"Not Unsafe" Does Not Equal Safe
An Evaluation of the HFEA's report on MST and PNT

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I. Introduction

On June 3, 2014, the United Kingdom's Human Fertility and Embryo Authority (HFEA) prepared an update report which was the third scientific review on the safety and efficacy of the potential techniques to prevent the transmission of mitochondrial disease from mother to child. The HFEA proposed two techniques to avoid the inheritance of mitochondrial disease: Maternal Spindle Transfer (MST) and Pro-nuclear Transfer (PNT). The UK Department of Health, part of the government, used the HFEA's update report and the consultation it released in February 2014 to understand the public's views of MST/PNT to present the methods to the UK Parliament. The Parliament can legalize MST/PNT in the UK by amending the current legislation which prohibits altering human eggs, known as the Human Fertilization and Embryology (HFE) Act (1990). The HFEA in the update report, after reviewing new developments with MST/PNT, concluded that there is no evidence to "suggest that these techniques are unsafe".[1] Despite this claim, significant shortcomings with the techniques and unresolved ethical concerns demonstrate that MST/PNT are not currently safe enough or ethically acceptable to be legalized and used in clinical practice.

II. Safety of MST and PNT

[1] "Third scientific review of the safety and efficacy of methods to avoid mitochondrial disease through assisted conception: 2014 Update", Human Fertilisation and Embryology Authority (HFEA) June 2014, http://www.hfea.gov.uk/docs/Third_Mitochondrial_replacement_scientific_review.pdf , 4.

MST and PNT would be used to prevent children from inheriting unhealthy mitochondria from their mothers which cause mitochondrial disease, rather than treating people who already have the disease. Although these techniques are often called "mitochondrial replacement", this term is misleading, as instead of replacing mitochondria, MST and PNT involve removing the nucleus from the egg or embryo of the woman with the mitochondrial disease and placing it into a donor egg or embryo with healthy mitochondria. MST involves removing the spindle from the nucleus of the mother's egg and transferring it to the donor egg, while PNT involves removing the pro-nuclei from a fertilized egg and transferring it to the donor embryo.[2] In the June 2014 report, the HFEA describes the new evidence regarding MST and PNT and assesses how safe and reliable these methods currently are. In their analysis, the HFEA concluded that the new evidence shows considerable progress with MST/PNT and that they are not unsafe and better than the alternatives, such as PGD. A close evaluation of their findings shows, however, that contrary to the HFEA's conclusion, MST/PNT may not be worth the risk given the growing evidence and concerns about their safety and reliability.

A) PGD: A Safer Alternative?

In assessing the value of MST and PNT, the update report first considered the value of pre-implantation genetic diagnosis (PGD) as an alternative to mitochondrial donation. PGD is a screening method that would allow parents to be able to have a genetically related child without the abnormal mitochondria which would cause mitochondrial disease. The procedure would first require in-vitro fertilization (IVF) to produce the embryos that will be tested. Once the embryos are produced, a single cell is removed from each embryo and is then used for genetic testing to

[2] *Mitochondrial Donation*, Health Science and Bioethics Department, Department of Health, 27 Feb. 2014, https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/285251/mitochondrial_donation_consultation_document_24_02_14_Accessible_V0.4.pdf>, 5.

determine which ones have and do not have abnormal mitochondria. After each embryo is tested, the ones with no mitochondrial DNA mutations or those with the lowest amounts are implanted in the mother's womb.[3]

As the HFEA reviewed the efficacy of PGD in avoiding the transmission of abnormal mitochondrial DNA, it said that PGD can reduce but not eliminate the chances of children being born with mitochondrial disease. In the update report, the HFEA noted that one of the faults of PGD is that it is not effective in cases where there is a high level of heteroplasmy (high ratio of abnormal mitochondrial DNA) or when the mother has highly homoplasmic (identical) abnormal mitochondria.[4] The HFEA expert panel also stated that girls born from PGD may still be at risk of having affected children because abnormal mitochondria might still be present in their eggs, since PGD involves choosing embryos with either no abnormal mitochondria or the ones with the lowest amount. Based on these weaknesses of PGD, the HFEA claimed that MST and PNT would be preferable because they would have a higher chance of preventing the transmission of the disease in the child and subsequent generations as well.

