Standard Operating Procedures
for
Streamlining Ethical Review of Research Projects

in Victoria and as part of National Mutual Acceptance

Version: August 2017

Scope

These Standard Operating Procedures (SOPs) describe the procedures and processes in place for the system of streamlined ethical review of multi-site research projects in Victoria and under the National Mutual Acceptance (NMA) initiative.

These SOPs describe the regulatory aspects of a clinical trial or health/medical research project. For guidance on the conduct of research, contact your organisation's research office or visit http://ichgcp.net.

These SOPs provide guidance only; they do not describe research processes in their entirety, and should not be relied upon as a sole source of information for conduct of a research project.

These SOPs provide general guidance for investigators, trial coordinators, sponsors, CROs and other parties in all sectors of clinical, health and medical research. Specific SOPs are also available for *Coordinators of Reviewing HRECs* and *Research Governance Officers*.

Research on humans must be conducted in a safe and ethically responsible manner. Ethical and scientific review should be in accordance with the *National Statement on Ethical Conduct in Human Research* (NHMRC, 2007).

For detailed guidance on research governance and site specific assessment (SSA), refer to *Research Governance and Site Specific Assessment – Process and Practice* (available to download from the websites below).

For queries regarding these SOPs, or the ethics and governance processes for research projects in Victoria and NMA, please contact the Coordinating Office.
Tel. 03 9096 7398 or email multisite.ethics@dhhs.vic.gov.au.

Clinical Trials and Research website: www2.health.vic.gov.au/about/clinical-trials-and-research/clinical-trial-research

Contents

Glossary	
ACT	Australian Capital Territory
AE	Adverse Event
AHEC	Australian Health Ethics Committee
ARPANSA	Australian Radiation Protection and Nuclear Safety Agency
AU RED	Australian Research Ethics Database
CAS	Central Allocation System (Victoria)
CCS	Central Coordinating Service (Queensland)
CIRA	Clinical Investigation Research Agreement
CPI	Coordinating Principal Investigator
CRG	Collaborative Research Group
CRO	Contract Research Organisation
CTN	Clinical Trial Notification
CTX	Clinical Trial Exemption
CTRA	Clinical Trial Research Agreement
DHHS	Department of Health and Human Services (Victoria)
FTIH	First Time in Human
HREA	Human Research Ethics Application
HREC	Human Research Ethics Committee
IMA	Interstate Mutual Acceptance (superseded by NMA)
LNR	Low and Negligible Risk
LNR VIC	Victorian Low and Negligible Risk application form
LNR VIC SSA	Victorian Low and Negligible Risk Site Specific Assessment application form
MA	Medicines Australia
MDF	Minimal Dataset Form
MOU	Memorandum of Understanding
MTAA	Medical Technology Association of Australia
NEAF	National Ethics Application Form
NHMRC	National Health and Medical Research Council
NMA	National Mutual Acceptance
NSW	New South Wales
PI	Principal Investigator
PICF	Participant Information and Consent Form
QLD	Queensland
RGO	Research Governance Officer
RSO	Radiation Safety Officer
SA	South Australia
SAE	Serious Adverse Event
SCD	Submission Closing Date
SEBS	Southern Eastern Border States
SOP	Standard Operating Procedure
SSA	Site Specific Assessment
SUSAR	Suspected Unexpected Serious Adverse Reaction
TGA	Therapeutic Goods Administration
USADE	Unanticipated Serious Adverse Device Effect
VIC	Victoria
VMIA	Victorian Managed Insurance Authority
VSM	Victorian Specific Module
WA	Western Australia
WASM	Western Australian Specific Module

SOP 01 Streamlined Ethical Review of Multi-site Research Projects

Purpose To describe the scope of streamlined ethical review of multi-site research projects in Victoria

1.1 Multi-site research means research to be conducted at more than one site including:
- Conduct of research at more than one organisation
- Research conducted jointly by investigators affiliated with different organisations
- A project conducted at an organisation where the investigator is affiliated with another organisation and where more than one organisation requires ethical review and approval of the same research project.

1.2 The streamlined system for ethical and scientific review of multi-site research projects applies to all human research, as defined in the *National Statement on Ethical Conduct in Human Research* (2007) (or any replacement of that document published by the National Health and Medical Research Council (NHMRC)), for which an application must be made to an HREC for the purpose of conducting research at a public health organisation. This will include low and negligible risk research review.

