Secondary Legislation Scrutiny Committee
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Dear Chairman,

I have been advised by Parliamentary officials that you are receiving submissions up to today, 6 January 2015, on the draft regulations to permit mitochondrial donation to prevent the transmission of serious mitochondrial disease from mother to child.

On behalf of the Christian Medical Fellowship, the UK's largest faith-based group of health professionals, I would like to take this opportunity to draw the Committee's attention to a number of recent warnings about the lack of evidence of safety and efficacy of the techniques involved, and to new evidence that mitochondria play a more significant role in a person's identity than has been previously thought.

There is a lack of data from species more closely related to humans that it would be wise to complete before proceeding to human clinical trials. What data there is from animals gives rise to further safety concerns. Several pre-clinical safety tests recommended by the HFEA have either been dismissed, or not concluded, published or peer reviewed.[1]

In introducing provision into the Human Fertilisation and Embryology Act 1990 (as amended) for regulations to be passed that will allow techniques which could be used to prevent the transmission of serious mitochondrial disease for a few women, the Government gave assurance that the power to make these regulations would only be considered '*once it was clear that the scientific procedures involved were **effective and safe'***.[2]

By 2014 the HFEA stated that '*no evidence was found to suggest that the techniques would be unsafe in humans'*.[3]

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[1] For example, the HFEA has admitted that: '*Current research using PNT in Macaques has yet to be shown to be successful'* however instead of waiting for evidence of safety and efficacy they have instead concluded that safety tests are no longer required to be carried out on non-human primates. Para 3.6.2. http://www.hfea.gov.uk/docs/Mito-Annex_VIII- science_review_update.pdf_

[2] http://www.hfea.gov.uk/6372.html

[3] http://www.hfea.gov.uk/8807.html, http://www.hfea.gov.uk/docs/2014-10-07_-_Polar_Body_Transfer_Review_-_Final.PDF

However this statement does not take full account of the mixed evidence currently available and neither does it take account of the lack of evidence for safety.

- Professor Evan Snyder, chair of the scientific panel advising the US Food and Drug Administration (FDA) on mitochondrial transfer, concluded in November 2014 that there are too many unresolved safety issues and that it is premature to proceed. Acting chairman of the FDA committee, Daniel Salomon has similarly said: 'I *think it is pretty ridiculous how little data there is to support any of this, and that worries me.'*[4]

- On the only occasion one of the proposed techniques (pronuclear transfer) was attempted in humans in China, it resulted in an abortion, a miscarriage and a stillbirth.'[5]

- Animal studies have yielded variable outcomes including some concerning results. When mitochondrial replacement has been carried out experimentally, it has been shown to alter the metabolism[6] and cognitive ability[7] of mice. In other species it results in male sterility,[8] accelerated ageing[9] and changes the expression of many hundreds of genes.[10]

- Even some who are closely in this research acknowledge that there may be significant incompatibilities, causing abnormalities: 'The *question of whether the manipulations associated with nuclear genome transplantation might induce epigenetic anomalies remains to be resolved'.*[11]

- Dr Paul Knoepfler has strongly warned about the epigenetic harm caused by nuclear

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[4] http://www.nytimes.com/2014/06/29/magazine/the-brave-new-world-of-three-parent-ivf.html?_r=1
[5] Zhang, J. *et al*. Pregnancy derived from human nuclear transfer. *Fertility and Sterility*, **80,** Suppl. 3, S56, (2003) http://www.nature.com/news/2003/031013/full/news031013-4.html
[6] http://europepmc.org/abstract/MED/9546205
[7] http://www.nature.com/ng/journal/v35/n1/full/ng1230.html
[8] http://www.cell.com/current-biology/abstract/S0960-9822(12)01442-X?cc=y, http://www.sciencedirect.com/science/article/pii/S096098221201442X
[9] http://www.ncbi.nlm.nih.gov/pubmed/22863313
[10] http://www.ncbi.nlm.nih.gov/pubmed/21566193
[11] Craven, Murdoch, Herbert, Turnbull et al, Mitochondrial DNA disease: new options for prevention. Hum Mol Genet. Oct 15 2011; 20(R2): R168–R174. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3179382/

transfer,[12] Reinhardt et al found evidence of mito-nuclear mismatch[13] while Burgstaller et al conclude that: '*The dynamics by which mitochondrial DNA (mtDNA) evolves within organisms are still poorly understood'* and they warn of: '*potential complications for therapies in human populations'* from the preferential replication of even tiny amounts of carry over of mutated mtDNA.[14]