Flaws with the HFEA's reasoning and analysis on the relative effectiveness of PGD show that it may actually be a more reliable option than MST/PNT. The first issue is that the number of people that PGD would not be useful for is very small. For example, the cases where PGD is not suitable, which the HFEA identified are when the mother has high levels of heteroplasmy or homoplasmy, are only about 20% of the approximately 3,500 women in the UK with abnormal mitochondrial DNA.[5] This means that PGD would be useful for at least 80%, or 2,800, of the

[3] "Third scientific review of the safety and efficacy of methods to avoid mitochondrial disease through assisted conception: 2014 Update", Human Fertilisation and Embryology Authority (HFEA) June 2014, http://www.hfea.gov.uk/docs/Third_Mitochondrial_replacement_scientific_review.pdf, 12.
[4] Ibid.
[5] Sara Barber, "Mitochondrial Donation", United Kingdom: House of Commons, Science and Environment, 31 March 2014, PDF, 4.

women wanting to having genetically related children without passing on mutated mitochondria. The fact that PGD is effective in 80% of cases shows that if the technique were to be improved, it could be used to detect abnormal mitochondria when there are high levels of heteroplasmy or homoplasmy and thus become even more efficient and reliable.

The other defect with PGD that the HFEA mentioned was that girls born from it might be at risk of having affected children. Although this is true since PGD would involve implanting the embryos with either none or the least amount of mutated mitochondrial DNA, MST/PNT would result in girls with the same risk. During MST/PNT, because the nucleus of the mother with the unhealthy mitochondria is enclosed in the karyoplast which contains part of the cytoplasm, some of the mutated mitochondrial DNA might carry over.[6] Consequently, MST/PNT can also lead to girls born from these methods at risk of passing the disease to their children. Even though PGD and MST/PNT have the same shortcoming, PGD can be seen as the better option because it is safer. Unlike MST/PNT, PGD has been successfully used to produce children without maternally inherited diseases since 1989.[7] Also, since PGD does not involve manipulating human eggs and embryos as MST/PNT do, it has far fewer risks associated with it. PGD can thus be viewed as a preferable alternative to MST/PNT because it is safer and more reliable, and if it is improved, it may be able to prevent the inheritance of mitochondrial disease for almost all cases.

B) Experiments with Animals and Results

MST and PNT have been tested for their safety and efficacy through animal experiments involving Rhesus Macaque monkeys, mice, and Drosophila (fruit flies). In the update report, the

[6] "Third scientific review of the safety and efficacy of methods to avoid mitochondrial disease through assisted conception: 2014 Update", Human Fertilisation and Embryology Authority (HFEA) June 2014, http://www.hfea.gov.uk/docs/Third_Mitochondrial_replacement_scientific_review.pdf, 24.
[7] Molina B. Dayal, "Preimplantation Genetic Diagnosis", *Preimplantation Genetic Diagnosis*, 4 November 2013, http://emedicine.medscape.com/article/273415-overview.

HFEA outlined the progress and results of animal experiments using MST/PNT over the past few years. For example, when MST was used with the Macaque monkeys, the HFEA reported that the four male monkeys that were born using MST and are now five years old (adulthood) do not have any abnormalities currently.[8] Based on the follow-up, the HFEA concluded that MST was successful with the Macaque monkeys. However, when PNT failed with the Macaque monkeys, the HFEA stated in 2013 that it was no longer necessary to conduct MST/PNT with non-human primates because the eggs and embryos of monkeys and humans are too different.[9] With regards to mice studies, the HFEA noted in the 2011 report that only one experiment used a mouse with mutated mitochondria and the researchers were able to perform PNT with it.[10] Other studies used substrains from mice with different mitochondrial DNA haplotypes. The HFEA also stated that even though additional mice experiments with different types of mitochondrial DNA mutations can be carried out, they can be criticized for not representing what would happen with humans.[11] In 2014, one of the members of the HFEA's expert panel, Dr. Edward Morrow, outlined the 2011 study which used about 160 fruit flies and found that the type of mitochondrial DNA can impact nuclear gene expression in males, making them infertile.[12] Dr. Murrow then argued that the fruit fly experiments are irrelevant to humans because genetic diversity is too low in humans to cause the same kind of results.

