This response was submitted to the call for evidence by the Nuffield Council on Bioethics on *Emerging techniques to prevent inherited mitochondrial disorders: ethical issues* between January 2012 and February 2012. The views expressed are solely those of the respondent(s) and not those of the Council.

Antenatal Results and Choices (ARC)

Mitochondrial transfer

Antenatal Results and Choices (ARC) is the only national charity providing specialized information and support to parents throughout antenatal testing and its consequences. A large proportion of our support work involves parents who are given the difficult news that their unborn baby has an anomaly. We provide ongoing support for as long as is needed whatever decision is made about the future of the pregnancy.

ARC has almost twenty five years' experience in helping parents who make the painful decision to end a wanted pregnancy after a prenatal diagnosis, including those who know they carry a heritable condition, including mitochondrial disorders. We know there are couples who would love to have their own children, but feel unable to pursue this knowing that they risk having an affected child because the prospect of facing termination is not acceptable to them. There is the added difficulty in the context of mitochondrial disorders in that diagnostic testing may deliver uncertain results. PGD can be an option for some but there are those women whose eggs will all contain too much abnormal mitochondria to be usable.

We are pleased to have the opportunity to respond to the consultation on the potential ethical implications of mitochondrial transfer techniques. Being a parent support organization, our comments are informed by the parent perspective rather than from a more abstracted ethical standpoint.

1. Emerging techniques such as PNT and MST involve replacing the mitochondrial genes that a child would have received through natural conception, with mitochondrial genes taken from a healthy donor. Is it acceptable, in this instance, to select genes that will then be inherited by future generations?

ARC firmly believes that the replacement of a small number of mitochondrial genes from a healthy donor that will be inherited is justified. These genes will allow the recipient and their potential offspring to live without life-limiting disorders, a hugely beneficial outcome.

2. *PNT involves removing the two pronuclei from a very early embryo containing a significant level of mutated mitochondria, at the one-cell stage before the genetic material in the pronuclei of the sperm and egg cells merges to form the mature nucleus of the embryo. The pronuclei are transferred into another embryo at the same stage of development, which contains healthy mitochondria and which has had its pronuclei removed. From the two-cell stage of embryonic development onwards, the embryo's cells contain one nucleus combining both parents' DNA. What ethical distinctions can we make between prospective treatments which would: a. transfer pronuclei between embryos? b. transfer the nucleus of a cell between embryos? c. seek to modify the nuclear DNA of an embryo?*

We can see no ethical distinction between the three prospective treatments, as the purpose seeks to allow the birth of a baby who has avoided inheriting a severe disorder.

3. All new techniques pass through research stages before being offered for treatment, but in the early stages of treatment might still be considered experimental. Is it reasonable to use experimental techniques such as these in treatment?

We would highlight IVF techniques again at this point. The early implementation of these techniques and then those involving PGD could be considered in this light and have proved to be of profound benefit. Over three decades of IVF treatment no significant harm has come to light and there is no reason to suspect that mitochondrial transfer will be any different.
4. *After the use of these techniques, children would inherit nuclear DNA (around 25,000 genes) from their parents, and mtDNA (13 genes) from the donor of the egg. What might the use of these*

techniques signify for the relationships of the resulting child to the three adults with whom it shares a genetic connection?

The child will inherit a karyotype (its genetic 'identity') from its two biological parents, which is by far the most important factor. It is of course significant that the 13 genes inherited from the mitochondrial donor means he or she can avoid a severe disorder, but the child's relationship with this person can be likened to someone who might have donated an organ.

5. How might mitochondrial DNA be associated with a person's identity?

The only association we can envisage is that the donated mitochondrial DNA enables an individual to avoid a life with a debilitating disorder.

6. *Could the relationships created between the people involved in these new techniques- particularly between the mitochondrial donor and a person born with their donated mitochondria- be seen as similar to those involved in:*

a. organ or tissue transplantation?
b. gamete donation?
c. a donation of other bodily material?
Or, should these relationships been seen as unique?

Although there are differences in that the genetic material donated will be passed on to future generations, we would say the relationship is closest to (a). The donation results in a positive effect on the child's physical health rather than an impact on their genetic identity or that of their future offspring.

7. Only daughters born as a result of these techniques would be able to pass their mtDNA on to subsequent generations. Would it be reasonable to permit prospective parents using these technologies to also use pre-implantation sex selection (preferring male embryos), if they requested it in order to limit the risks of transmitting any adverse side effects of the techniques to future generations?

Although we cannot pretend to be experts in the science involved, it would seem to be unnecessary to encourage sex selection in this circumstance.

8. *If mitochondrial donation were to be approved for medical treatment in the UK, what government or regulatory policies, and/or professional guidelines would be needed to promote ethically sound practices?*

We do not foresee any particular measures above and beyond the current regulatory framework around reproductive technologies.

9. *If mitochondrial donation were not to be approved for translation from research into medical treatment in the UK, what ethical concerns, if any, would follow?*

We would view it as unethical to prevent use of a treatment that will allow couples to have healthy children who would otherwise be unable to do so. It would be hard to imagine how this might be justified to prospective parents who risk passing on mitochondrial disorders when they see other carriers of genetic conditions who successfully have children through current licensed technologies. It is unimaginable now that the IVF techniques that have resulted in thousands of healthy children might have been prohibited on 'ethical grounds'.

10*. Is it desirable for a record of the donation to be kept and managed by the relevant authorities, and if so, what should be recorded and to whom should this information be made available?*

It would be desirable for records to be kept in order to facilitate follow up of the health of the recipient and their offspring. There doesn't seem to be any compelling reason why the donor should not remain anonymous.