July 2015

Re: Regulating mitochondrial donation

We, the organisations listed above, support the translation of research into the clinic to make a difference to people's lives. We welcome evidence-based proportionate regulation which promotes access to, and the uptake of, life changing medical technologies, whilst ensuring the safety and interests of patients and providing a clear framework for clinicians.

Mitochondrial donation has the potential to give families affected by mitochondrial disease a chance of having healthy children, and we therefore welcome the consultation on the regulatory framework to bring this important innovation into the clinic. As much of the consultation is directed at seeking the specific views of clinicians and patients, we have written to comment on those elements most relevant to our expertise.

We welcome the importance placed on long-term follow-up which, as with all new medical innovations, is an essential aspect of assessing and refining mitochondrial donation. Although long-term research is not within the responsibilities of the HFEA, the outcomes of such studies must be of paramount interest to the HFEA. However, clinical and research follow-up are distinct and must be carefully distinguished. Follow-up mechanisms within the remit of the HFEA will be in terms of clinical provisions, for the specific benefit of the child conceived, not in terms of long-term research. We hope and expect that clinics will have considered research follow-up of the child born in order to monitor any possible effects and future generations. Similarly, we hope that the outcomes of mitochondrial donation techniques for the individual, family and society will be similarly considered through long-term research. We would not however advocate research follow-up participation as an obligation of treatment; the research relationship is rightly voluntary.

Appropriate justification for any regulation must be demonstrated and reflect scientific and social evidence, ethical considerations and clinical practice. If not justified, restrictions may lead to unnecessary delays in access to treatment without a corresponding contribution to improving patient safety and welfare. A number of aspects of the mitochondrial donation licensing provisions outlined in the consultation documentation and at the accompanying HFEA workshop appear not to be clearly justified and may be unduly inflexible. As one example, the proposed restrictions on donor age could limit eligible donors. We understand that the scientific basis for such restriction is not compelling; there is not a strong evidence base that age increases the risk of inheriting unhealthy mitochondria. If there are other valid factors behind this reasoning, these must be demonstrated. Where there is a strong justification however, recommendations should clearly reflect this; provisions caveated in terms of "wherever possible" lack clarity, which is unhelpful for clinical practice.

We understand that a proposal moved at the HFEA workshop was that only patients who have undergone pre-implantation genetic diagnosis (PGD) should be eligible for mitochondrial donation. We do not understand the reasoning to justify such a pre-requisite, which could undermine the very purpose of mitochondrial donation techniques; mitochondrial donation has the potential to be used for women whose eggs contain very high levels of, or exclusively, mitochondrial DNA mutation, which are not suitable for PGD. Mitochondrial donation is likely to be a safer option than PGD when levels of mitochondrial DNA mutation are borderline, both for the child born, but particularly for subsequent

generations if the child is female. Mitochondrial donation also avoids the need to make the difficult decision about which embryos to replace during PGD or termination for those considering prenatal testing. In some circumstances PGD might be an option patients wish to consider, but it should not be a pre-requisite.

Regulations for mitochondrial donation should specifically consider the technology being licensed and frameworks for similar technologies should not be applied without appropriate consideration of the unique aspects of mitochondrial donation. For example, the proposal that there should be mitochondrial donor family limits because of concerns regarding genetic relatedness. Although mitochondria donors will ostensibly undergo the same process as gamete donors, namely egg retrieval, the purpose and genetic relatedness is very different. Directly transposing provisions from one technology to another may bring unnecessary restrictions, and could also risk that unique considerations for licensing mitochondrial donation could be overlooked.

We appreciate that ensuring evidence-based proportionate regulation is a challenging balance and would welcome an opportunity to discuss this further with you.