Mitochondrial Donation Licence Application Form – Application for a Clinical Trial Licence

Overview of the mitochondrial donation licensing scheme

In Australia, research into mitochondrial donation techniques and its use can only be undertaken when it is authorised by a mitochondrial donation licence issued by the National Health and Medical Research Council's (NHMRC) Embryo Research Licensing Committee (ERLC) in accordance with the *Research Involving Human Embryos Act 2002* (Cth) (RIHE Act).

A mitochondrial donation licence permits the creation and development of an embryo, the creation of embryos containing the genetic material provided by more than two people, the alteration of a cell, and in certain circumstances the placement of an embryo created using a permitted mitochondrial donation technique in a woman.

Mitochondrial donation licences will initially be granted to permit certain research and training and to support a clinical trial to deliver mitochondrial donation to affected families. The initial three types of mitochondrial donation licence are a:

- pre-clinical research and training licence
- clinical trial research and training licence
- clinical trial licence.

Once clinical trials have demonstrated the safety and effectiveness of the mitochondrial donation techniques there will be an option for the Parliament of Australia to allow further mitochondrial donation licences that would allow the licence holder to use mitochondrial donation techniques in clinical practice. This would allow accredited assisted reproductive technology (ART) centres that are licensed under the scheme to offer mitochondrial donation in clinical practice.

The scheme also creates the Mitochondrial Donation Donor Register, which is maintained by the Department of Health, and stores details about persons born as a result of a mitochondrial donation procedure and their mitochondrial donors.

The mitochondrial donation licensing scheme is separate to the general licence scheme for use of excess ART embryos in research not involving mitochondrial donation techniques. Importantly, material created under a general licence[1] cannot be used under a mitochondrial donation licence and material created under a mitochondrial donation licence cannot be used under a general licence.

Embryos created under a mitochondrial donation clinical trial licence are specifically created for placement in the body of a particular trial participant.[2] In the event that an embryo created for a woman under a mitochondrial donation clinical trial licence becomes excess to the woman's reproductive needs, it may be used under another mitochondrial donation licence for research and training, however, it cannot be donated to another woman for use in reproductive treatment.

Organisations wishing to undertake research and training in the creation or use of human embryos using a mitochondrial donation technique or run a clinical trial involving a mitochondrial donation technique must apply to ERLC for a licence. ERLC will undertake a comprehensive assessment of each application against the criteria set out in the RIHE Act and issue or refuse licences accordingly.

1 General licence means a licence issued under section 21 of the *Research Involving Human Embryos Act 2002* (Cth).
2 *Research Involving Human Embryos Act 2002* (Cth) sections 10(2)(e) and 28P.

Role of the NHMRC Embryo Research Licensing Committee

Section 13 of the RIHE Act establishes ERLC, a Principal Committee of NHMRC. ERLC regulates research involving human embryos in accordance with the RIHE Act and with regard to the *Prohibition of Human Cloning for Reproduction Act 2002* (Cth).

The functions of ERLC are to:

(i) consider applications for licences to conduct research involving human embryos

(ii) consider applications for licences to conduct research, undertake training and conduct a clinical trial involving mitochondrial donation

(iii) issue (subject to conditions) or not issue such licences

(iv) maintain a publicly available database containing information about licences issued

(v) 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

(vi) report to the Parliament of Australia on the operation of the RIHE Act and the licences issued under this Act

(vii) perform such other functions as are conferred on it by the RIHE Act or any other relevant law.

The use of mitochondrial donation is regulated by a licensing scheme, which allows for licences for research and clinical practice involving mitochondrial donation. ERLC is responsible for administering the licensing scheme.

Criteria ERLC must consider when determining whether to issue a licence

ERLC must consider and be satisfied of specific matters before making a determination to issue a mitochondrial donation licence.[3] When considering licence applications, ERLC must be satisfied that:

- appropriate protocols are in place to enable proper consent to be obtained before a human egg or human sperm is used in carrying out the technique and to enable compliance with any restrictions on such a consent[4] and
- the relevant activity or project has been assessed and approved by a Human Research Ethics Committee (**HREC**) constituted and acting in compliance with the National Statement.[5]

ERLC must also have regard to the following:

- restricting the number of embryos, human eggs or zygotes, to that likely to be reasonably necessary to achieve the goals of the activity or project[6]
- any relevant guidance set out in the *Ethical guidelines on the use of assisted reproductive technology in clinical practice and research* (the ART Guidelines) and the *National Statement on Ethical Conduct in Human Research* (the National Statement)[7]
- the assessment of the proposed project by the relevant HREC, and[8]
- whether the applicant has complied with the conditions of any other mitochondrial donation licence issued to them.[9]

ERLC may also seek and have regard to advice from any person having appropriate expertise in considering the application.[10]

3 *Research Involving Human Embryos Act 2002* (Cth) section 28J.
4 *Research Involving Human Embryos Act 2002* (Cth) section 28J(2)(a).
5 *Research Involving Human Embryos Act 2002* (Cth) section 28J(2)(b).
6 *Research Involving Human Embryos Act 2002* (Cth) section 28J(3)(a)
7 *Research Involving Human Embryos Act 2002* (Cth) section 28J(3)(b); *Research Involving Human Embryos Regulations 2017* (Cth) regulation 7H.
8 *Research Involving Human Embryos Act 2002* (Cth) section 28J(3)(c).
9 *Research Involving Human Embryos Act 2002* (Cth) section 28J(3)(d)
10 *Research Involving Human Embryos Act 2002* (Cth) section 28J(4).

