Should the Government press ahead its proposals, we do not agree that the definition of 'parenthood' can be limited to the two chromosome providers. Though mtDNA comprises a very small proportion of total DNA, it would impossible for a child to be created through MST or PNT without an emptied unfertilised or fertilised egg from a donor parent. Both the donor mother and the persons providing nuclear DNA would play a key, albeit different role, in enabling the child to come into existence, and neither contribution should be regarded as insignificant. Furthermore, as with the chromosome providers, the donor mother will be genetically related to the child and will provide identifiable genetic material that will be passed down to future generations. **All three individuals who participate in the creation of the child, and who share a genetic connection with the child, should be regarded as a 'parent'.** Comparisons should not be drawn between mitochondrial donation and organ donation, since the latter does not enable a new human life to be created, but simply helps prolong the life of an existing person.

Introducing a third parent in the life of a child would however lead to complex, legal and social conflicts, and create the potential for lasting emotional damage to both the child and the donor parent. The only justifiable course of action therefore is to abandon these proposals.

Question 6: Regulation 10 provides that the HFEA should tell a person aged 6, on request, if they were born following mitochondrial donation. Do you agree with this?

Your Comments:

The ethical and safety concerns surrounding MST and PNT are such that neither procedure should be permitted in the UK (please see our answers to Questions 3 and 9).

Should the Government press ahead with the proposals, we agree that a person aged 16 or above should be informed, on request, if they were born through mitochondrial donation. We do not agree, however, that the identity of the donor parent should be withheld from the applicant, and it is unclear how such a restriction would be compatible with his or her human rights. As mentioned above, although mtDNA comprises a very small proportion of total DNA, it cannot be denied that any resulting child will inherit genetic material from three adults, and effectively have three, instead of two, biological parents. The donor's genetic connection to the child, and indeed her role in enabling the child to come into existence, should not be minimised or ignored.

A child has the right to know the identity of all its three genetic parents, and the existence of any donor siblings. Children have a natural curiosity about their genetic heritage, and studies have shown that donor offspring commonly experience emotional distress at the lack of information about their donor parent.

Question 7: Regulation 10 also provides that the information that the HFEA should provide in response to such a request should not identify the mitochondrial donor and be limited to screening tests carried out on the donor and about her family medical history, and any other non-identifying information that the donor has provided with the intention that it is made available in these circumstances. Do you agree with this approach?

Your Comments:

As mentioned above, we do not agree that the identity of the donor parent should be withheld from the applicant, and it is unclear how such a restriction would be compatible with his or her human rights. Though mtDNA comprises a very small proportion of total DNA, it cannot be denied that any resulting child would inherit genetic material from three adults, and effectively have three, instead of two, biological parents. The donor's genetic connection to the child, and indeed her role in enabling the child to come into existence, should not be downplayed or ignored.

A child has the right to know the identity of all its three genetic parents, and the existence of any donor siblings. Children have a natural curiosity about their genetic heritage, and studies have shown that donor offspring commonly experience emotional distress at the lack of information about the donor parent.

Question 8: Regulation 13 provides that the HFEA should tell a mitochondrial

donor, on request, when a child has been born from their donation, how many and their sex. Do you agree with this approach?

Your Comments:

The ethical and safety concerns surrounding MST and PNT are such that neither procedure should be permitted in the UK (please see our answers to Questions 3 and 9).

Should the Government press ahead with its proposals, we agree that the second mother should be informed, on request, of the birth of any child to whom she is genetically related.

We do not agree however, that the identity of the child should be withheld from the donor mother. As mentioned above, though mtDNA comprises a very small proportion of total DNA, it would impossible for a child to be created through mitochondrial donation without an emptied unfertilised or fertilised egg from the donor parent. Both the donor mother and the persons providing nuclear DNA would play a key, albeit different, role in enabling the child to come into existence, and neither contribution should be regarded as insignificant. Furthermore, as with the two chromosome providers, the donor mother will be genetically related to the child and provide identifiable genetic material that will be passed down to future generations. **All three individuals who participate in the creation of the life of the child, and who share a genetic connection with the child, should be regarded as a 'parent'.** This would however lead to complex, legal and social conflicts and create the potential for lasting emotional damage to both the child and the donor parent. The only justifiable course therefore is to abandon these contentious proposals.

Question 9: Do you have comments on any other aspect of the draft regulations?

Your Comments:

In addition to the serious health risks emphasised in our response to Question 3, we have particular concerns about the significant ethical and social implications of these proposals:

- If regulatory approval for the proposed technique is given, it will be difficult to prevent further genetic modification of children to 'enhance' other traits such as intellect and appearance. More than 30 members of the Council of Europe Parliamentary Assembly Group recently signed a written Declaration stating that the technique was a eugenic practice that was "incompatible with international law and human dignity". The Declaration referred to the Council of Europe's Convention on Human Rights and Biomedicine, which indicates in Article 13 that "an intervention seeking to modify the human genome may only be undertaken for preventive, diagnostic or therapeutic purposes and **only if its aim is not to introduce any modification in the genome of any descendants**"[1].

[1] http://www.assembly.coe.int/ASP/Doc/XrefViewPDF.asp?FileID=20204&Language=EN

- The routine use of mitochondria donation, and the research needed for MST and PNT, will result in the destruction of thousands of human embryos. IVF procedures are integral to mitochondrial donation, and each application of PNT will necessitate the destruction of at least two human embryos. **All human life is intrinsically valuable, and should be protected from the moment of conception.** The proposal would also contravene the Council of Europe's Convention for the Protection of Human Rights and Dignity of the Human Beings with Regard to the Application of Biology and Medicine (ETS - No.164) which expressly says that "the creation of human embryos for research purposes is prohibited" (Article 18).

- As mentioned earlier, any child born through mitochondria replacement will inherit genetic material from three different adults, and effectively have three instead of two biological 'parents' (two mothers and a father). There are widespread concerns about the profound, adverse effects on a child's physiological well-being, including the impact on his or her sense of identity,that could arise from a genetic, parental connection with three, instead of two, individuals. Furthermore, many children who are born from donor gametes express a desire to know more about their full genetic heritage, and express frustration about the lack of information available about their donor parent (please see our answer to Question 5).

- Since the long term effects of mitochondria donation are impossible to predict, the unforeseeable consequences of the technique cannot be established without first experimenting with the procedure on humans, and thus, placing the health and lives of both present and future generations at significant risk.

The ethical and safety concerns surrounding mitochondrial donation are such that no other country in the world has permitted MST or PNT, with several countries, including France and Germany, expressly prohibiting the techniques. Nearly all European countries, except Britain, have signed the Council of Europe Convention on Biomedicine and Human Rights which prohibits human genome modification. **The UK Government should not ignore international best practice, and should abandon these ill-thought through proposals.**