Australian Government
Department of Health

Legalising Mitochondrial Donation in Australia

Public Consultation Paper

Cover image credit: Oregon Health & Science University

Overview – legalising mitochondrial donation in Australia

What is mitochondrial donation?	Mitochondrial donation is an IVF-based assisted reproductive technology. It has the potential to prevent mitochondrial DNA disease in babies born to mothers who may otherwise pass on the disease.
Will it be legalised in Australia?	Mitochondrial donation is currently not allowed in Australia. The Australian Government is proposing to introduce mitochondrial donation in a staged and closely monitored way. This paper outlines how the Australian Government proposes to do that. The aim is to allow families to access the technique as quickly as possible, at a carefully selected and regulated clinic. Ongoing research will also be allowed to increase Australian-based knowledge and expertise. This phase is expected to last for 10+ years. Once the technique has been demonstrated successfully over a number of years, and the results have been evaluated by experts, there would be an option to allow for licensed clinics across Australia to offer mitochondrial donation.
Consultation process	Your feedback and comments on the proposal are sought. All comments and submissions will be carefully considered by the Australian Government. A summary of the comments and submissions will be published on the Department of Health website at the conclusion of the consultation period. After the consultation period, the Australian Government plans to introduce legislation to introduce mitochondrial donation, for consideration by the Parliament.
Timeframe	If you would like to submit a short comment or a submission, please provide it by **3pm, Monday 15 March 2021**. Comments or submissions can be made via the consultation hub or by emailing to mito@health.gov.au. All questions should be provided by email to mito@health.gov.au.
Further information	For more information on mitochondrial donation, please go to the Department of Health website: www.health.gov.au/mito

Background

What is mitochondrial disease?

Mitochondria are small DNA-containing structures in human cells. They produce 90 per cent of the energy that the body needs to function and are inherited almost exclusively through the maternal line (passed from a mother to her children) through the mitochondria present in the mother's egg cells.

Mitochondrial disease refers to a group of inherited conditions that can significantly lower an individual's health and life expectancy, and may be fatal. It is caused by mutations or inherited abnormalities in an individual's mitochondrial DNA which impacts the ability of the mitochondria to function normally. These abnormalities may be inherited either through the mitochondrial DNA (which is contained in the mitochondria inherited from the mother) or through the nuclear DNA (which is inherited from both parents).

The severity of symptoms and prognosis for the disease depends on the type and number of mutations and how the affected mitochondria are distributed among an individual's tissues and organs. Common symptoms include developmental delays, seizures, weakness and fatigue, muscle pain, vision and hearing loss, multiple organ failure and heart problems, leading to morbidity and in severe cases, premature death.

The risk of developing serious illness due to a mitochondrial genetic defect is considered to be between one in 5,000 and one in 10,000. However, around one in 200 Australians are estimated to carry a mitochondrial genetic defect[1] and approximately one child is born each week with a severe form of the disease.

Currently there is no known cure for mitochondrial disease and treatment options are mostly limited to management of symptoms.

What is mitochondrial donation?

Mitochondrial donation is a new assisted reproductive technology which can help some parents to avoid transmitting mitochondrial DNA disease to their biological children.

The term collectively refers to a number of specific techniques aimed at ensuring only healthy mitochondrial DNA is passed on to an embryo.

Used in conjunction with in-vitro fertilisation (IVF), mitochondrial donation techniques allow for an embryo to be produced using the nuclear material from a man and woman and the mitochondria in an egg donated by another woman. This approach minimises the risk of transmission of the abnormal mitochondria from the mother to her child.

It cannot, however, be used to cure existing mitochondrial disease or to prevent mitochondrial disease caused by mutations in the nuclear DNA.