Contrary to what the HFEA said about the implications of the animal experiments on MST/PNT, the results actually demonstrate how unsafe these techniques might be. With the experiments using Macaque monkeys, the HFEA's reasons for why those studies would not

[8] "Third scientific review of the safety and efficacy of methods to avoid mitochondrial disease through assisted conception: 2014 Update", Human Fertilisation and Embryology Authority (HFEA) June 2014, http://www.hfea.gov.uk/docs/Third_Mitochondrial_replacement_scientific_review.pdf, 18.
[9] Ibid., 22.
[10] Ibid., 17.
[11] Ibid., 21.
[12] Ibid., 17.

reflect what would occur with humans remain unclear and insufficient. Instead, the fact that the HFEA dismissed the monkey experiments after the failure of PNT shows that it may have been more so a refusal to acknowledge the potential risks associated with PNT, as there is no evidence to show that the same failure could not occur with human embryos. Furthermore, the HFEA's initial conviction that MST is efficient based on the follow-ups with four male monkeys that are five years old is also unconvincing, as these results do not show possible long-term harmful side effects MST might have.

The HFEA's update report also does not accurately present the flaws and worries with the mice studies. For example, the one mouse study with abnormal mitochondria conducted in 1993 showed that PNT used with the two strains resulted in impaired growth and less expression of liver-specific proteins, however, the same experiment conducted in 2009 did not result in these defects.[13] While the HFEA claims that differences in the methods may have caused the variance in results, one study contradicting the other is not sufficient to show that MST/PNT would not have harmful results with certain genetic strains. The Human Genetics Alert organization in the UK also expressed concerns with this, as they argued that the varied results of mice studies show that the efficacy of MST/PNT depended on the genetic background of the mice, implying that MST/PNT might also not be equally safe for all human beings.[14]

With the Drosophila studies, Dr. Morrow's assessment that the results are irrelevant to humans due to the differences between humans and fruit flies is similar to the HFEA dismissing the Macaque monkeys because of the failure of PNT. However, the resulting sterility in the male fruit flies and the growing indication that mitochondrial DNA and nuclear DNA have important

[13] Ibid., 17.
[14] *Human Genetics Alert Submission to HFEA Update on Safety of MST/PNT January 2013*, Human Genetics Alert, <hhttp://www.biopoliticaltimes.org/downloads/HGA%20submission%20to%20HFEA%20update%20on%20safety%20of%20MST%20and%20PNT.pdf>, 2.

interactions cannot be ignored simply because of the differences between fruit flies and humans. Instead, this should be taken seriously, since there is no evidence to show that these same results cannot occur with humans. While the results of the mice and fruit flies studies are alarming, there is also a significant lack of long-term experiments with different animals using MST/PNT. The amount of research and experimentation usually performed to test new scientific procedures in the past demonstrate why the animal studies conducted so far with MST/PNT are not enough to accurately determine their safety. For example, before IVF was first used with humans, a variety of extensive studies with IVF were conducted with animals including hamsters, rabbits, rats, and mice throughout the 1950s, 60s, and 70s.[15] The U.S. Food and Drug Administration (FDA) also identified in their safety hearings regarding MST/PNT that more studies with different kinds of animals are needed before these techniques can be used with humans, as they said that "the full spectrum of risks…has yet to be identified".[16] Thus, contrary to the HFEA's conclusions, the results of the animal experiments as well as the lack of long-term studies with different animals actually demonstrate how unsafe and unreliable MST/PNT currently are, as the experiments that have been conducted so far are unsettling and insufficient to prove MST/PNT ready for humans.

C) Experiments with Human Zygotes and Results

According to the update report, a limited number of experiments using human eggs and embryos have been conducted. The HFEA reported that in 2013, MST was carried out on sixty-five human eggs with thirty-three additional eggs as controls. The HFEA reported that 53% of

[15] "Black-footed Kittens Born through IVF", Understanding Animal Research, 17 March 2011, http://www.understandinganimalresearch.org.uk/news/2011/03/black-footed-kittens-born-through-ivf/.