Consent to the use of human eggs, human sperm and reproductive or genetic material or cell for mitochondrial donation

It is a condition of all mitochondrial donation licences that each *responsible person* who is the biological donor of the human egg or human sperm or whose reproductive material, genetic material or cell is used under the licence, has given proper consent to that use, and that the licence holder has reported in writing to ERLC that such consent has been obtained, and any restrictions to which the consent is subject.[11]

A mitochondrial donation licence holder must also collect specified information about children born as a result of a mitochondrial donation procedure and their mitochondrial donors for storage on the Mitochondrial Donation Donor Register.[12] Accordingly, a mitochondrial donation licence holder is required to obtain consent to the collection, use and storage of certain information from the person who is the mitochondrial *donor*[13] in relation to the mitochondrial donation procedure.

A mitochondrial donation licence holder should ensure that pre-treatment counselling is provided by counsellors with full Australian and New Zealand Infertility Counsellors Association (ANZICA) membership in order to ensure ART procedures using mitochondrial donation techniques are conducted in a way that is respectful of all involved.[14] Clinical decisions must respect, primarily, the interests and welfare of the persons who may be born, as well as the long-term health and psychological welfare of all participants including mitochondrial donors and any gamete donors.

Approval is required from ERLC before the creation and placement of an embryo under a clinical trial licence[15] and ERLC will require a report to be prepared setting out the required pre-treatment counselling provided to trial participants.[16] Note that pre-treatment counselling and the preparation of this report may require input from a multi-disciplinary team with expertise in genetics, gamete donation in ART, and disease specialists.

Confidentiality

All those who participate in the mitochondrial donation scheme and in ART activities more generally are entitled to privacy to the degree that is protected by law. Licence applicants should familiarise themselves with the applicable laws and the relevant provisions of the ART Guidelines.

No identifying information is to be provided to ERLC as part of a licence application.

Included with this application form is a collection notice addressing the Australian Privacy Principles (APP) 5.2 matters for mitochondrial donation licence applicants and staff and the HREC Chairperson. All mitochondrial donation licence applicant representatives must confirm that the collection notice has been provided to all persons identifiable in the application and detail in the licence application the measures they have in place to protect individual privacy.

In the consent reports to ERLC referred to above (see **Consent to the use...**) a licence holder must not include in a report to ERLC the name, or any other information that could be used to discover the identity of a *responsible person or mitochondrial donor*.[17] However this information must be collected and kept by the licence holder as part of the consent process.

Ethics committee approval

ERLC cannot approve a mitochondrial donation licence application unless the activity or project proposed in the application has been assessed and approved by a HREC that is constituted in accordance with and acting in compliance with the National Statement.[18]

11 *Research Involving Human Embryos Act 2002* (Cth) section 28N(1) and (1A).
12 *Research Involving Human Embryos Act 2002* (Cth) section 28R(1) and (3).
13 A donor in relation to a particular use of a mitochondrial donation technique is the donor of the egg which contains the mitochondria used in the mitochondrial donation technique.
14 *Research Involving Human Embryos Act 2002* (Cth) section 28P(4).
15 *Research Involving Human Embryos Act 2002* (Cth) section 28P(1) and (2).
16 *Research Involving Human Embryos Act 2002* (Cth) section 28P(4)(d).
17 *Research Involving Human Embryos Act 2002* (Cth) section 28N(2).
18 *Research Involving Human Embryos Act 2002* (Cth) section 28J(2)(b).

What does a clinical trial licence authorise?

Subject to specific approval being granted a clinical trial licence authorises a licence holder to conduct a clinical trial to use a permitted mitochondrial donation technique to determine whether the permitted technique is sufficiently safe and effective to use in clinical practice. Specifically, it would allow a licence holder to undertake permitted activities with a permitted technique at an accredited ART centre for the purpose of:

(i) creating a human embryo for a trial participant, using the permitted technique specified in the licence, with the intention of minimising the risk of the embryo inheriting mitochondria that would predispose any resulting child to mitochondrial disease; and

(ii) placing the embryo in the body of the trial participant for the purposes of achieving her pregnancy.[19]

Approval to create an embryo for a woman or to place an embryo created for a woman in that woman's body cannot be applied for, or granted, at the time that a clinical trial licence is applied for.[20] Once a clinical trial licence holder is ready to apply for an approval it may apply to ERLC using the prescribed application form available at **https://www.nhmrc.gov.au/mitochondrial-donation-0**

The only mitochondrial donation techniques that may be permitted for use under a clinical trial licence are:[21]

(i) maternal spindle transfer (**MST**)[22]

(ii) pronuclear transfer (**PNT**)[23]

The activities that may be permitted by a clinical trial licence are:

(i) creation of human embryos other than by fertilisation of a human egg by a human sperm, using the permitted technique specified in the licence, and use of such embryos

(ii) creation and use of human embryos that contain genetic material provided by more than 2 persons, using the permitted technique specified in the licence:

  (a) by fertilisation of a human egg by a human sperm outside the body of a woman, or

  (b) other than by the fertilisation of a human egg by a human sperm

(iii) alteration of the genome of a human cell (within the meaning of section 15 of the *Prohibition of Human Cloning for Reproduction Act 2002*) using the permitted technique specified in the licence, in such a way that the alteration is heritable by descendants of the human whose cell was altered

(iv) placement in the body of a woman of any of the following kinds of human embryo created using the permitted technique specified in the licence:

  (a) a human embryo created by a process other than the fertilisation of a human egg by human sperm

  (b) a human embryo that contains genetic material provided by more than 2 persons

  (c) a human embryo that contains a human cell (within the meaning of section 15 of the *Prohibition of Human Cloning for Reproduction Act 2002*) whose genome has been altered in such a way that the alteration is heritable by descendants of the human whose cell was altered

(v) use of any material (other than an excess ART embryo) created, developed or produced under a mitochondrial donation licence.[24]

The activities permitted by a clinical trial licence are only able to be conducted using the permitted mitochondrial donation technique authorised in the licence.

A person cannot apply for a clinical trial licence relating to a particular mitochondrial donation technique unless the person has held a clinical trial research and training licence relating to that technique.[25]

A person applying for a clinical trial licence must be a corporate entity. Where there are multiple applicants they must all be corporations. As the activities permitted by a clinical trial licence must be undertaken at an accredited ART centre the legal entity holding that accreditation may also be an applicant on the licence application, or absent this the applicant must produce proof of any relevant commercial agreement in place that enables it access to and use of the facilities of an accredited ART centre.

