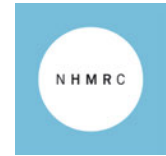




Australian Government
National Health and Medical Research Council



Senate Standing Committees on Community Affairs
Legislation Committee
Department of the Senate
PO Box 6100
Parliament House
CANBERRA ACT 2600

Dear Chair

Inquiry into the Mitochondrial Donation Law Reform (Maeve's Law) Bill 2021

Thank you for the opportunity to make a submission to the Community Affairs Legislation Committee Inquiry into the Mitochondrial Donation Law Reform (Maeve's Law) Bill 2021. I make this submission as the CEO of the National Health and Medical Research Council (NHMRC) and on behalf of the NHMRC Embryo Research Licensing Committee (ERLC) and the Australian Health Ethics Committee (AHEC).

In addition to this submission, I invite the Committee to consider my CEO Statement, [*Should Australia introduce mitochondrial donation?*](#), along with NHMRC's two reports released in June 2020 to inform discussion in Australia about mitochondrial donation:

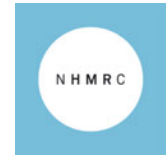
- [*Mitochondrial Donation Community Consultation Report*](#) which provides an overview of the views on the technology across the Australian community
- [*Mitochondrial Donation Expert Working Committee Expert Statement to the NHMRC CEO on the science of mitochondrial donation*](#) which provides an expert consideration of the science of mitochondrial donation.

I am available to attend the Inquiry in person to expand on this submission. If this would be helpful please contact my Executive Assistant, Karen Elliott,

Yours sincerely

Professor Anne Kelso AO
Chief Executive Officer

16 July 2021



Submission to the Community Affairs Legislation Committee Inquiry into the Mitochondrial Donation Law Reform (Maeve's Law) Bill 2021

Introduction

Mitochondrial donation is an assisted reproductive technology that seeks to reduce the risk of a child inheriting mitochondrial disease from a woman carrying the condition. Current Australian legislation prohibits the use of mitochondrial donation in clinical practice, and limits research into mitochondrial donation using human embryos.

In 2018 the Senate Community Affairs Reference Committee conducted the *Inquiry into the science of mitochondrial donation and related matters*. The Australian Government response to the Inquiry Report was tabled on 20 February 2019. The Hon Greg Hunt MP, the Minister for Health and Aged Care, asked the National Health and Medical Research Council (NHMRC) to deliver on the first two recommendations. NHMRC established the Mitochondrial Donation Expert Working Committee to provide expert advice on the science of mitochondrial donation, and invited contributions from the Australian community to a public consultation on the social and ethical considerations. The [Mitochondrial Donation Expert Working Committee Expert Statement to the NHMRC CEO on the science of mitochondrial donation](#) and the [Mitochondrial Donation Community Consultation Report](#) were released in June 2020.

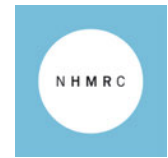
The Mitochondrial Donation Law Reform (Maeve's Law) Bill 2021 proposes to allow mitochondrial donation in Australia. NHMRC has two Principal Committees—the Embryo Research Licensing Committee and the Australian Health Ethics Committee—which would each play an important role in the oversight and implementation of the proposed reforms to introduce mitochondrial donation in Australia.

The science of mitochondrial donation

Mitochondrial disease refers to a group of conditions caused by mutations in either mitochondrial DNA or nuclear DNA. Mitochondrial donation is an assisted reproductive technology (ART) that seeks to reduce the risk of transmitting—from mother to child—mutations in mitochondrial DNA that cause mitochondrial disease. The term collectively refers to a number of techniques which involve the creation of an embryo containing nuclear DNA from a woman (the mother) and a man (the father), and mitochondrial DNA from an egg donated by another woman (the donor). Figure 1 provides a conceptual overview of the main mitochondrial donation techniques.

Different mitochondrial donation techniques involve transferring the nuclear DNA at different stages. One technique, maternal spindle transfer (MST), involves transferring the mother's nuclear DNA to an unfertilised donor egg with the nucleus removed and then fertilising the egg. Another technique, pronuclear transfer (PNT), involves transferring the parents' nuclear DNA from a fertilised egg to a fertilised donor egg with the nucleus removed. There are also other mitochondrial techniques, which differ in the stage of development at which they are carried out and the origin of the nuclear DNA being transferred.