[16] Cellular, Tissue, and Gene Therapies Advisory Committee, "Oocyte Modification in Assisted Reproduction for the Prevention of Transmission of Mitochondrial Disease or Treatment of Infertility", FDA Briefing Document, 25-26 February 2014, http://www.fda.gov/downloads/advisorycommittees/committeesmeetingmaterials/bloodvaccinesandotherbiologics/cellulartissueandgenetherapiesadvisorycommittee/ucm385461.pdf.

the eggs displayed abnormal fertilization, but the remaining embryos developed to blastocysts.[17] A second study, also done in 2013, used MST with human eggs which were artificially activated instead of fertilized, to specifically see how much mitochondrial DNA is carried over and found that it was largely less than 1%.[18] According to the HFEA, less than 5% of carry-over mutated mitochondrial DNA would not lead to the disease reoccurring.[19] With PNT, the HFEA reported that the University of Newcastle Group used normally fertilized human zygotes, and their studies revealed the importance of timing and the two zygotes being at the same stage. The HFEA stated that these details are important but difficult to achieve if using PNT in clinical practice, since the eggs would need to be fertilized immediately after they are collected and then PNT would need to be carried out right away.[20] The HFEA also reported that the Newcastle Group's studies with PNT and normally fertilized eggs show less than 2% of carry-over mitochondrial DNA and that they are currently working on using MST with human eggs as well.[21] Based on these studies, the HFEA concluded that considerable progress has been made and suggested further experiments to ensure the safety and efficiency of MST and PNT.

The limited number of experiments with human eggs and embryos and the lack of studies with eggs from women with abnormal mitochondria refute the HFEA's claims and leave various unanswered questions. For example, in the 2013 study that involved sixty-five human eggs, the fact that less than half of the eggs developed to blastocysts is not sufficient to show that MST is reliable. Similarly, the fact that they developed to blastocysts is not enough to demonstrate that MST would not impair the embryos as they develop further and grow older. According to an

[17] "Third scientific review of the safety and efficacy of methods to avoid mitochondrial disease through assisted conception: 2014 Update", Human Fertilisation and Embryology Authority (HFEA) June 2014, http://www.hfea.gov.uk/docs/Third_Mitochondrial_replacement_scientific_review.pdf, 18.
[18] Ibid., 19.
[19] Ibid., 25.
[20] Ibid., 20.
[21] Ibid., 20.

article in Nature magazine, their study of the impact of MST on human embryos showed that 52% of the embryos had chromosomal abnormalities.[22] The second study that used artificially activated eggs to see how much mutated mitochondrial DNA would carry over also does not reflect what would happen in clinical practice, as there is no evidence to show that the less than 1% carry-over with artificially activated eggs would also occur with normally fertilized eggs.

The subject of carry-over abnormal mitochondria also raises the question: how can it be ensured in clinical practice that no more than 5% of mutated mitochondrial DNA is carried over during MST/PNT? The same question applies to the HFEA's statement regarding the importance of timing and matching the stages of the two zygotes, as the HFEA mentioned that this would be difficult to achieve in clinical practice, but failed to state how clinics can surpass this obstacle. Ultimately, the greatest weakness with MST/PNT experiments that makes them unreliable for clinical practice is the fact that so far, there have been no experiments using MST or PNT with eggs from women with mitochondrial disease. Until MST/PNT are successfully used with eggs from women with abnormal mitochondrial DNA to create healthy embryos that are observed for generations, there is no evidence to show that these techniques would be safe with actual people.

III. Ethical Concerns

A) Altering the Human Genome

One of the ethical concerns that several scientists and bioethicists have raised is that MST and PNT would alter the human genome because they are types of germ-line modification. The human genome can be defined as the entire genetic information of an individual, including the

[22] "Mitochondrial Transfer (Three-Parent Children)", *Column 164WH: Commons Debates: Daily Hansard - Westminister Hall*, 12 March 2014, http://www.publications.parliament.uk/pa/cm201314/cmhansrd/cm140312/halltext/140312h0002.htm#14031278000002.

DNA in the chromosomes and the mitochondria.[23] MST/PNT would change the human genome because the donor's mitochondrial DNA would alter the genetic ancestry of the child born from MST/PNT and all following generations. Since MST and PNT imply genetic modification, these methods can lead to unforeseeable consequences on subsequent generations. The HFEA and the UK Department of Health (DH) have responded to these concerns by claiming that MST/PNT are not genetic modification because they involve substituting the unhealthy mitochondria with the healthy mitochondria, rather than altering genetic information.[24] Also, while the HFEA and the DH recognize that MST and PNT are techniques of germ-line therapy, they claimed in the consultation report that MST/PNT do not violate the United Nation's prohibition on altering the human genome because they do not regard these methods as harming human dignity.[25]