19 *Research Involving Human Embryos Act 2002* (Cth) section 28E(1).
20 *Research Involving Human Embryos Act 2002* (Cth) section 28P(2).
21 *Research Involving Human Embryos Regulations 2017* (Cth) regulation 7B item 2.
22 A definition of the technique is set out in the *Research Involving Human Embryos Regulations 2017* (Cth) regulation 7C.
23 A definition of the technique is set out in the *Research Involving Human Embryos Regulation 2017* (Cth) regulation 7D.
24 *Research Involving Human Embryos Act 2002* (Cth) section 28E(2).
25 *Research Involving Human Embryos Act 2002* (Cth) section 28H(3).

Clinical trial licence reporting and record keeping obligations

The holder of a clinical trial licence has a legal obligation to notify ERLC and the Secretary of the Department of Health of specific adverse events for a trial participant and children born as a result of the use of a mitochondrial donation technique.[26] This is an ongoing obligation that continues after the licence expires, is suspended, revoked or surrendered.

An *adverse event* includes:

- for a trial participant – a failed embryo development, a miscarriage, a premature birth of a child, or the birth of a child with a birth defect, a genetic abnormality or a diagnosis at birth of mitochondrial disease, and
- for a child of a trial participant – a diagnosis at any time of mitochondrial disease.[27]

This obligation ensures that the Secretary of the Department of Health and the ERLC can effectively monitor the safety and effectiveness of mitochondrial donation techniques used in reproduction. This obligation is distinct from Reproductive Technology Accreditation Committee (RTAC) obligations that apply to accredited ART centres to report serious adverse events to RTAC and the certifying body.

The main purpose of monitoring is to understand any risks that may be presented by the use of mitochondrial donation techniques. Whilst any future engagement by trial participants and children is voluntary the holders of a licence are required to have in place, and comply with, protocols for seeking the ongoing engagement of these persons, for example by explaining to these persons the benefits to themselves and others of their participation in ongoing monitoring.

As soon as practicable after becoming aware of the birth of a child born as a result of a pregnancy achieved using a mitochondrial donation technique the clinical trial licence holder (including if the licence is no longer in effect) must notify the Secretary of the Department of Health and ERLC of the birth.[28] The licence holder must provide the prescribed information to the Secretary for inclusion in the Mitochondrial Donation Donor Register,[29] however the licence holder must not provide any identifying details to ERLC.[30]

This includes information about mitochondrial donors as well as any children born as a result of a pregnancy achieved using a mitochondrial donation technique.[31]

Restrictions and prohibitions

A clinical trial licence **does not authorise**:

(i) any use of a human embryo that would result in the development of a human embryo for a period of more than 14 days outside the body of a woman, excluding any period when development is suspended[32]

(ii) the use of a human egg or human sperm without the written consent of the *responsible person* or against any restrictions on that consent[33]

(iii) the use of any material created, developed or produced under the licence that is not expressly permitted by the licence[34]

(iv) creating a human embryo for the woman who is a trial participant using the mitochondrial donation technique to which the licence relates without an approval from ERLC[35]

(v) placing a human embryo created for the woman using the mitochondrial donation technique to which the licence relates in the body of the woman for the purposes of achieving her pregnancy without an approval from ERLC.[36]

All licences will be subject to conditions. Mandatory conditions are set out in the RIHE Act sections 28N, 28P and 28Q. Additional licence conditions may also be imposed by ERLC. A copy of the standard conditions for mitochondrial donation licences [37] is available on the NHMRC website at **https://www.nhmrc.gov.au/mitochondrial-donation-0**

26 *Research Involving Human Embryos Act 2002* (Cth) section 28S(3). In making a notification the licence holder must not disclose the identity of a trial participant or patient a child of a trial participant or patient; *Research Involving Human Embryos Act 2002* (Cth) section 28S(5).
27 *Research Involving Human Embryos Act 2002* (Cth) section 28S(8) and *Research Involving Human Embryos Regulations 2017* (Cth) regulation 7M.
28 *Research Involving Human Embryos Act 2002* (Cth) section 28R(5).
29 *Research Involving Human Embryos Act 2002* (Cth) section 29A.
30 *Research Involving Human Embryos Act 2002* (Cth) section 28R(6).
31 *Research Involving Human Embryos Act 2002* (Cth) section 28R(1) and (3).
32 *Research Involving Human Embryos Act 2002* (Cth) section 28E(3).
33 *Research Involving Human Embryos Act 2002* (Cth) section 28N(1) and (1A).
34 *Research Involving Human Embryos Act 2002* (Cth) section 11A.
35 *Research Involving Human Embryos Act 2002* (Cth) section 28P(1)(a).
36 *Research Involving Human Embryos Act 2002* (Cth) section 28P(1)(b).
37 Licence conditions are subject to review by ERLC.