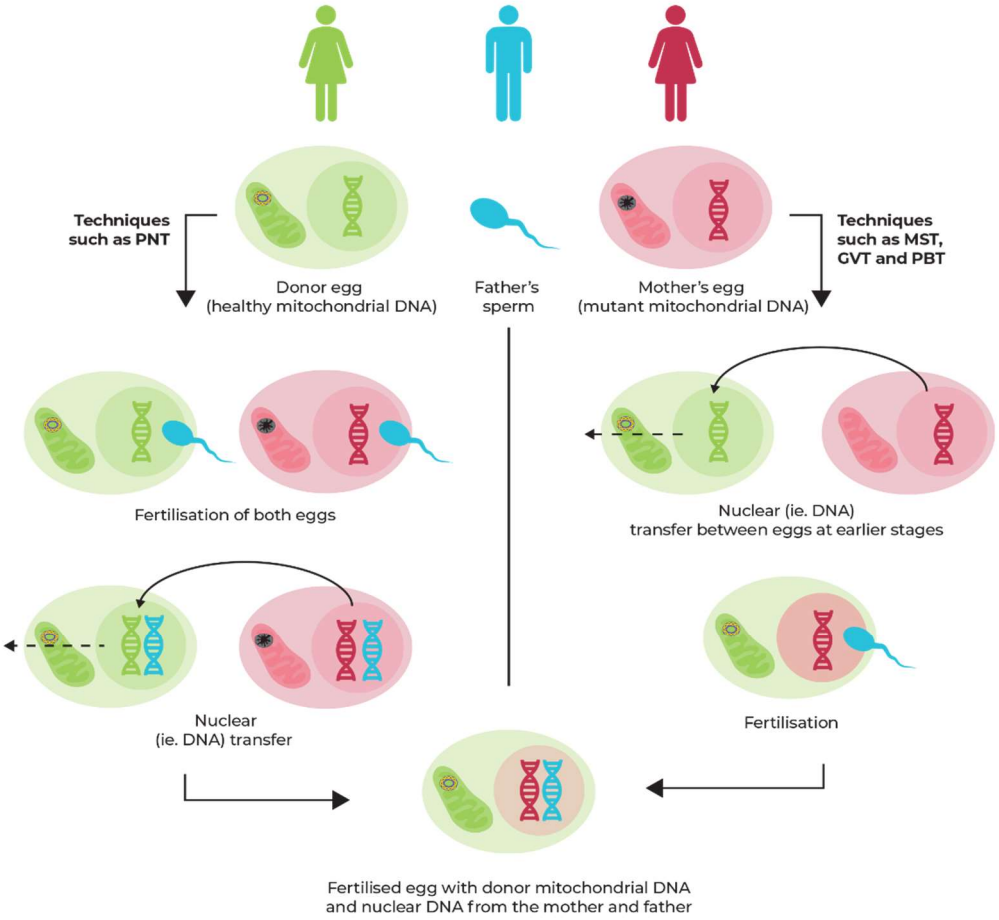
The science of mitochondrial donation is complex. For this reason, an expert committee was established by the National Health and Medical Research Council (NHMRC) to provide further advice to the Government on the safety and efficacy of this technology.

Immediate and long-term risks for the child and longer term implications for subsequent generations are not yet fully understood.

Figure 1 illustrates how the genetic contents and mitochondria from 3 individuals (donor, green; father, blue; and mother, pink) are combined using various mitochondrial donation processes.

[1] Source: Mito Foundation, https://www.mito.org.au/mito-info/, How Common is it?

Figure 1: The mitochondrial donation process[2]



Public consultation to date

In 2018, the Senate Community Affairs References Committee undertook an inquiry into the *Science of mitochondrial donation and related matters*. The inquiry looked at the impacts of mitochondrial disease, the science of mitochondrial donation, legal and ethical considerations and regulation.

The final report recommended further consultation should be undertaken with the community, relevant experts and the states and territories before mitochondrial donation was introduced into Australian clinical practice. In 2019-20, the NHMRC undertook a series of community and expert consultation activities in response to these recommendations.

[2] Mitochondrial donation techniques - PNT (pronuclear transfer); MST (maternal spindle transfer); GVT (germinal vesicle transfer); PBT (polar body transfer)

Proposal - how mitochondrial donation will be introduced in Australia

The Australian Government wants to make mitochondrial donation available in Australia. The aim is to give impacted families greater reproductive choices and reduce the burden of disease for future generations.

The Government plans to proceed slowly, through a 2-Stage implementation approach.