Experts have criticized the HFEA and the DH's dismissal of the concerns regarding germ-line modification for the purpose of preventing the inheritance of mitochondrial disease. For example, the Council for Responsible Genetics, based in New York, raised questions about what kind of harmful implications MST/PNT may have for the human germ-line and how this may impact future generations. The HFEA and DH's claim that MST and PNT do not constitute genetic modification is also untrue, as although the genes themselves are not being changed, the original genetic makeup of an individual is being altered by replacing the nucleus of the donor with that of the mother. Similarly, their statement that MST/PNT would pose no threat to human dignity is unsupported because the potential for MST/PNT to hurt entire future generations itself compromises human integrity. Recognizing these harmful implications, many nations around the

[23] "Center for Biomolecular Science and Engineering", *What Is the Human Genome?* University of Santa Cruz, last accessed 24 June 2014, http://cbse.soe.ucsc.edu/research/human_genome.
[24] *Mitochondrial Donation*, Health Science and Bioethics Department, Department of Health, 27 Feb. 2014, https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/285251/mitochondrial_donation_consultation_document_24_02_14_Accessible_V0.4.pdf>, 13.
[25] Ibid., 14.

world, such as Australia and Canada, have outlawed germ-line modification. Also, 186 countries had signed UNESCO's Universal Declaration on the Human Genome and Human Rights (1997), prohibiting changes to the human genome that would threaten human dignity.[26] The international community thus views MST/PNT, for their unpredictable and possibly dangerous consequences on future generations, as types of germ-line modification that are currently too risky to pursue.

B) A Child with Three Parents

Another ethical concern with MST/PNT is that it would lead to a child having three parents because he/she would have DNA from three different people: the father, nuclear DNA from the mother, and mitochondrial DNA from the donor. The HFEA and the DH responded to this concern in the consultation report by arguing that the mitochondrial DNA that comes from the donor is too insignificant to allow the donor to be seen as a parent of the child. They claim that since nuclear DNA, which comes from the mother and father, is the primary type of DNA that impacts a person's characteristics and appearance, only the mother and the father would be considered parents of the child.[27] The HFEA and the DH conclude that because mitochondrial DNA would not affect the child's traits, the donor would not be considered the child's parent.

Despite the HFEA and the DH's claims, scientists still believe that MST/PNT may result in a child having three biological parents because of growing evidence regarding the exact role of mitochondrial DNA. According to new research, the HFEA and the DH's statement that the mitochondrial DNA does not impact an individual's traits is inaccurate, as scientists do not have complete knowledge about the exact roles of mitochondria in the cell or the interaction between

[26] "The Universal Declaration on the Human Genome and Human Rights", United Nations Education, Scientific, and Cultural Organization, 11 November 1997, http://portal.unesco.org/en/ev.php-URL_ID=13177&URL_DO =DO_TOPIC&URL_SECTION=201.html.

[27] *Mitochondrial Donation*, Health Science and Bioethics Department, Department of Health, 27 Feb. 2014, https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/285251/mitochondrial_donation_consultation_document_24_02_14_Accessible_V0.4.pdf>, 13.

mitochondrial DNA and nuclear DNA. While mitochondria have traditionally been characterized as the energy providers of the cell, new evidence demonstrates that mitochondrial DNA might play a role in determining the traits of individuals. According to the European Journal of Human Genetics, there is growing evidence that mitochondrial DNA impacts nuclear gene expression, which indicates that it may influence personal traits.[28] Based on this, the interaction between mitochondrial DNA and nuclear DNA is especially important to understand because the donated mitochondria might interact differently with the mother's nuclear DNA, leading to harmful side effects. The lack of knowledge on the specific roles of mitochondrial DNA and their potential influence on individual traits reveals that there is insufficient information to dismiss the concern that MST/PNT may lead to a child having three biological parents, which may lead to destructive medical and/or emotional effects on the child.