Explanation of Key Terms

Word	Definition
Accredited ART Centre	Accredited ART Centre means a person or body accredited to carry out assisted reproductive technology by the Reproductive Technology Accreditation Committee of the Fertility Society of Australia. [38]
APP	Australian Privacy Principles available at **https://www.oaic.gov.au/privacy/australian-privacy-principles/**
ART Guidelines	NHMRC *Ethical guidelines on the use of assisted reproductive technology in clinical practice and research* available at **https://www.nhmrc.gov.au/art#block-views-block-file-attachments-content-block-1**
Constitutional corporation	A constitutional corporation is either a foreign corporation or a trading or financial corporation formed within the limits of the Commonwealth.
ERLC	Embryo Research Licensing Committee is a principal committee of the NHMRC established under section 13 of the *Research Involving Human Embryos Act 2002* (Cth).
Excess ART embryo	Excess ART embryo means a human embryo that: (a) was created by assisted reproductive technology, for use in the assisted reproductive technology treatment of a woman, and (b) the woman for whom it was created and her spouse at the time the embryo was created (if any) has: (i) given written authority for use of the embryo for a purpose other than a purpose relating to the assisted reproductive technology treatment of the woman concerned, and the authority is in force at that time; or (ii) determined in writing that the embryo is excess to their needs, and the determination is in force at that time. (see *Research Involving Human Embryos Act 2002* (Cth) section 9)
Human cell	**Human cell** includes a human embryonal cell, a human fetal cell, human sperm or a human egg. (see *Prohibition of Human Cloning for Reproduction Act 2002* s15).
HREC	Human Research Ethics Committee constituted in accordance with the National Statement. For more information on human research ethics committees see **https://www.nhmrc.gov.au/research-policy/ethics/human-research-ethics-committees**
Mitochondrial Donor	If a particular use of a mitochondrial donation technique results in the creation of a zygote that: (c) has nuclear DNA from a woman and a man; and (d) contains mitochondria from a human egg of a different woman; the woman mentioned in paragraph (b) is the *donor* in relation to that use of the technique.

38 See *Research Involving Human Embryos Act 2002* (Cth) section 8.

Word	Definition
Mitochondrial donation technique	**Mitochondrial donation technique** means a technique, prescribed by the regulations for the purposes of this definition, that: (a) can be used to minimise the risk of a woman's offspring inheriting mitochondria from that woman that would predispose the offspring to mitochondrial disease; and (b) involves using assisted reproductive technology to create a zygote that: i. has nuclear DNA from the woman and a man; and ii. contains mitochondria from a human egg of a different woman; and (c) does not involve: i. intentionally modifying nuclear DNA or mitochondrial DNA; or ii. using any cell, or any component part of a cell, of an animal; or iii. creating a chimeric embryo (within the meaning of the *Prohibition of Human Cloning for Reproduction Act 2002*) or a hybrid embryo.
National Statement	NHMRC *National Statement on Ethical Conduct in Human Research 2007* (Updated 2018) available at **https://www.nhmrc.gov.au/about-us/publications/national-statement-ethical-conduct-human-research-2007-updated-2018#block-views-block-file-attachments-content-block-1**
Permitted technique	A permitted technique is a prescribed technique that is permitted for use under a mitochondrial donation licence. The mitochondrial donation techniques prescribed in the *Research Involving Human Embryos Regulations 2017* are: (a) maternal spindle transfer (b) pronuclear transfer (c) germinal vesicle transfer (d) first polar body transfer (e) second polar body transfer. Only certain techniques may be used under particular licences and each licence may only authorise one permitted technique.
Proper consent	In relation to the use of a human egg or a human sperm, the use or creation of a zygote or human embryo, or the creation, development or production of genetic or reproductive material for the purposes of mitochondrial donation, proper consent means consent that is obtained in accordance with: (a) guidelines issued by the CEO of NHMRC under the *National Health and Medical Research Council Act 1992*, and prescribed by the regulations, and (b) the ART guidelines. (See *Research Involving Human Embryos Act 2002* (Cth) section 28N; *Research Involving Human Embryos Regulations 2017* (Cth) regulation 7J.)
Responsible person	In relation to a human egg, the person who was the biological donor of the egg. In relation to a human sperm, the person who was the biological donor of the sperm. In relation to any reproductive or genetic material that is created, developed or produced as authorised by a mitochondrial donation licence, each person whose reproductive or genetic material or cell was used, or is proposed to be used, in the creation, development, production or use of the material.
Trial participant	Is a woman whose pregnancy is sought to be achieved through the use of a mitochondrial technique under the clinical trial licence.

Contact Details

For further information or queries relating to this Licence Application Form contact Embryo Research Licensing:

Email: **embryo.research@nhmrc.gov.au**

GPO Box 1421,
CANBERRA ACT 2601

Tel: 1300 064 672 in Australia
+61 2 6217 9000 for international callers.

Important Note

- You are advised to familiarise yourself with the requirements of the *Research Involving Human Embryos Act 2002* and the *Prohibition of Human Cloning for Reproduction Act 2002*.
- You are also advised to consider any relevant State or Territory legislation and, if necessary, seek independent legal advice.
- If additional information is provided as part of the application please include the names of any files that are provided as attachments to the application form.
- When completed and signed by all relevant parties the form should be saved as a PDF file and submitted by email to Embryo Research Licensing at **embryo.research@nhmrc.gov.au**

Annexure 1
Clinical trial licence application form

ALL SECTIONS OF THIS FORM MUST BE COMPLETED

Section 1 – Applicant details

1.1	APPLICANT INFORMATION
1.1.1	**Applicant Organisation.**[39]
	Organisation name
	Street Address
	Postal Address
	Courier Address
	ABN or ACN
1.1.2	**Organisation Representative.**
	Title
	Given Names
	Surname
	Position
	Contact number(s)
	Email address
1.1.3	**Contact person for licence application.**[40]
	Title
	Given Names
	Surname
	Position
	Contact number(s)
	Email address
1.1.4	**Is the applicant an accredited ART centre?** **If so please provide a copy of:** **(a) the Reproductive Technology Accreditation Committee (RTAC) accreditation, and** **(b) any other accreditation licence, approval or other recognised certification of the proposed facility/ies.**[41]

39 Note a person cannot apply for a clinical trial licence unless the person is a constitutional corporation [*Research Involving Human Embryos Act 2002* (Cth) section 28H(2)(b)]. Where there is more than one corporate entity applying for the licence include its details as well.
40 The contact person must consent to acting in this role before their details are provided in an application.
41 This may include NATA accreditation of diagnostic laboratories, the licensing of day procedure centres, or any other state and territory, or commonwealth licensing requirement.