The technology aims to reduce the risk of children inheriting some forms of mitochondrial disease. Mitochondrial donation cannot be used to reduce the risk of



transmitting mitochondrial disease caused by mutations in nuclear DNA. The techniques cannot be used to cure people with existing mitochondrial disease.

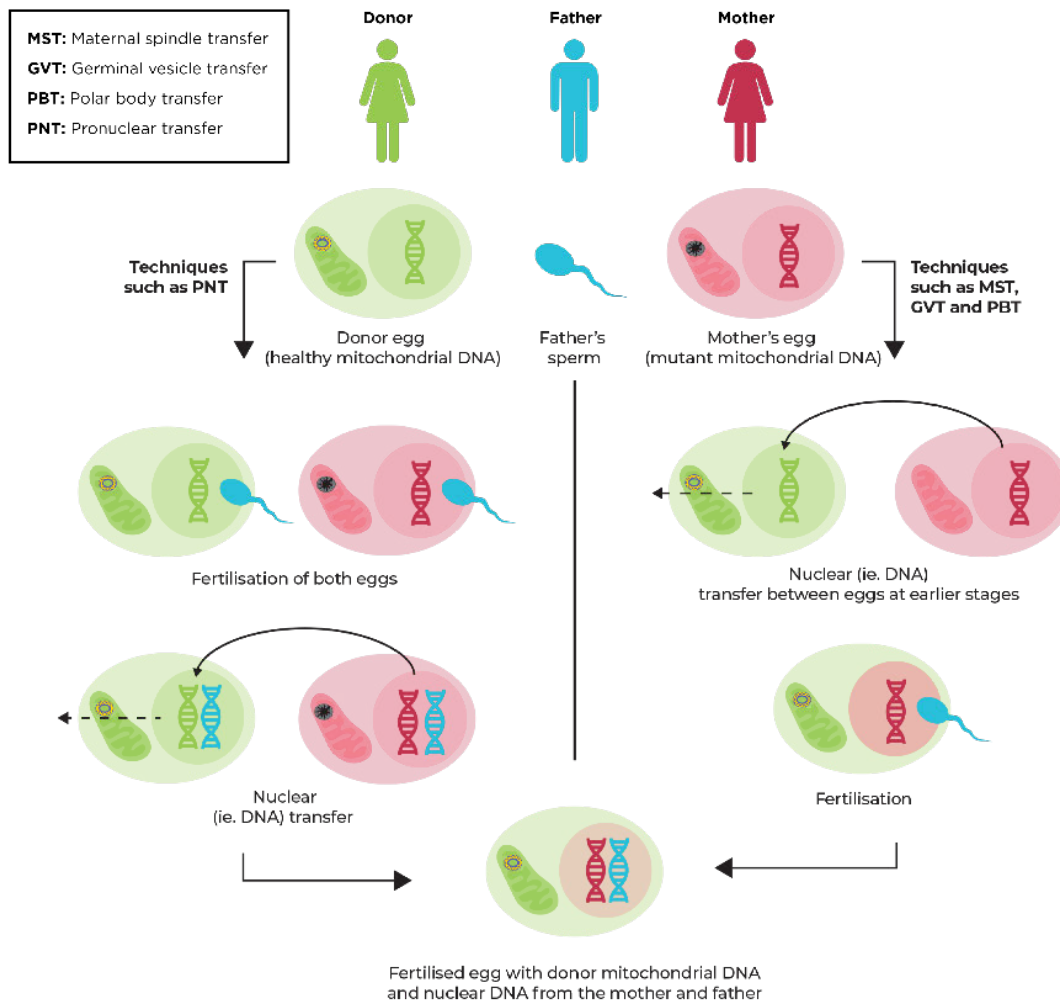


Figure 1: A conceptual overview of the main mitochondrial donation techniques

The conceptual overview of the main mitochondrial donation techniques at Figure 1 shows the contribution of the father (blue), mother (pink) and mitochondrial donor (green). The mitochondria are shown on the left in each cell with a small circle representing the mitochondrial DNA. The nuclear DNA is represented by the double helices on the right in each cell. The pronuclear transfer technique is shown on the left and maternal spindle transfer technique is shown on the right.