- Dr Paul Knoepfler also warns that: '*The UK and the specific leaders making this decision, should they rush forward on this, could well find themselves on the wrong side of history on this one with horrible consequences*.'[15] Indeed: '*there is an equal or arguably greater chance that it will tragically produce very ill or deceased babies*.'[16]

Since the interactions between the mitochondrial genome and the nuclear genome are so poorly understood still, it is premature to proceed with human mitochondrial transfer, particularly in view of the fact that this would introduce unknown, irreversible and transmissible changes to the human genetic code down generations. It seems particularly ironic that trying to create genetically related children free of mitochondrial disease for a few women (10 or so at year[17]) will put their own daughters, and granddaughters, at risk and in need of embryo screening. [18]

Advocates of these techniques can tend to downplay the relevance of the mitochondria in the individual's genetic make-up, yet we can all agree that there will be three adults with whom a baby shares a parental genetic connection, even apparently minor.

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[12] http://www.ipscell.com/2012/12/my-concerns-about-nature-paper-on-genome-transfer-for-mitochondrial-disease/

[13] http://www.hfea.gov.uk/8178.html

[14] http://www.cell.com/cell-reports/abstract/S2211-1247%2814%2900395-7?_returnURL=http%3A%2F%2Flinkinghub.elsevier.com%2Fretrieve%2Fpii%2FS2211124714003957%3Fshowall%3Dtrue

[15] http://www.ipscell.com/2014/11/open-letter-to-uk-parliament-avoid-historic-mistake-on-rushing-human-genetic-modification/

[16] http://www.ipscell.com/2014/11/open-letter-to-uk-parliament-avoid-historic-mistake-on-rushing-human-genetic-modification/

[17] House of Lords Answers to Written Parliamentary Questions, Hansard. 6th May 2014.

[18] As a result of these unknown long-term health and safety concerns, the HFEA recommends that: 'Until *knowledge has built up that says otherwise, the panel recommends that any female born following MST or PNT should be advised, when old enough, that she may herself be at risk of having a child with a significant level of mutant mtDNA, putting this child or (if a female) subsequent generations at risk of mitochondrial disease. Thus, we recommend that any female born following MST or PST is advised that, should she wish to have children of her own, that her oocytes or early embryos are analysed by PGD in order to select for embryos free of abnormal mtDNA'.*
http://www.hfea.gov.uk/docs/Mito-Annex_VIII- science_review_update.pdf

However Bayliss presents evidence that the contribution of the mtDNA is important in shaping a person's narrative and determining who a person will be.[19] The Committee will also no doubt be aware that the New Scientist recently revised its position on mitochondrial donation, suggesting the role of mtDNA may have been underestimated: *'Recent research suggests that they play a key role in some of the most important features of human life. This raises the ethically troubling prospect ... that children conceived in this way will inherit vital traits from three parents.'* [20]

A child has the right to identify and know who his/her three genetic parents are. Denying such knowledge may not be compliant with their human rights. This is already a right granted to children who are adopted so would create a situation where children resulting from three parent embryos techniques are being discriminated against.

Lastly, we note that over 60 countries specifically prohibit human germline engineering because of its profound social, ethical and unpredictable safety consequences for future generations. A statement by the Council of Europe warns that the creation of children with genetic material from more than two progenitor persons is incompatible with human dignity and international law. [21]

We therefore strongly recommend that Government wait until these techniques have passed more safety tests, in order to ensure these techniques do not cause more harm than benefit, before legislation is passed.

Yours faithfully,

Philippa Taylor

The Christian Medical Fellowship

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[19] Baylis F. The ethics of creating children with three genetic parents. *Reproductive BioMedicine Online* 2013;26:531-534.

[20] *Three-parent babies: It's more messy than we thought,* New Scientist, 18 September 2014 http://www.newscientist.com/article/mg22329871.600-threeparent-babies-its-more-messy-than-we-thought.html#.VDVfJWd0zcs

[21] http://www.bionews.org.uk/page_352766.asp