1.1.5	**If the applicant is not an Accredited ART Centre detail the Accredited ART Centre where the licensed activities will be undertaken.**
	Accredited ART Centre name
	Street address
	Postal address
	ABN or ACN
	Attach proof of RTAC accreditation
1.1.6	**Accredited ART Centre Organisation Representative if different from the applicant.**
	Title
	Given Names
	Surname
	Position
	Contact number(s)
	Email address
1.1.7	**If the applicant is not an accredited ART centre provide proof of:** **(a) the accredited ART centre's consent to use the accredited ART centre and a copy of the agreement between the applicant and the accredited ART centre providing for the use of an accredited ART centre for the licensed activities,** **(b) the Reproductive Technology Accreditation Committee (RTAC) accreditation, and** **(c) any other accreditation licence, approval or other recognised certification of the proposed facility/ies[42]**
	Attach a copy of all documentation and note attachment numbers in this box.

42 This includes NATA accreditation of diagnostic laboratories, the licensing of day procedure centres, or any other state and territory, or commonwealth licensing requirement.

1.2 PROPOSED AUTHORISED PERSONS

1.2.1 Principal supervisor(s)[43]

Title
Given Names
Surname
Position
Contact number(s)
Email address
Role in proposed activity
[Describe the person's role in the proposed activity, including information about whether the person will be creating or using embryos or using human cells.]

Qualifications and experience

The principal supervisor should be able to demonstrate:

- a high level of professional and scientific expertise
- relevant experience managing large multidisciplinary projects across a range of sites
- relevant experience managing a clinical trial
- relevant qualifications and/or experience in embryology.

Attach a full curriculum vitae and note the attachment number in this box.

43 Where there is a joint or alternate supervisor include their details as well.

1.2.2	**Principal investigator(s)**[44]
	Title
	Given Names
	Surname
	Position
	Contact number(s)
	Email address
	Role in proposed activity *[Describe the person's role in the proposed activity, including information about whether the person will be creating or using embryos or using human cells.]*
	Qualifications and experience The principal investigator must be able to demonstrate: • a high level of professional and scientific expertise • relevant experience managing a clinical trial • relevant qualifications and/or experience in embryology • demonstrable knowledge of mitochondrial donation techniques developed through previous mitochondrial donation licences (include the licence details under which the experience in mitochondrial donation was gained).
	Attach a full curriculum vitae and note the attachment number in this box.

1.2.3	**The Principal Investigator confirms they have been given a copy of the *Mitochondrial Donation Licensing Scheme – Privacy and the protection of your personal information* notice.**
	Yes ☐ No ☐

44 Where there is more than one investigator include their details as well.

1.2.4 Nominated Embryologist(s) who will use the technique permitted under the licence.

Only the embryologists authorised in the licence may use the mitochondrial donation technique under the licence.[45]

Title
Given Names
Surname
Position
Contact number(s)
Email address
Role in proposed activity *[Describe the person's role in the proposed research and what activities they will be trained in using the permitted technique.]*
Professional certification or qualification details *(e.g Medical Laboratory Scientist ANZSCO 234611 Specialisation: IVF Embryologist CLMS certification.)*
Embryologist(s)'s consent to being nominated. *[Describe how the embryologist(s)' consent to being nominated has been recorded in the organisation's records.]*

45 *Research Involving Human Embryos Act 2002* (Cth) section s28H(5).

Details of clinical trial research and training licence under which the embryologist used the relevant mitochondrial donation technique.

Requirements for nominated embryologist(s).

Evidence of embryologist(s)' demonstrated technical competence in the use of the proposed technique.

Provide evidence of the embryologist's professional qualifications and relevant professional experience. If attachments are included note the attachment number here.

Details of the outcomes/results achieved by the embryologist in using a mitochondrial donation technique for the permitted activities under the clinical trial research and training licence.

Evidence that the nominated embryologist(s) understand their obligations under the *Research Involving Human Embryos Act 2002* (Cth)[46].

46 *Research Involving Human Embryos Act 2002* (Cth) section 28J(5)(b); *Research Involving Human Embryos Act 2002* (Cth) sections 28N(1)-(3), 28P(9) and 28Q and set out obligations relevant to embryologists.

1.2.5 The nominated embryologist confirms that they have been given a copy of the *Mitochondrial Donation Licensing Scheme – Privacy and the protection of your personal information* notice.

Yes ☐ No ☐

1.2.6 Other persons who will carry out activities that are authorised by the licence.[47]

ERLC cannot issue a licence unless satisfied that the staff other than embryologists who would carry out activities directly connected with the clinical trial are appropriately qualified and trained to do so.[48]

Title

Given Names

Surname

Position

Contact number(s)

Email address

Role in proposed activity

Evidence of relevant qualifications and training

Attach a brief curriculum vitae for each staff member. The CV should indicate relevant embryology or other skills.

Role in proposed activity

1.2.7 Other persons confirm they have been given a copy of the *Mitochondrial Donation Licensing Scheme – Privacy and the protection of your personal information* notice.

Yes ☐ No ☐

47 You are required to identify and certify that all other persons who would assist the embryologist in using the technique, for example in activities such as storing embryos and removing them from storage, have the appropriate expertise to assist in the activities permitted by the licence. It is not necessary to identify staff with only a peripheral role, such as administrative support staff. Staff must consent to provision of their details in an application.

48 *Research Involving Human Embryos Act 2002* (Cth) section 28J(5)(d).

1.3 SPECIFIED SITES

1.3.1 Site(s) of the proposed activities (if multiple sites are listed in the application the applicant must specify which sites will conduct which activities).

Organisation name
Contact name[49]
Contact Number
Contact email address
Street number and name
Suburb
State and Postcode
Building Name
Level/room
Postal address
Activities to occur at this site

1.3.2 Site(s) for storage of records associated with proposed activities (including original consent documents).

Organisation Name
Contact Name[50]
Contact Number
Contact email address
Street number and name
Suburb
State and Postcode
Postal Address

1.3.3 ART clinic(s) or other organisations from which human cells will be obtained (only required if different from the applicant organisation or the accredited ART centre at which the licensed activities will occur).