C) Slippery Slope

Other ethical and moral issues that surround MST and PNT include that these types of germ-line therapy could lead to a dangerous slippery slope. In the consultation report, the DH and the HFEA did not address the slippery slope neither in the section on ethical concerns nor in the draft regulations. Various experts have argued that MST/PNT can lead to immoral utilization of such technologies, including possibilities for genetic engineering in humans and the creation of "designer" babies.[29] This concern is particularly true with MST/PNT, as the HFEA indicated in the update report that certain mutations of mitochondrial DNA interacting with nuclear DNA

[28] Martin P. Horan et al., "From Evolutionary Bystander to Master Manipulator: The Emerging Roles for the Mitochondrial Genome as a Modulator of Nuclear Gene Expression", Nature Publishing Group, 24 Apr. 2013, http://www.nature.com/ejhg/journal/v21/n12/full/ejhg201375a.html.
[29] Marcy Darnovsky et al., "CGS : Is the UK Being Too Hasty Over Three-Parent Babies?" *Center for Genetics and Society*, 3 June 2014, http://www.geneticsandsociety.org/article.php?id=7797.

could lead to some type of "selectable advantage".[30] Although this may be avoided by matching the mitochondrial DNA haplotypes of the donor and the mother, it shows how MST/PNT have the potential to make the slippery slope a reality if proper precautions are not taken, which the HFEA admits clinics may not be able to achieve. Scientists worry that MST and PNT may bring about a renewed form of eugenics which would cause human society to be divided by genetic inequalities. For the slippery slope argument to not become a reality, proper regulations and laws must be enforced, which, as explored further below, are significantly lacking in the HFEA's draft regulations included in the consultation report.

IV. The Parliamentary Process

A) Legalizing MST/PNT in the UK

The legalization of MST/PNT in the UK is currently being debated in the UK Parliament and is dependent on the Parliamentary vote for approval. In the UK, the Human Fertilization and Embryology (HFE) Act of 1990, which was amended in 2008 to allow the Parliament to permit MST/PNT in the future, prohibits implanting an egg or embryo in a woman if the mitochondrial or nuclear DNA has been changed. Based on this power, the DH included a Regulatory Triage Assessment (RTA) in the consultation report, which held that the HFE Act should be amended by expanding the definition of "permitted eggs and embryos" to include eggs and embryos that have gone through MST/PNT.[31] The DH has presented this subject as well as the HFEA's draft regulations for the Parliament to debate. Also, the UK Secretary of State for Health, Jane Ellison,

[30] "Third scientific review of the safety and efficacy of methods to avoid mitochondrial disease through assisted conception: 2014 Update", Human Fertilisation and Embryology Authority (HFEA) June 2014, http://www.hfea.gov.uk/docs/Third_Mitochondrial_replacement_scientific_review.pdf, 33.
[31] *Mitochondrial Donation*, Health Science and Bioethics Department, Department of Health, 27 Feb. 2014, https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/285251/mitochondrial_donation_consultation_document_24_02_14_Accessible_V0.4.pdf>, 36.

confirmed that the regulations will go through the regular affirmative parliamentary procedure to change the law, which includes having a full debate in the House of Commons on the issue.[32]

B) Parliamentary Debate in the House of Commons

A debate on the subject of MST/PNT took place in the House of Commons, consisting of elected Members of Parliament (MP) who consider and discuss new laws. The debate took place on March 12, 2014, and included discussion on the safety, ethical concerns, and draft regulations regarding MST/PNT. Two of the MPs who led the debate, Jacob Rees-Mogg and Robert Flello, expressed their opposition to MST/PNT as they mentioned the various safety and moral issues the UK public would face. For example, Jacob Rees-Mogg argued that MST/PNT "ends up being a multi-generational experiment with the lives of people" and that "in a country nervous about genetically modified crops we are making the foolhardy move to genetically modified babies".[33] Robert Flello agreed with Rees-Mogg's concerns as he said that "there is a Pandora's box of problems" with MST/PNT, specifically speaking about the unpredictable consequences these methods could have.[34]

Flello and Rees-Mogg also criticized the science and studies, as they recognized that the results of the animal experiments revealed flaws of MST/PNT and that current research does not show what harmful long-term effects there might be. From a moral and legal perspective, the ministers further worried about the impact of having three genetic parents on the child and the potential of MST/PNT to lead to a renewed form of eugenics. Jane Ellison, the Secretary of State for Health, argued against Flello and Rees-Mogg with the same science and reasoning detailed in

[32] "Mitochondrial Transfer (Three-Parent Children)", *Column 164WH: Commons Debates: Daily Hansard - Westminister Hall*, 12 March 2014, http://www.publications.parliament.uk/pa/cm201314/cmhansrd/cm140312/halltext/140312h0002.htm#14031278000002.
[33] Ibid.
[34] Ibid.

the consultation and update reports.[35] By doing so, her comments did not add anything new or substantial to show MST/PNT as safe or ethically acceptable techniques. While further in-house debates will be conducted for MST/PNT as the House of Commons contemplates this, the March 2014 debate reveals that there is fervent opposition to legalizing MST/PNT within Parliament.

