ADVICE FOR PREPARING AN APPLICATION TO VARY A LICENCE

These notes provide detailed information about how to prepare an application to vary a NHMRC Licence under the *Research Involving Human Embryos Act 2002*. The numbering used corresponds to the numbering on the Embryo Research Licence (ERL) Application form.

HUMAN RESEARCH ETHICS COMMITTEE APPROVAL

Applications to vary aspects of the licensed activity or to change the consent process or consent documents must be approved by the institution's HREC and the assessment provided to the NHMRC Licensing Committee before the committee can finalise its decision. Consideration of the variation should reflect the issues and guidelines considered when the HREC approved the original licence application.

OTHER CONSIDERATIONS

The NHMRC Licensing Committee assesses applications to vary a licence in the same way it considered the original licence application.

As with the initial licence application, applicants should make themselves aware of any relevant State and Territory legislation and, where necessary, seek independent legal advice.

The information provided should be as comprehensive as possible – failure to provide adequate information is likely to result in delays in the NHMRC Licensing Committee reaching a decision about the variation.

The NHMRC Licensing Committee will make every effort to finalise its decisions in a timely manner. Administrative variations (see Chapter 3 of the Information Kit) can generally be considered out-of-session. Significant variations will require more time, as they are likely to be considered at a face-to-face meeting of the NHMRC Licensing Committee.

For significant variations the relevant sections of the approved licence application should be edited. New or altered information should be highlighted and the document should be resubmitted to the NHMRC Licensing Committee.

Applicants must consider whether the requested variation, if approved, can be implemented immediately or whether a transition period may be required. Situations where a transition period may be required include:

- Approval of a new Principal Supervisor in circumstances where a handover period will occur;
- Approval of a new site for the licensed activity where the activity may operate at both old and new sites for a period;
- Changes to the process or documents used for obtaining proper consent to use eggs or embryos required by changes to the licensed activity. It may not be practical to require the new processes or documents to be used with people who have already started the consent process.

If a transition period is required, note this at the relevant point in the application.

The licence holder may be required to provide additional written information to assist the NHMRC Licensing Committee to reach a decision about the variation.

A Working Group of the NHMRC Licensing Committee may ask to meet or have a teleconference with the applicant to clarify the information provided.

Documents that may be useful when preparing an application to vary a licence are listed below.

Legislation available from the Federal Register of Legislation website (https://www.legislation.gov.au/):

- *Research Involving Human Embryos Act 2002* (the RIHE Act);
- *Prohibition of Human Cloning for Reproduction Act 2002* (the PHCR Act); and
- Research Involving Human Embryos Regulations 2017.

Guidelines available from the NHMRC website (http://www.nhmrc.gov.au):

- *National Statement on Ethical Conduct in Human Research (2007) - updated May 2015* (the National Statement);
- *Ethical guidelines on the use of assisted reproductive technology in clinical practice and research, 2017* (the ART Guidelines);
- *Objective criteria for embryos that are unsuitable for implantation;*
- *Australian code of practice for the care and use of laboratory animals for scientific purposes 8th edition 2013;* and
- *The Australian Code for the Responsible Conduct of Research 2007* (the Code).

The National Statement and the ART Guidelines are prescribed by the Research Involving Human Embryos Regulations 2017 in relation to licence applications.

Specific Information
The following sections provide details of the information required for applications to vary specific parts of the licence. The numbering used corresponds to the numbering on the Licence Application form.

It is not possible for the NHMRC Licensing Committee to foresee all potential licence variations and to provide instructions for all eventualities. If the variation required is not covered by the information below please provide additional details in an attachment or covering letter.

Section 1 – Applicant Information

1.1 — Applicant Organisation (Licence Holder)

Changes to the organisation's address and other contact details must be notified to the NHMRC Licensing Committee.

1.1.1 — Applicant organisation (Licence Holder)
Any changes to the licence holder (for example, sale of an IVF clinic or merger of two companies etc.) may have significant consequences for the conduct of a licensed activity. If this situation occurs, provide full details of the change and its implications for continuation of the licensed activity. Refer to the Instructions for Completing the ERL Application Form for more information on the responsibilities of licence holders.

1.1.2 — Organisation representative
A change to the organisation representative during the life of the licence must be notified to the NHMRC Licensing Committee but is not considered to be a variation to the licence unless that person is also an Authorised Person under the licence (see Section 1.2 below).

1.1.3 — Contact person
A change to the Contact person during the life of the licence must be notified to the NHMRC Licensing Committee but is not considered to be a variation to the licence unless that person is also

an Authorised Person under the licence (see Section 1.2 below). The contact person must be familiar with the details of the project, application and licence.