Under Stage 1, mitochondrial donation will be allowed for use in research and training settings and for clinical delivery in a carefully chosen, licensed, and monitored clinic. Separately, research will allow for increased knowledge and expertise on mitochondrial donation.

Availability of mitochondrial donation under Stage 1, will allow the relatively small number of impacted families who are ready to start a family now, the choice of using mitochondrial donation.

Stage 2 will only be implemented once the licensed techniques have been demonstrated successfully over a number of years during Stage 1, and the results have been evaluated by experts. If implemented, Stage 2 will allow for licensed clinics across Australia to offer mitochondrial donation.

A summary is provided in the table below. More detailed information is on the next page.

How mitochondrial donation will be introduced in Australia		
Legalised by Parliament	Legislation will be introduced for consideration by Parliament.	2021
Implementation Stage 1	Mitochondrial donation allowed for research and training – specific criteria apply.	10 years +
	A clinic selected and licensed by a special committee of the NHMRC to deliver mitochondrial donation to impacted couples. Key clinical staff will require specialised training in the technique prior to commencing. Detailed criteria for who can deliver treatment, who can access treatment, and how they must be monitored and supported throughout the process, will also apply.	
Implementation Stage 2	Mitochondrial donation permitted in licensed clinics across Australia. States and territories to opt-in to National Framework at this stage, if desired.	Following evaluation of Stage 1

Stage 1:

Legalising mitochondrial donation for research, training, and use in a clinic

Under Stage 1 mitochondrial donation will be legalised for certain research and training purposes, and to support selection and licensing of a clinic for delivery of mitochondrial donation to impacted families.

The use of specified mitochondrial donation techniques under Stage 1 would be subject to strict licensing conditions, which would be overseen by the existing Embryo Research Licensing Committee (ERLC) of the NHMRC.

Initially Stage 1 will include completion of ERLC licensing protocols for mitochondrial donation and identification of a suitable clinic to deliver mitochondrial donation to couples under Stage 1.

The clinic will commence with an establishment phase which will require a clinical research and training licence from the ERLC. This licence will allow the clinic to create human embryos using approved mitochondrial donation techniques. The clinic will then need to refine their mitochondrial donation and patient protocols and demonstrate proficiency in the relevant technique, before moving to mitochondrial donation for impacted families under a separate clinical licence.

Once established, patients seeking to access mitochondrial donation through the clinic will also require approval from the ERLC. Under this process, the clinic would have responsibility for providing a clinical recommendation to the ERLC for each patient, aligned to the current licensing conditions used in the UK.

It is expected that Stage 1 will take approximately 10 - 12 years, based on the relatively small number of families that may be assisted through this technology, and the potential for participants to require multiple IVF procedures before a successful pregnancy is achieved.

Throughout Stage 1, ongoing monitoring and evaluation of the clinic will occur.

Separately, research and training licences could also be granted to researchers to undertake broader research focused on mitochondrial donation techniques that aim to avoid the transmission of serious mitochondrial DNA disease. This would enable Australian researchers to work on refining other, potentially lower risk, techniques for future use.

There are several benefits to implementing mitochondrial donation in this staged way:

- Mitochondrial donation can be offered relatively quickly – in comparison to across-the-board implementation – enabling current patients to get faster access to treatment options in Australia.
- It will provide the necessary safeguards and ensure delivery of the highest quality clinical care and support for patients.
- It will build the Australian evidence base and expertise for mitochondrial donation. It will also enable further evidence and data to be gathered in relation to the safety and efficacy of the techniques, and associated issues such as feasibility, service delivery, cost and impacts, prior to introducing more broadly.
- Limiting access in this manner in the first instance also follows the model used in the UK, where mitochondrial donation has been formally legalised under a carefully regulated licensing regime.

Stage 2:

Expanding mitochondrial donation to clinics across Australia

Provided Stage 1 can demonstrate evidence of the safety, efficacy and clinical utility of the technology, the Australian Government will move to Stage 2, where mitochondrial donation will be allowed in other licensed clinics across Australia.

Given the limited number of families per annum who are expected to seek these services, it is anticipated that only a small number of highly specialised clinics will seek to offer these services. Mitochondrial donation services will be provided by these clinics under a clinical licence from the ERLC and in accordance with any authorising state or territory law.