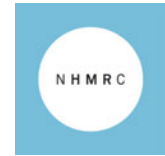
Expert Statement on the science of mitochondrial donation

The [Mitochondrial Donation Expert Working Committee Expert Statement to the NHMRC CEO on the science of mitochondrial donation](#) provided advice on three questions identified in Recommendation 2 of the Senate Community Affairs References Committee's report on the *Inquiry into the science of mitochondrial donation and related matters*. The Expert Statement did not make a recommendation on whether or not mitochondrial donation should be introduced into Australian clinical practice.



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1. Whether mitochondrial donation is distinct from germline genetic modification

The Committee advised that the term “germline genetic modification” has conceptual drawbacks and would not be appropriate for classifying mitochondrial donation.

The Committee advised, however, that it is essential to recognise that mitochondrial donation introduces changes to the genome of the embryo with the potential to be inherited by future generations. These changes would be transmitted through the female line because the mitochondria in the embryo come from the egg, not the sperm. The Committee noted that, while there is scope to prevent the transmission of genetic changes resulting from mitochondrial donation by restricting the clinical procedure to male offspring only, there are ethical, scientific and practical considerations that make this practice problematic.

2. Is there any new information to indicate that research findings from the United Kingdom that the science of mitochondrial donation is safe for introduction into controlled clinical practice, cannot be applied in the Australian context?

The Committee advised that incremental developments have been made on some aspects of the science since the 2016 UK Human Fertilisation and Embryology Authority (HEFA) scientific review. However, there is no significant new evidence about the safety and efficacy of mitochondrial donation since the 2016 HEFA scientific review.

3. Whether other approaches to inheriting mitochondrial disease should also be the focus of Australian research.

The Committee noted that mitochondrial donation techniques are not the focus of significant Australian research. This may be due to lack of opportunities, a decline in skills-based expertise or legislation prohibiting clinical use of mitochondrial donation.

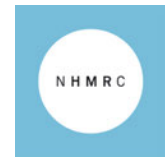
The Committee advised that further *in vitro*, animal and clinical research into the safety and efficacy of the two techniques for mitochondrial donation (pronuclear transfer and maternal spindle transfer) would enable the techniques to be better understood and refined. Emerging mitochondrial donation techniques, including polar body transfer and germinal vesicle transfer, would require further research to refine the techniques and evaluate whether the level of safety and efficacy would make these techniques appropriate for introduction into clinical practice.

The Committee advised that research into gene editing techniques for the purpose of preventing the transmission of mitochondrial disease should not be a priority at this time in Australia.

Legal status of mitochondrial donation in Australia

Mitochondrial donation is currently prohibited in Australia. The *Prohibition of Human Cloning for Reproduction Act 2002* (PHCR Act) and the *Research Involving Human Embryos Act 2002* (RIHE Act) provide the legislative framework for prohibited practices in the use of ART, and for research involving human embryos. Among other things, the PHCR Act prohibits:

- the creation of human embryos by fertilisation with genetic material from more than two people
- heritable alterations to the genome of human embryos for reproductive purposes.



The PHCR Act also prohibits the creation of a human embryo by fertilisation for a purpose other than achieving pregnancy in a woman. Parents can consent to donate 'excess ART embryos' for use in research in Australia (excess ART embryos are defined in the legislation). The PHCR Act limits the scope of research that can be undertaken into mitochondrial donation. The RIHE Act provides a regulatory framework for the use of donated excess ART embryos and does not allow their implantation into a woman.

NHMRC's Embryo Research Licensing Committee (ERLC) is responsible for administering the regulatory framework.

Embryo Research Licensing Committee (ERLC)

Section 13 of the RIHE Act establishes ERLC. It was first established in May 2003 and is a Principal Committee of NHMRC. ERLC regulates research involving human embryos in accordance with the RIHE Act and with regard to the PHCR Act.

The functions of ERLC are to:

- consider applications for licences to conduct research involving human embryos
- issue (subject to conditions) or not issue such licences
- maintain a publicly available database containing information about licences issued
- monitor licensed activities and ensure compliance with the legislation through the appointment of inspectors and take necessary enforcement action, such as cancelling or suspending licences
- report to the Parliament of Australia on the operation of the RIHE Act and the licences issued under this Act
- perform such other functions as are conferred on it by the RIHE Act or any other relevant law.

Maeve's Law would expand the functions of ERLC to include licensing of mitochondrial donation research, training and a clinical trial. More information on ERLC's role and functions under the mitochondrial donation reforms is presented below.