1.2 — Proposed Authorised Persons

1.2.1 — Principal supervisor
The departure of a Principal Supervisor is a significant variation to a licensed activity. Standard licence condition 2301 requires that the departure of the Principal Supervisor must be notified to the NHMRC Licensing Committee within 7 days and, unless there is already another Principal Supervisor authorised by the licence, the licensed activity must cease until the NHMRC Licensing Committee has approved a new Principal Supervisor (Condition 4301).

- Provide the reasons for the variation, information about the new Principal Supervisor (as specified in the Licence Application form) and the arrangements in place to ensure continuity of the project and ongoing compliance with the licence conditions.

1.2.2 — Staff who will use excess ART embryos or human eggs, or create or use other embryos
It is necessary to vary the licence to add new authorised persons. It is a breach of the licence conditions if an unauthorised person conducts or participates in a licensed activity.

- Provide the information requested in the Licence Application Form and wait for approval from the NHMRC Licensing Committee before allowing the person to participate in the licensed activity.

The approval of an application to train an embryologist under a training licence has the effect of making them an authorised person for the period of their training.

If authorised persons leave the licence holder organisation or cease to be involved in the licensed activity for other reasons, their departure must be reported in the next six-monthly report. The NHMRC Licensing Committee will vary the licence at the next available opportunity.

1.3 — Specified Sites

1.3.1 — Site (or sites) of the proposed use
Addition of a new site or moving to a new site for conducting the licensed activity is a significant variation. Provide the following information:

- the date of effect
- why the new site is required and whether it has the necessary equipment and personnel
- whether the new site is in addition to or a replacement for the previous site
- whether there are any other related variations such as changes to the list of authorised persons and sites of storage of laboratory records.

Where a move takes place over a period of time and it is proposed that the licensed activity continues during this period, it will be necessary to ensure that the licence allows for the period of overlap by licensing both the old and new sites for the relevant period.

1.3.2 — Site (or sites) of records (other than patient records) associated with the proposed use
See comments for 1.3.1 above if variations to the site of storage of laboratory records are required.

1.3.3 — ART clinic or other organisation from which the excess ART embryos or human eggs or other material will be obtained

- Provide details of the reasons for the variation including information about how consent processes will be conducted at the new site (if applicable).

1.3.4 — Site (or sites) of patient records (including original consent documents) associated with the proposed use

Changes to the sites of storage of patient records are generally considered to be administrative variations.

- Provide the old and new addresses and the date of the move. Licence documents will be updated to reflect the change.

If patient records relating to licensed activities are archived to a commercial storage facility please describe how records will be made available if required during a monitoring inspection.

SECTION 2 — PROJECT DESCRIPTION

2.1 — Proposed use of excess ART embryos or human eggs, or creation or use of other embryos

If the proposed variation required changes to the categories of activities authorised by the licence the NHMRC Licensing Committee would generally consider that this should be submitted as a new application rather than a variation to an existing licence. Consult Embryo Research Licensing for advice before preparing the application for such a variation.

2.2 — Proposed commencement date of variation

The new/varied activity must not commence until authorised by the varied licence.

2.3 — Extension of duration of activity

Provide a realistic timeframe for the duration of the proposed extension to the licence duration. The NHMRC Licensing Committee will then determine an appropriate expiry date for the extended licence if approved.

The request for an extension to the duration of the licence must include the reasons for requiring the extension and an analysis of whether the project is likely to be completed within the revised timeframe.

The justification for the extension will refer to progress with the licensed activity to date (and/or reasons for lack of progress) and may include published papers, the biannual reports to the NHMRC Licensing Committee and other material as appropriate. The justification will also need to address the state of the art in other relevant research groups. A project which may have had a reasonable likelihood leading to a significant advance in knowledge when the licence was issued may have been overtaken by other research by the time an extension is required.

The NHMRC Licensing Committee will also consider the licence holder's compliance history when making decisions about extensions to licences.

2.4 — Title of proposed activity

The NHMRC Licensing Committee does not envisage that the title of a licensed activity would change significantly during the life of a licence. If variations are proposed such that it would be necessary to change the title of the licence, the committee considers it is likely that an application for a new licence would be more appropriate. Consult Embryo Research Licensing for advice in this situation.

2.5 — Short lay statement about the nature of the proposed use

Any changes to the lay statement should be minor, providing more detail or clarifying the project. An application which seeks to significantly expand or change the scope of the original licence may not be considered as a variation.

