Today the UK government announced that its House of Commons will vote this coming Tuesday 3 February on whether to approve regulations legalizing controversial germline modification techniques known as "mitochondrial donation" or "3-person IVF."

In response, the Center for Genetics and Society has released the following open letter to all UK Members of Parliament.

CGS Executive Director Marcy Darnovsky adds, "Allowing a form of human inheritable genetic modification will put the UK at odds with every other country that has ever considered it, as well as multiple international human rights treaties. Advocates say that approving these techniques will make the UK a scientific pioneer. In fact, it risks becoming a pariah."

For more information on mitochondrial manipulation or "3-person IVF" techniques, please see our resource page .

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Five things to know about "mitochondrial donation" before you cast your vote An open letter to all Members of Parliament

29 January 2015

Dear Members of Parliament,

On Tuesday, 3 February, you will be asked to help decide whether the UK should become the only country in the world to explicitly allow the inheritable genetic modification of humans. Although the proposed goal of the techniques in question – to prevent the transmission of mitochondrial diseases – is noble, the techniques will in fact put women and children at risk for severe complications, divert resources from promising alternatives and treatments, and set a policy precedent that experimentation on future generations is an acceptable biomedical /

fertility development.

Unfortunately, there has been much misinformation about the safety and efficacy of these techniques, and about what is at stake. Here are five critical facts of which you may not be aware.

1. **Mitochondria do a lot more than provide cellular energy**. New data show that due to the production of thousands of special RNAs by mitochondria, which affect the expression of nuclear genes, mitochondrial DNA have direct influence over numerous complex traits (1). They are not simply "batteries," but contribute to determining who we are. The common analogy between replacing defective mitochondria and putting new batteries into a camera obscures this important biological reality, and highlights the fact that the proposed technology poses risks that are poorly understood.

1. **These techniques also pose known risks to any resulting children, and may not be effective** . Scientists around the world have raised many cautions; here we mention several. An expert scientific committee convened by the US Food and Drug Administration in February 2014 concluded that using these techniques based on current evidence would be premature (2). Genetic screening of IVF embryos was acknowledged to be a safer and viable alternative for the vast majority of women who may be candidates for the techniques to have genetically related healthy children (3).

In the UK, the HFEA's final safety review said it was "essential" to conduct experiments on whether even a tiny percentage of mutated mitochondria could be preferentially replicated in embryos produced by these techniques, leading to the very disease the techniques are supposed to prevent (4). A subsequent report in the prestigious journal *Cell* by Burgstaller et al. confirmed that this is in fact common and could lead to serious problems for any resulting child (5). These findings have not been adequately addressed. Furthermore, the transfer of a nucleus from one egg or embryo into another is known to cause so-called epigenetic modifications, which change gene function and could create lasting medical issues (6). And finally, although a study of pronuclear transfer in a non-human primate model was originally required, this was later dropped after an attempt by scientists in the U.S. failed to produce even a single viable embryo (7).

1. **These techniques will put women at risk.** Pregnancy is dangerous for women with serious mitochondrial disease (8); egg retrieval and IVF raise additional concerns (9). Current predictions suggest that women considering this procedure should expect to undergo at least four cycles of painful egg extractions that pose their own medical risks (10).

2. **Under the proposed arrangement, we will not know if these techniques work or are safe** . The vote would not enable a human clinical trial as is being discussed in the U.S., but would permit clinics to begin offering a risky and experimental fertility procedure. The proposed regulations do not require any follow-up of resulting children, or include any plan to deal with unintended consequences (10) .

1. **Assertions of "broad public support" for this proposal are at best based on a selective reading of the evidence** . In fact, the majority of people who responded to the HFEA's open consultation said they oppose changing the law (11, 12). Independent polls found support to be as low as 18% (13).

It is the duty of regulators to reject drugs, devices, and procedures that don't meet safety standards. At this time, it is simply wishful thinking to present these techniques to women as a way to have a healthy child. Rather than subjecting women and any children resulting from these techniques to serious risks, and chipping away at what has been a long-respected international consensus against human germline modification, the UK's innovative scientific minds could strengthen their existing efforts to treat those who are currently suffering from mitochondrial diseases. We appeal to you to consider the points above and to reject these regulations.

Sincere thanks and kind regards,

Marcy Darnovsky, PhD
Executive Director, Center for Genetics and Society

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