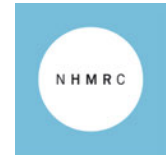
The Minister for Health appoints the members of ERLC in consultation with the states and territories. Appointments are on a part-time basis for a period not exceeding three years with members eligible for reappointment. The membership of ERLC comprises the following:

- a person with expertise in a relevant area of law
- a member of the Australian Health Ethics Committee
- a person with expertise in research ethics
- a person with expertise in a relevant area of research
- a person with expertise in assisted reproductive technology
- a person with expertise in consumer issues relating to disability and disease
- a person with expertise in consumer issues relating to assisted reproductive technology
- a person with expertise in the regulation of assisted reproductive technology
- a person with expertise in embryology.



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Mitochondrial Law Reform (Maeve's Law) Bill 2021

The introduction of the Bill into law would allow mitochondrial donation to be introduced in Australia to reduce the risk of some forms of severe mitochondrial disease being inherited from an affected mother.

The introduction of this technology would be undertaken in a phased approach over a number of years. Initially this would involve ensuring that equipment, processes and protocols are developed for using mitochondrial donation techniques safely and effectively and that embryologists are competent in the techniques. A clinical trial could then occur, potentially leading to the birth of children and the ongoing monitoring of their health.

NHMRC notes that Maeve's Law provides a pathway for mitochondrial donation to be introduced into clinical practice in the future, after the use of mitochondrial donation techniques has been monitored and evaluated through a clinical trial over a number of years.

The use of mitochondrial donation would be regulated by a licensing framework, which extends the licensing framework currently overseen by ERLC and allows for new types of licence for research and clinical practice involving mitochondrial donation. ERLC would be responsible for administering five new licences to cover these uses:

- pre-clinical research and training licences
- clinical trial research and training licences
- clinical trial licences
- clinical practice research and training licences
- clinical practice licences.

The amendments to the RIHE Regulations under Maeve's Law would permit the use of PNT and MST mitochondrial techniques under a mitochondrial donation clinical trial research and training licence or a clinical trial licence. Three other mitochondrial donation techniques would be permitted under pre-clinical research and training licences.

ERLC would not immediately consider licences for clinical practice because no techniques are authorised for use under the clinical practice research and training licences and clinical practice licences at the commencement of these reforms. Clinical practice would require a future amendment to the RIHE Regulations, which would be based on expert advice and the outcomes of the clinical trial. Transition of the technique into clinical practice would also require the cooperation of states and territories which regulate clinical ART practice.

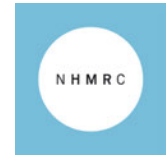
ERLC's role in administering this new licensing framework would include:

- developing appropriate licence application and reporting forms
- establishing appropriate protocols for the assessment and issue of licences
- developing appropriate application forms for the creation of embryos and the placement of created embryos in the bodies of women
- developing adverse events reporting forms



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- establishing robust protocols to ensure the technique is only used for women whose mitochondrial DNA is affected and would put her offspring at risk of serious medical conditions
- establishing appropriate licence conditions
- conducting assessments of licence applications, including the assessment of protocols for obtaining proper consent from the parents and donor before an egg or sperm is used
- ongoing monitoring of issued licences, including licensees' reporting of adverse events affecting patients and children.

NHMRC supports ERLC in its work through:

- development of supporting documentation for the consideration of licence applications and applications to vary licences
- undertaking monitoring and compliance activities on behalf of ERLC
- preparing ERLC's biannual reports to Parliament
- undertaking horizon scanning activities to ensure ERLC is aware of relevant scientific, ethical and regulatory developments.

NHMRC is also supporting ERLC in its initial preparations for the new licensing framework through managing the drafting of:

- licence application and reporting forms (including adverse events reporting)
- application forms for the creation of embryos and placement of created embryos in the bodies of women
- standard licence conditions.

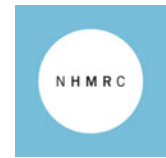
While ERLC currently administers embryo research and training licences, administering licences for mitochondrial donation will differ from the current work of ERLC in that it will be the first time ERLC has had responsibility for issuing licences:

- which involve the creation of embryos by fertilisation specifically for research purposes (clinical trial research and training licence and clinical trial licence)
- for which the intended result is the live birth of a child or children (clinical trial licence and clinical practice licence).