2.6 — Detailed description of the proposed project

In circumstances where a licence holder is proposing a variation to the project design, provide details on the following:

- **Aims/goals** – describe how the proposed variation remains consistent with the specific aims or goals of the project authorised by the current licence. Include a clear statement of the new or varied hypothesis to be tested (if applicable). Include the reasons for requesting the proposed change
- **background** – describe the progress to date for the licensed activity and the reasons for the proposed change to the project. Include an analysis of changes to the state of knowledge in the area since the licence was issued and refer to relevant literature
- **methodology and experimental design** – describe the revised research plan in detail, including as appropriate, a detailed description of the experimental design, techniques to be used and methods of statistical analysis
- **outcomes** – describe how the proposed changes will affect the outcomes and endpoints of the activity already licensed.

It is essential that sufficient detail is provided to allow the NHMRC Licensing Committee to gain a clear understanding of the aims of the proposed variation, the precise nature of the activity and the reasons for the proposed changes. It will also be valuable to note the aspects of the project which will not change.

2.7 — Excess ART embryos, other embryos or human eggs likely to be used and justification for the number requested

2.7.1 to 2.7.3 — Number of excess ART embryos, other embryos or human eggs likely to be necessary to achieve the goals of the proposed activity

- Record the number of excess ART embryos, other embryos or human eggs likely to be necessary to achieve the goals of the proposed activity if varied as requested in this application.

2.7.4 to 2.7.6 Justification for the number of excess ART embryos, other embryos or human eggs requested above

- Explain **why** the varied number of excess ART embryos, other embryos or human eggs is considered to be necessary to achieve the goals of the proposed activity or project (refer to s. 21(4)(a) of the RIHE Act). If the application requests substantially larger numbers of embryos or eggs, also provide information about the likely availability of the required numbers. This may include information about the numbers of potential donors approached and the numbers giving consent during the licence to date.

  If any of the details originally provided have changed since the licence was issued (or since a previous variation was approved), provide revised information. Refer to the Instructions for Completing the Application Form for more information.

2.8 — Likelihood of significant advance in knowledge or improvement in technologies for treatment

2.8.1 to 2.8.3 — Likelihood of a significant advance in knowledge or improvement in technology as a result of the use of the excess ART embryos or human eggs or creation or use of other embryos

If any of the details in sections 2.8.1 to 2.8.3 have changed since the licence was issued (or since a previous variation was approved), provide revised information. Refer to the Instructions for Completing the Application Form for more information.

2.9 Justification for why the advances described above could not reasonably be achieved by other means

Since scientific progress in this area is very rapid, any applications to vary the licensed activity or to increase the number of excess ART embryos, other embryos or human eggs must include a reappraisal of the necessity for conducting the licensed research in the light of the requirement to explain why the advances could not reasonably be achieved by other means (see section 21(4)(b) of the RIHE Act).

SECTION 3 — OBTAINING PROPER CONSENT FOR THE USE OF EXCESS ART EMBRYOS OR HUMAN EGGS, OR CREATION OR USE OF OTHER EMBRYOS

Applicants must reconsider the approved consent process and documents in the light of any requested variation to the licensed activity. The NHMRC Licensing Committee considers that any variations which require a major change to the consent process would be better presented as an application for a new licence. However, licence holders may prefer to make a case for consideration of the change as a variation to an existing licence. Consult Embryo Research Licensing for advice in this situation.

The NHMRC Licensing Committee recognizes that minor changes to consent documents may be necessary from time to time. Such changes could include:

- changes to the process or contact person for making complaints or enquiries
- changes to phone numbers or addresses listed in the consent documents
- correction of typing errors
- minor amendments to improve clarity, or
- a change to the name of the HREC.

If minor changes are required, the licence holder should edit the process and/or documents and obtain approval from the HREC if required by organisation policy.

- If allowed by the licence conditions, it is not necessary to obtain approval from the NHMRC Licensing Committee before commencing use of the amended version(s), provided the process and documents remain consistent with the versions previously approved by the NHMRC Licensing Committee and the applicable consent checklist. However, the licence holder will be required by the licence conditions to provide the current version for checking if requested by NHMRC inspectors and will also be required to report on any changes in the 6-monthly reports required by Condition 3001.
- If the licence conditions do not permit this approach to managing consent processes and documents, it will be necessary to obtain approval from the NHMRC Licensing Committee before using amended versions.

3.1 — Overview of proper consent process

If proposed variations to the licensed activity require changes to the consent process or documents, refer to the Instructions for Completing the Application Form for the information required about the consent process. Indicate clearly those aspects of the process which will change and those which will stay the same. Complete a new copy of the applicable Consent Checklist and include it with the variation application.