Transition to Stage 2 will only occur with the agreement of the Commonwealth Minister for Health, based on recommendations from suitably qualified experts or committees.

The intention is that the provision of mitochondrial donation clinical services under Stage 2 will remain tightly regulated, with the individuals seeking access to the procedure needing to obtain approval, and the clinic performing the procedure needing to obtain a licence, broadly in line with the UK model.

A national regulatory framework will come into play when transition to Stage 2 occurs. Delivery of mitochondrial donation in clinical practice in a particular jurisdiction will require a state or territory to 'opt in' to this national framework (by enacting their own legislative changes) before this would be permitted by law.

Legalising mitochondrial donation in Australia

Proposed legislative amendments and regulatory framework

Mitochondrial donation is currently prohibited in Australia under the *Prohibition of Human Cloning for Reproduction Act 2002* (PHCR Act) and the *Research Involving Human Embryos Act 2002* (RIHE Act).

Legalising mitochondrial donation for research and training and reproductive use in Australia will therefore require amendments to both of these Acts. An appropriate regulatory framework to oversee licensing and monitoring of mitochondrial donation in Australia will be also established under Stage 1. As noted above, a national regulatory framework will apply in Stage 2.

In addition, given that reproductive technology is regulated at both a Commonwealth and jurisdictional level in Australia, implications and flow on effects to corresponding state and territory laws have also been considered.

Proposed amendments to Commonwealth laws

The Australian Government intends to introduce amendments to both the PHCR Act and the RIHE Act that will permit well established mitochondrial donation techniques to be used in limited circumstances, under strict licensing conditions.

These changes will allow for the creation of human embryos using approved mitochondrial donation techniques, and the use of these embryos for research and training, and for clinical purposes (i.e. to achieve a pregnancy in women who would otherwise pass on to their biological children severe mitochondrial DNA disease).

The proposed amendments to the PHCR Act and the RIHE Act will also provide for a national framework that, under Stage 2, will allow for regulated mitochondrial donation techniques to be offered in clinical practice more broadly, through appropriately licensed clinics.

Since reproductive technology is also governed by state and territory laws, each individual state or territory would first choose to 'opt in' to the national framework (by enacting their own legislative changes) before mitochondrial donation could be offered as a clinical service, permitted by law in that jurisdiction.

Commencement of Stage 2 will not be automatic. Instead, the Government will build further safeguards into the legislation that will require the formal approval of the Commonwealth Minister for Health, by disallowable legislative instrument, before Stage 2 could legally commence.

The Minister's decision will be based on the recommendations of a suitably qualified person(s) or committee and the demonstrated outcomes of Stage 1.

In addition, the legislation will include a requirement for an independent review of the Commonwealth's legislation to be undertaken on a regular basis. This review would further safeguard the proposed legislative changes, enabling the legislation to keep up to date with the evolving science.

Importantly, the proposed legislation will only apply to mitochondrial donation techniques that aim to prevent the transmission of mitochondrial DNA disease caused by disease-causing mitochondrial DNA being passed on from the mother to future generations. It will do this by permitting and regulating approved mitochondrial donation techniques to be used for the purpose of minimising the risk of transmission of serious mitochondrial DNA disease.

Additional details on the amendments proposed can be found in Appendix 1.

Addressing sensitivities

The Australian Government is aware that some in the community are concerned about the legalisation of mitochondrial donation in Australia. The NHMRC and Senate Inquiry processes identified a number of sensitivities, including a number of ethical issues and safety concerns.

The Australian Government is aware of these sensitivities and is seeking to introduce mitochondrial donation in a way that finds a balance between helping couples to have healthy biological children while managing the risks and minimising potential harms.

The staged approach proposed for introducing mitochondrial donation in Australia aims to address these issues in a number of ways. Firstly, the strict licensing and regulatory regime proposed will ensure that the use of these techniques is limited to the purpose of preventing the transmission of severe mitochondrial DNA disease.