Organisation Name
Contact Name[51]
Contact Number
Email address
Street name and number
Suburb and state
Licence number(s) and Project Name(s)

49 The contact person must consent to acting in this role before their details are provided in an application.
50 The contact person must consent to acting in this role before their details are provided in an application.
51 The contact person must consent to acting in this role before their details are provided in an application.

1.4 CURRENT AND PREVIOUS LICENCES

1.4.1	Details of current or previous clinical trial research and training licence(s) held by applicant. (Include licence number and details of embryologist nominated under the licence.)

1.4.2	Details of the outcomes/results achieved in using a mitochondrial donation technique for the permitted activities under the clinical trial research and training licence.

1.4.3	**Details of any previous general licence or other mitochondrial donation licence that has been granted or details of any application(s) for a licence under the RIHE Act that has been refused.**

Section 2 – Project Description

	PROJECT DETAILS
2.1	**Title of the proposed research activity**

2.2	**Proposed commencement date of licensed activities**

2.3	**Proposed duration of licensed activities**[52]

2.4	**Permitted technique** A mitochondrial donation licence may permit the licence holder to undertake multiple activities however each licence may only permit the use of one mitochondrial donation technique. If you wish to use multiple techniques additional licence applications are required.[53]

Tick **one** technique proposed to be used:

- ☐ (a) maternal spindle transfer[54];
- ☐ (b) pronuclear transfer[55];

52 Note that if a licence holder of a clinical trial licence ceases being a constitutional corporation ERLC is taken to have revoked the licence at the time the licence holder ceased being a constitutional corporation [*Research Involving Human Embryos Act 2002* (Cth) section 28V(3)].
53 *Research Involving Human Embryos Act 2002* section 28H(6).
54 As defined by the *Research Involving Human Embryos Regulations 2017* section 7C.
55 As defined by the *Research Involving Human Embryos Regulations 2017* section 7D.

2.5 Proposed activities

A clinical trial licence **does not authorise** the creation of an embryo for a woman or the placement of an embryo created for a woman in that woman's body without a further approval from the ERLC.[56]

Tick the activity or activities being applied for:

- ☐ (a) creation of human embryos other than by fertilisation of a human egg by a human sperm, using the permitted technique specified in the licence, and use of such embryos
- ☐ (b) creation of human embryos that contain genetic material provided by more than 2 persons, using the permitted technique specified in the licence:
  - (i) by fertilisation of a human egg by a human sperm outside the body of a woman; or
  - (ii) other than by the fertilisation of a human egg by a human sperm

  and the use of such embryos
- ☐ (c) alteration of the genome of a human cell using the permitted technique specified in the licence, in such a way that the alteration is heritable by descendants of the human whose cell was altered
- ☐ (d) placement in the body of a woman of any of the following kinds of human embryo created using the permitted technique specified in the licence:
  - (i) a human embryo created by a process other than the fertilisation of a human egg by human sperm
  - (ii) a human embryo that contains genetic material provided by more than 2 persons
  - (iii) a human embryo that contains a human cell (within the meaning of section 15 of the *Prohibition of Human Cloning for Reproduction Act 2002*) whose genome has been altered in such a way that the alteration is heritable by descendants of the human whose cell was altered
- ☐ (e) use of any material (other than an excess ART embryo) created, developed or produced under a mitochondrial donation licence.

2.6 If the applicant intends to use any material (other than an excess ART embryo) created, developed or produced under another mitochondrial donation licence provide details of the material that is intended to be used and the licence under which it was created[57].

56 *Research Involving Human Embryos Act 2002* section 28P(1).

57 Any material created, developed or produced under another mitochondrial donation licence that is intended to be used in the present application must have been provided by the responsible person with proper consent. In the case of material created, developed or produced under a mitochondrial donation licence related to research and training proper consent would need to include future use in a clinical reproductive setting. This may mean that re-consent for such purposes may need to be sought from existing donors.

2.7 Short description of proposed activity in plain English

Please note that in the event that a licence is granted the information provided here will be used in the public licence database. Please clearly identify any information that is not suitable for publication in the database.

NHMRC will confirm the content of the database entry with licence holders before the licence record is published.

2.8 Facilities, equipment and processes to be used to undertake licensed activities.

ERLC must be satisfied that the applicant's facilities, equipment and processes for using the permitted technique under the licence are suitable for that purpose.[58]

58 *Research Involving Human Embryos Act 2002* (Cth) section 28J(5)(c).

2.9 Detailed description of proposed project[59]

Provide a detailed outline of the proposed project. Include information on the following aspects of the proposed activity:

- aims – describe the specific aims of the project, including a clear statement of the hypothesis to be tested (if applicable)
- background – describe the significance of the project in relation to the existing state of knowledge and include a short review of relevant literature
- methodology and trial design – including as appropriate, a detailed description of the trial design, techniques to be used and methods of statistical analysis, and
- outcomes – including defined endpoints of the proposed activity.

If the project is being undertaken in conjunction with another organisation provide details of the respective organisation's roles in the project.

59 NOTE: In the event of the application being sent to external experts, any confidential commercial information would be removed from the application. Therefore, the project description should be able to be understood when this information is removed. The application should clearly identify any confidential commercial information. (See section 6 below).

PROJECT REQUIREMENTS

In deciding whether to issue the licence, ERLC must have regard to restricting the number embryos, human eggs or zygotes to that likely to be necessary to achieve the goals of the activity or project proposed in the application.[60] ERLC may impose a condition on the licence limiting the number of embryos or human eggs or zygotes that may be used in the proposed activity.[61]

2.10 Proposed number of embryos likely to be created to achieve the goals of the proposed activity and an explanation of why the number proposed is necessary.