To undertake this work, ERLC may need to call on external expertise, including people with expertise in mitochondrial disease, people with expertise in clinical trials, and other experts as required. The Bill allows for ERLC to access such expertise as required.

In their initial discussions on the implementation of the Bill, members of ERLC for the past triennium (2018-2021) noted:

- the importance of counselling for potential parents and donors
- the need to ensure authorised embryologists are competent and remain so for the duration of their authorisation under a licence
- the importance of appropriate processes for obtaining proper consent.



Social and ethical considerations for mitochondrial donation

The [Mitochondrial Donation Community Consultation Report](#) provides the outcomes of NHMRC's community consultation on the social and ethical issues related to the introduction of mitochondrial donation in Australian clinical practice.

The main considerations highlighted throughout the consultation were:

- the rights of the child, future adult and future generations—the interests and wellbeing of people who may be born as a result of using mitochondrial donation
- the status of the embryo—mitochondrial donation involves the use of human embryos, which are generally regarded as morally significant
- the role and rights of women donating eggs—mitochondrial donation relies on the donation of eggs from women unaffected by mitochondrial DNA disease
- community considerations in the use of mitochondrial donation—there are a range of perspectives in the community on the use of emerging technologies, access and equity and potential impacts now and in the future.

The community (individuals and stakeholder groups) provided a variety of reasons both for and against the introduction of mitochondrial donation during the community consultation, which reflected the broader social and ethical issues under consideration.

The opportunity for the birth of healthy children free from mitochondrial disease, avoiding the impact of the disease on a sufferer and their family, were themselves considered ethical issues. This perspective places significant importance on the benefits of mitochondrial donation (outweighing the risks) to prevent disease and suffering caused by mitochondrial disease.

There was considerable focus in the community on how to implement mitochondrial donation in a fair and ethical way to reduce the burden of disease—for example, taking into account equity of access, rights of donors, and the importance of research and appropriate regulatory oversight. Many in the community agreed that mitochondrial donation should initially be part of a clinical research study and that use of mitochondrial donation would only be appropriate for some circumstances, such as when there is a significant risk of disease.

Common themes among respondents who were concerned about, and in some cases opposed to, the introduction of mitochondrial donation were ethical concerns about:

- the use of and destruction of embryos in the techniques
- the unknown risks to children born of this technology and for future generations due to changes to the human genome
- the creation of embryos with genetic material from more than two people, with perceived implications for individual identity and the constitution of the family
- the limited supply of, and/or unethical incentives to obtain, donated eggs
- manipulating or altering genetic material in embryos and/or that the technology may be, or lead to, genetic engineering.

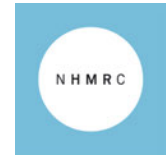
Australian Health Ethics Committee (AHEC)

AHEC is the only national body in Australia with statutory responsibilities for providing advice on ethical issues related to health and for developing human research guidelines.



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The *National Health and Medical Research Council Act 1992* (NHMRC Act) established AHEC as a Principal Committee of NHMRC. The functions of AHEC are:

- to advise the Council on ethical issues relating to health
- to develop and give the Council human research guidelines
- any other functions conferred on the Committee in writing by the Minister after consulting the CEO
- any other functions conferred on the Committee by the NHMRC Act, the regulations or other law.

The Minister for Health appoints the members of AHEC. Appointments are on a part-time basis for a period not exceeding three years with members eligible for reappointment. Under the NHMRC Act, the membership of AHEC comprises:

- the Chair
- a person with knowledge of the ethics of medical research
- a person with expertise in law
- a person with expertise in philosophy
- a person with expertise in religion
- a person with experience in medical research
- a person with experience in public health research
- a person with experience in social science research
- a person with experience in clinical medical practice
- a person with experience in nursing or allied health practices
- a person with knowledge of the regulation of the medical profession
- a person with understanding of consumer issues
- a person with understanding of the concerns of people with a disability
- no more than 2 other persons with expertise relevant to the functions of AHEC.

The passage of Maeve's Law through the Australian Parliament would lead to important work for AHEC to provide ongoing advice on the ethical implementation of mitochondrial donation. This would include undertaking a limited and focused revision of the *Ethical guidelines on the use of assisted reproductive technology in clinical practice and research* to incorporate guidance specifically on the use of mitochondrial donation in Australian clinical practice.

AHEC will have an ongoing role in providing advice on ethical issues associated with mitochondrial donation and other emerging technologies involving human embryos.