3.2 — Documents to be provided to obtain proper consent

Provide new versions of the consent documents if required. Versions which highlight the changes (or show them as “track-changes”) are usually the most effective method of presentation. If not

already required at 3.1 above, complete a new copy of the applicable Consent Checklist and include it with the variation application.

3.3 — Payment of reasonable expenses

Provide details of any changes to the information previously supplied.

SECTION 4 – COMPLIANCE ISSUES

4.1 — Tracking system

Provide information about any proposed changes to the tracking system.

SECTION 5 — HREC EVALUATION OF THE PROPOSAL

The HREC is required to approve all proposed variations to an issued licence which change the licensed activity, the consent process or consent documents. The NHMRC Licensing Committee does not require the HREC to be involved in variations to sites of the licensed activity or records storage or changes to authorised personnel (unless the changes to personnel adversely affect the ability of the licence holder to conduct the licensed activity). However, if local procedures require the HREC to consider all variations, the local procedures should be followed.

If applicable, the HREC assessment of the variation must be provided to the NHMRC Licensing Committee before the application to vary the licence can be finalised. It is desirable that the HREC assessment accompanies the application for the variation.

5.1 — HREC contact information

5.1.1 — Name of HREC
5.1.2 — Chairperson of HREC
5.1.3 — Secretary (or other contact person) of HREC
Please provide information about any changes as necessary. Changes to HREC contact details during the life of the licence should be notified to the NHMRC Licensing Committee but are not considered to be a variation to the licence.

5.2 — HREC consideration of application

See information above in the introduction to this section and complete this section if required by the nature of the variation.

5.2.1 - Date of HREC approval
Provide the date on which the HREC gave approval to the proposal to vary the licence.

5.2.2 — HREC evaluation and approval/clearance
If applicable, a statement signed by the chair of the HREC must be appended. The statement should be similar to the statement included in the original licence application. Refer to the Instructions for Completing the Licence Application form for more information.

SECTION 6 – AEC EVALUATION OF THE PROPOSAL

If required by the nature of the licence and the requested variation please provide any new or changed information.

6.1 — AEC contact information

6.1.1 — Name of AEC
6.1.2 — Chairperson of AEC
6.1.3 — Secretary (or other contact person) of AEC
Please provide information about any changes as necessary. Changes to HREC contact details during the life of the licence should be notified to the NHMRC Licensing Committee but are not considered to be a variation to the licence.

6.2 — AEC evaluation and approval

6.2.1 - Date of AEC approval
Provide the date on which the AEC gave approval to the proposal to vary the licence. Please also indicate the date on which the validity of the approval ceases.

6.2.2 — Compliance with NHMRC Australian code of practice for the care and use of animals for scientific purposes 8th edition 2013
Refer to the Instructions for Completing the Application Form for details of the information required.

6.2.3 — AEC evaluation and approval/clearance
Please attach a statement signed by the Chair confirming that the committee has approved the proposed variation to the use of animals in the project.

SECTION 7 — CONFIDENTIAL COMMERCIAL INFORMATION

If any information provided as part of an application to vary a licence is considered to be commercially confidential please complete Section 7. If the variation changes information already provided please update and resubmit the earlier statement.

7.1 — Identification of information
7.2 — Justification for treatment of information as confidential commercial information

Refer to the Instructions for Completing the Application Form for details of the information required.

SECTION 8 — SIGNATURES

Applications to vary a licence should be signed by either the Organisation Representative or the Principal Supervisor or the Contact Person as considered appropriate by the licence holder.

The HREC assessment should be signed by the HREC Chair or Secretary.

SECTION 9 — INDEX OF SUPPORTING INFORMATION

Provide an index of all supporting information attached to the variation application.

VARIATION APPLICATION CHECKLIST

Use the checklist below to ensure that all steps in the variation application process have been completed.

	Yes	No
Has a detailed proposal been developed and submitted to the HREC for approval (if required by the type of variation)?		
Has the variation been approved by the HREC (if required by the type of variation)?		
Has the variation application been proof-read?		
Do the consent documents and process continue to accurately reflect the project described in the application form and are new versions (including a new version of the completed consent checklist) provided if required?		
Will a transition period be required if the variation is approved?		
Is the signed written evaluation prepared by the HREC attached (if applicable)?		
Has the application been signed as outlined in section 8?		
Are all other relevant documents/approvals detailed in the variation application including CVs, consent documents, project description, relevant published articles as applicable attached to the application?		
Has the application been submitted to: embryo.research@nhmrc.gov.au?		