A clinical trial licence does not authorise the creation of an embryo for a woman or the placement of an embryo created for a woman in that woman's body without a further approval from ERLC.[62]

2.11 Proposed number of human eggs or zygotes likely to be necessary to achieve the goals of the proposed activity and explanation of why the number proposed is necessary.

60 *Research Involving Human Embryos Act 2002 (Cth) section 28J(3)(a).*
61 *Research Involving Human Embryos Act 2002 (Cth) section 28N(5).*
62 *Research Involving Human Embryos Act 2002 section 28P(1).*

PROJECT PROTOCOLS

ERLC cannot issue a licence unless satisfied that the applicant has in place protocols:

- for using the licensed technique safely and effectively in a clinical trial for the purposes of minimising the risk of the women's offspring inheriting mitochondria that would predispose them to mitochondrial disease.[63]
- to ensure that trial participants or patients (as the case requires) have been fully informed about:
  - (i) the risks involved in using mitochondrial donation techniques, and
  - (ii) alternatives to using mitochondrial donation techniques.[64]

2.12 Protocols for clinical trial

Detail the protocols that will be in place for using the technique safely and effectively in the clinical trial for the purposes of minimising the risk of women's offspring inheriting mitochondria that would predispose them to mitochondrial disease.

Provide attachments if necessary and note the attachment numbers in this box.

Detail the protocols that will be in place for ensuring that clinical trial participants have been fully informed about:

(i) the risks involved in using mitochondrial donation techniques, and

(ii) alternatives to using mitochondrial donation techniques.

Provide attachments if necessary and note the attachment numbers in this box.

63 *Research Involving Human Embryos Act 2002* (Cth) section 28J(5)(a).
64 *Research Involving Human Embryos Act 2002* (Cth) section 28J(5)(g).

Section 3 – Obtaining proper consent

PROPER CONSENT

ERLC cannot issue a licence unless satisfied that proper protocols are in place so that proper consent is obtained before human gametes or genetic or reproductive material are used in carrying out the technique(s) authorised by the licence.[65]

When developing the consent process and documents, please consult:

- *Research Involving Human Embryos Act 2002* (Cth);
- ART Guidelines;
- National Statement; and
- any other relevant advice or guidelines issued by the NHMRC.

3.1.1 Overview of process for the responsible persons and mitochondrial donors to give proper consent for the use of their human eggs or human sperm under the licence.

Provide a detailed description of how and when proper consent will be obtained and recorded and how you will ensure that you notify ERLC that proper consent has been obtained before each human egg or human sperm is used under the licence.

Provide attachments and note the attachment numbers in this box.

3.1.2 Documents to be provided to obtain proper consent from responsible persons and mitochondrial donors

Attach copies of all documentation to be provided to responsible persons and mitochondrial donors to obtain proper consent and note attachment numbers in this box. Do not attach any signed consent forms or forms containing personal information about donors.

65 *Research Involving Human Embryos Act 2002* (Cth) section 28J(2).

3.1.3 Describe how you will ensure that any conditions on the consent given are adhered to.

3.1.4 Payment of reasonable expenses[66]

Specify the amount, if any, to be paid to research participants and/or donors and provide a justification for the level of reimbursement of reasonable expenses.

Describe what measures will be put in place to ensure that only reasonable expenses as defined by the *Prohibition of Human Cloning for Reproduction Act 2002* are paid and that no other inducement is offered.

Attach a copy of all documentation used and note attachment numbers in this box.

66 Note that under section 21 of the *Prohibition of Human Cloning for Reproduction Act 2002*, giving or receiving benefits, or offering to give or receive benefits, in excess of reasonable expenses, is a serious offence punishable by imprisonment for up to 15 years.

Section 4 – Compliance Matters

4.1	Detail the policies, procedures or protocols that are in place for ensuring that: (a) a human embryo is not allowed to develop for more than 14 days outside the body of a woman (b) no human egg or human sperm is used without the written consent of the donor or against any restrictions on that consent (c) any material created, developed or produced under the licence is not used unless expressly permitted by the licence (d) no human embryos are created for a woman who is a trial participant using the mitochondrial donation technique to which the licence relates without an approval from ERLC (e) a human embryo created for a woman who is a trial participant using the mitochondrial donation technique to which the licence relates is not placed in the body of the woman for the purposes of achieving her pregnancy without an approval from ERLC.

Provide attachments if necessary and note the attachment numbers in this box.

4.2 Detail the policies, procedures or protocols that are in place for the disposal of material produced by the activities authorised by the licence.

Mitochondrial donation licences may be subject to conditions relating to the disposing of material produced by using the relevant mitochondrial donation technique [28N(5)(f)] and 11A].

Provide attachments if necessary and note the attachment numbers in this box.

4.3 Describe the tracking system that will be used to identify the human eggs or human sperm used, or embryos created or used in the proposed activity.

Maintenance of a tracking system that links individual embryos, zygotes, eggs and sperm to a specific licence and donors will be a condition of a licence granted and NHMRC Inspectors will audit the system during their inspections.

Provide attachments if necessary and note the attachment numbers in this box.

Section 5 – Information updating

	It will be a licence condition of any mitochondrial donation licence granted that the licence holder notify ERLC of any changes to information provided in support of a mitochondrial donation licence application.
5.1	Identify any policies procedures or protocols that are in place for ensuring that any changes to any of the information provided are reported to ERLC

Provide attachments if necessary and note the attachment numbers in this box.

Section 6 – Requirements for ongoing monitoring protocols and notification of adverse events

The holder of a clinical trial licence must have in place, and comply with, protocols for:

- **monitoring the pregnancies of trial participants**
- **monitoring the ongoing health and development of children born as a result of the use of a mitochondrial donation technique**
- **seeking the ongoing engagement of trial participants and children, in relation to such monitoring, and**
- **notifying ERLC of any adverse events, for those participants or children, that the licence holder becomes aware of.**[67]

6.1 Provide a copy of protocols and any necessary explanatory material for:

(a) monitoring the pregnancies of trial participants

(b) monitoring the ongoing health and development of children born as a result of the use of a mitochondrial donation technique

(c) seeking the ongoing engagement of trial participants and children (or their legal guardian), in relation to such monitoring, and

(d) notifying ERLC of any adverse events, for those participants or children, that the licence holder becomes aware of.