IV. Looking Forward: Problems with the Regulatory Framework

A) The Draft Regulations

The HFEA prepared draft regulations and included them in the consultation report which represent the type of regulations that Parliament would be voting on, which include provisions for what would be considered "permitted" eggs and embryos for MST/PNT. The HFEA held that the eggs and embryos that would be permitted include those that are at severe risk of developing mitochondrial disease.[36] Likewise, the HFEA outlined that the donor information would be kept anonymous and information would only be given if there was a mutual desire for the donor and family to meet.[37] The HFEA also stated in the draft regulations that even after Parliament would legalize mitochondrial donation, clinics would still need approval and licensing from the HFEA before applying the methods.[38] Furthermore, the HFEA strongly recommended that follow-ups be conducted with children born using MST/ PNT to monitor any side effects.[39]

B) Problems with the Draft Regulations

The HFEA's regulatory framework and guidelines did not address a number of remaining questions. For instance, what would be the criteria that clinics will be assessed for to be approved by the HFEA? Also, given the current necessity for further research on MST and PNT, what kind

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[35] Ibid.
[36] *Mitochondrial Donation*, Health Science and Bioethics Department, Department of Health, 27 Feb. 2014, https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/285251/mitochondrial_donation_consultation_document_24_02_14_Accessible_V0.4.pdf, 30.
[37] Ibid., 34.
[38] Ibid., 31.
[39] Ibid., 24.

of human trials would be allowed, and on what scale? Will there be a period of waiting between the Parliament approving mitochondrial donation and the techniques being used clinically? Other points in their guidelines are also flawed, such as their recommendation for follow-ups. How will these follow-ups be authorized and enforced? Will all of the families that try MST and PNT for the first few years be required to have follow-up medical visits, and is it ethically permissible to use the first few patients as guinea pigs?

The HFEA's draft regulations about not revealing donor information are also concerning. Who will enforce this rule and how? Is it ethically righteous to keep the donor anonymous even with growing evidence that children born from MST/PNT have three genetic parents? An even larger issue that the DH and the HFEA completely ignored in the draft regulations is the slippery slope argument. The HFEA did not include any regulations on how to prevent the slippery slope argument from becoming a reality. How will these methods be controlled and regulated so that they are used only for preventing the transmission of mitochondrial disease? Who will enforce such regulation, and what specific laws will be in place so that it is clear to every fertility clinic that may attempt to use the technology for genetic enhancement? The HFEA did not address any of these regulatory issues and instead simply expressed the need for regulation without outlining any specific rules that should be enforced.

V. Conclusion

The safety issues and ethical concerns with mitochondrial donation that are currently unresolved show that MST and PNT are unfit to be approved and legalized for clinical practice. Although the HFEA concluded in the update report that considerable progress was achieved with MST and PNT, ongoing safety concerns about the potential harmful side effects these techniques may have on the child and subsequent generations demonstrate that they are not safe enough to

be legalized. If approved, MST/PNT are projected to be used with about ten to twenty families in the UK each year, but harmful consequences of these methods could impair entire generations.[40] At the same time, other options such as adoption, egg donation, and PGD are comparatively safe and reliable alternatives to mitochondrial donation and are readily available to people wanting to have children without transmitting mitochondrial disease. The risks, ethical concerns, and lack of proper regulations show that it would be premature for mitochondrial donation to be legalized at this time. The ongoing efforts of scientists and researchers to understand MST/PNT show that the HFEA proclaiming that MST/PNT are not unsafe does not mean that they are safe, and until they are proven to be safe, it would be too large of a medical and ethical risk to take at this time.

[40] *Mitochondrial Donation*, Health Science and Bioethics Department, Department of Health, 27 Feb. 2014, https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/285251/mitochondrial_donation_consultation_document_24_02_14_Accessible_V0.4.pdf, 45.