The proposed approach for Australia will also require prospective parents to attend pre-treatment counselling, where the potential risks will be fully explained. This approach would allow for parents to make their own informed decisions, and provides for reproductive choice. One risk that will need to be raised with prospective parents, is the potential for mitochondrial DNA disease to re-emerge in future generations and the option to reduce this risk (where possible) by choosing to only implant male mitochondrial donation embryos.

In addition, the proposed amendments to current legislation will not permit the manipulation or alteration of the nuclear DNA, which is the genetic material responsible for an individual's personal characteristics and traits.

The wellbeing and rights of the child have also been raised as a key area of concern for some members of the community. Mitochondrial donation promotes the health and wellbeing of any

resulting children through the prevention of severe mitochondrial DNA disease. However some argue that it will be impossible to protect the interests of children born through this process.

To address this, the legislation will ensure that the privacy of families and children is maintained and that ongoing monitoring will be undertaken through the mainstream health care system with no invasive testing being undertaken for routine monitoring purposes. Mandatory reporting of any adverse events will be required however.

Donor rights and responsibilities have also featured strongly in consultation processes undertaken both in Australia and overseas. To address these issues, it is proposed that donor rights and responsibilities for Australian mitochondrial donation egg donors would be largely aligned to current assisted reproductive technology (ART) regulations. This would include that:

- Mitochondrial donation egg donors would not be considered legal parents in line with current ART sperm and egg donors under the *Family Law Act 1975*; and
- Children conceived by mitochondrial donation would have the right to apply for identifying information about their donor at an appropriate age.

Appendix 1

Additional information - proposed amendments to Commonwealth laws

Research and training

Two classes of research and training will be included under the legislation:

- Clinical research and training in approved techniques for the purposes of establishing the initial pilot; and
- Pre-clinical research and training for the purposes of building expertise and evidence to ensure the most effective technique is able to be used in the future.

Both classes of research and training (clinical and pre-clinical) will require a Commonwealth licence.

Mitochondrial donation techniques

Initially, only two mitochondrial donation techniques, maternal spindle transfer (MST) and pronuclear transfer (PNT) will be approved techniques in the legislation and can be applied immediately, subject to a licence being granted. These are the two techniques which have been legalised for clinical practice in the UK.

The primary legislation would also allow for additional techniques to be prescribed by delegated legislation in the future (if proved to be safe and effective), noting that the legislation will set some boundaries around the purpose and/or sorts of techniques that could be prescribed under delegated legislation.

Clinical application

The legislation will allow for clinical mitochondrial donation techniques for human reproduction to be provided in a licensed clinic in Stage 1, subject to a clinical licence.

A clinical licence will only be granted for approved clinical mitochondrial donation techniques that have already been the subject of a clinical research and training licence and for which there is sufficient evidence of their safety and efficacy.

<u>Stage 2</u>

Clinics wishing to provide mitochondrial donation as a clinical service for preventing transmission of severe mitochondrial DNA disease, will be required to do so under Commonwealth licence and in accordance with any authorising state or territory law.

Regulation of mitochondrial donation

Regulation of Stage 1 will be undertaken primarily through existing mechanisms, with some changes required to ensure that the relevant expertise is available to inform decisions regarding licensing of mitochondrial donation in both research and training and clinical settings.

This will include amendments to the PHCR Act and the RIHE Act, and the introduction of associated delegated legislation and licensing conditions. These will include compliance with accreditation and licensing criteria such as development and introduction of patient consent and clinical care protocols; monitoring and reporting protocols; workforce training and proficiency; and data storage of patient and donor information.

Where appropriate, the more detailed conditions will be specified through delegated legislation as well as through guidelines and/or codes of practice in line with the current system in Australia.

The role of the current ERLC will also be expanded under the RIHE Act to include licensing and oversight of research and training licences, a clinical licence for Stage 1, and future clinical practice licences using mitochondrial donation techniques under Stage 2.

Whilst the consideration of research and training licences would largely be within the current competence of the ERLC, the addition of clinical application will require additional expertise.

To fulfil this broader role, the powers of the ERLC will be expanded to ensure this committee has access to the appropriate skills and information required to make informed decisions in granting embryo research licences related to the use of mitochondrial donation, in both the research and training setting and for clinical human reproductive purposes (and in the future, clinical practice).