Provide attachments and note the attachment numbers in this box.

6.2 Policies, protocols or procedures for ensuring proper record keeping for information about mitochondrial donors and any children born as a result of a pregnancy achieved under a mitochondrial donation licence.

A licence holder is required to keep records of information collected during the trial for 25 years.[68]

Provide attachments and note the attachment numbers in this box.

67 *Research Involving Human Embryos Act 2002* (Cth) section 28S(1).
68 *Research Involving Human Embryos Act 2002* (Cth) section 28R(4); *Research Involving Human Embryos Regulations 2017* (Cth) regulation 7K.

Section 7 – Information about mitochondrial donors and children born from the use of mitochondrial donation technique

ERLC cannot issue a licence unless satisfied that:

- **the applicant is likely to be able to comply with obligations relating to the collection and storage of information about donors and any children born from the technique, and**
- **the applicant has protocols in place to ensure that each donor in relation to a use of a technique is aware that any children born as a result of pregnancy through the technique will be able to obtain information about the donor from the Mitochondrial Donation Donor Registry.**[69]

7.1 **Provide details of how the information that must be collected under section 28R(1) of the *Research Involving Human Embryos Act 2002* (Cth) will be collected and updated throughout the duration of the licence and beyond.**

A licence holder must collect:

- the mitochondrial donor's full name
- the mitochondrial donor's residential address at the time the donor gave consent to the use of their egg
- the mitochondrial donor's date and place of birth
- the mitochondrial donor's email address
- any other information the donor gives the licence holder for the purposes of the Mitochondrial Donation Donor Register
- any other information prescribed by the regulations.

It is an offence under the *Research Involving Human Embryos Act 2002* (Cth) to intentionally or recklessly fail to comply with this obligation.[70]

Provide attachments if necessary and note the attachment numbers in this box.

69 *Research Involving Human Embryos Act 2002* (Cth) section 28J(5)(e) and (f).
70 *Research Involving Human Embryos Act 2002* (Cth) section 28R(8).

7.2 Provide details of how the applicant will satisfy the requirements under section 28R(3) of the *Research Involving Human Embryos Act 2002* (Cth) throughout the duration of the licence and beyond.

A licence holder must use their best endeavours to collect the name, sex, date of birth and any other information prescribed in the regulations for each child born as a result of a pregnancy achieved under a mitochondrial donation licence.

It is an offence under the *Research Involving Human Embryos Act 2002* (Cth) to intentionally or recklessly fail to comply with this obligation.[71]

7.3 Outline protocols to ensure that each mitochondrial donor is aware that any children born as a result of pregnancy achieved from the use of mitochondrial donation technique will as a result be able to obtain information about the mitochondrial donor from the Mitochondrial Donation Donor Registry.

71 *Research Involving Human Embryos Act 2002* (Cth) section 28R(8).

Section 8 – Information updating

	It will be a licence condition of any mitochondrial donation licence granted that the licence holder notify ERLC of any changes to information provided in support of a mitochondrial donation licence application.
8.1	Identify any policies procedures or protocols that are in place for ensuring that any changes to any of the information provided are reported to ERLC
	Provide attachments if necessary and note the attachment numbers in this box.

Section 9 – HREC evaluation of the proposal

9.1	Name of HREC
9.2	Chairperson of HREC Note that the Chairperson of the HREC is required to sign this application at Section 5
	Title
	Given names
	Surname
	Postal Address
	Courier Address
	Contact number
	Email address

9.3	Secretary (or other contact person) of HREC
	Title
	Given names
	Surname
	Postal address
	Courier address
	Contact number
	Email address
	Relationship to Applicant organisation
9.3.1	I have been given a copy of the *Mitochondrial Donation Licensing Scheme – Privacy and the protection of your personal information* notice.
	Yes ☐ No ☐
9.4	**HREC evaluation and approval/clearance.**
	Attach the HREC evaluation and approval/clearance of the proposed activity and indicate the attachment number here.

Section 10 – Confidential Commercial Information

10.1	**Does this application contain confidential commercial information?**
	Yes ☐ No ☐
10.2	**Identification of information**
	Provide attachments if necessary and note the attachment numbers in this box.

10.3	Justification for treatment of information as confidential commercial information
	Provide attachments if necessary and note the attachment numbers in this box.

Section 11 – Signatures

11.1 Organisation representative

I confirm that the *Mitochondrial Donation Licensing Scheme – Privacy and the protection of your personal information* (the privacy notice) has been provided to every person identifiable in this application form.

I acknowledge that I have read and understood the privacy notice.

I declare that to the best of my knowledge, having made reasonable inquiries, the information provided in this application is true and correct and not misleading.

I understand that providing misleading information to NHMRC is an offence under Commonwealth law.

Signature

Date

Printed name

Position

11.2 Principal supervisor
(If joint or alternate Principal Supervisors are named at 1.2.1, each one should sign the form here. Duplicate the section if required)

I acknowledge that I have read and understood the privacy notice.

I declare that to the best of my knowledge, having made reasonable inquiries, the information provided in this application is true and correct and not misleading.

I understand that providing misleading information to NHMRC is an offence under Commonwealth law.

Signature

Date

Printed name

Position

11.3 Chairperson of HREC

I acknowledge that I have read and understood the privacy notice.

I declare that the proposed research outlined in this application has been assessed and approved by the HREC that I chair and the information contained herein about that assessment is true and correct.

Signature

Date

Printed name

Position

Section 12 – Index of supporting information

PROVIDE AN INDEX OF SUPPORTING DOCUMENTATION WITH ATTACHMENT NUMBERS