1.3 The streamlined system is principally for use in public health organisations; however, private organisations may accept the review of a reviewing HREC in the streamlined system. No formal agreement is required by the private organisation but there must be a written agreement between the private organisation and the reviewing HREC.

1.4 Victorian organisations that are a signatory to a Memorandum of Understanding (MOU) with the Department of Health and Human Services will become participating organisations. Participating organisations must agree to the following:
- Accept the ethical and scientific review of a reviewing HREC and not undertake any further review by the organisation's HREC
- All research proposals must undergo a process of site specific assessment (SSA) that will be conducted by the participating site as part of an institution's research governance responsibilities
- Consistency of HREC review standards and processes, and ongoing participation in professional development of ethics committee members and related stakeholders
- A research project must not commence at a site unless the following has been completed:
  - The project has received ethical approval from a reviewing HREC
  - SSA has been conducted at the site where the research is to be undertaken
  - The Chief Executive or delegate has seen the HREC approval and endorsed the SSA giving authorisation for the project to be conducted at the site.

1.5 The streamlining initiative is designed to facilitate one ethics review for research at multiple sites. These SOPs also equally apply to single-site research projects with regards to policy and processes around preparing ethics and site assessment applications and post-approval reporting and monitoring.

SOP 02 National Mutual Acceptance

Purpose To outline the National Mutual Acceptance (NMA) initiative, its scope and state-specific requirements

2.1 National Mutual Acceptance (NMA) is a national initiative for mutual acceptance of ethical and scientific review in public hospitals for multi-centre clinical trials. Development of NMA is a phased approach – currently the Australian Capital Territory, New South Wales, Queensland, South Australia, Victoria and Western Australia are participating.

Multi-centre research projects being submitted for ethical and scientific review, and taking place in one or more of the participating jurisdictions, are eligible for single ethical and scientific review at public health organisations.

2.2 Each proposal for a multi-centre research project conducted across the participating states will be ethically and scientifically reviewed once only by a public health organisation HREC that is nominated by state/territory health departments and certified by the NHMRC. The exception is for those projects that require specialist review.

2.3 NMA superseded the Interstate Mutual Acceptance (IMA) initiative that was in place for NSW, QLD and VIC. Multi-centre clinical trials that received ethics approval as part of the IMA initiative will remain under the arrangements in place at the time of that ethics approval.

2.4 The scope for NMA includes all research projects, both clinical trials (e.g. interventional research involving a drug/device trial, radiation therapy, surgery, treatment or diagnostic procedure and studies associated with ongoing activities relating to trials that have been conducted) and non-clinical trials (e.g. clinical research, post-trial activities such as observational research and evaluation of a trial, other post-marketing surveillance activities, and registries).

2.5 Certain research projects are excluded from mutual acceptance because of State specific requirements; details can be found in the **NMA Fact Sheet** and **NMA Standard Principles for Operation** (both available from www2.health.vic.gov.au/about/clinical-trials-and-research/clinical-trial-research) These projects will continue to be reviewed under the current local jurisdictional arrangements.

2.6 The application submission process depends on the jurisdiction to which the applicant chooses to submit the research project for ethical and scientific review. In ACT, NSW, SA and WA, the selection of the certified HREC is at the discretion of the applicant. In QLD, applications are allocated by using a website booking system: www.health.qld.gov.au/ohmr/html/regu/cen_coord_serv.asp, and in VIC applications are allocated by the Central Allocation System (CAS) on 03 9096 7395.

2.7 The Victorian-Specific Module (VSM) is a mandatory document in addition to the HREA. As part of the ethics application process, a completed VSM is required to address Victorian-specific legislation.

If a research project is being submitted for HREC review under the NMA initiative and there is a Victorian site participating in the research project, the VSM must be submitted, along with the HREA, to the reviewing HREC.

If the CPI is based outside Victoria, it is recommended that the VSM is completed and endorsed by a Victorian PI based at a participating Victorian site, as they will have familiarity with the relevant legislation. The interstate CPI may sign the VSM, or alternatively the PI may endorse it.

2.8 The Victorian Low and Negligible Risk application form (LNR VIC) is a state-specific form and must **not** be used for a NMA application. All NMA applications, including those that are considered low risk, must be submitted using the HREA.

SOP 03 Coordinating Principal Investigator, Principal Investigator, Reviewing HREC Coordinator and Research Governance Officer

Purpose To describe the roles and responsibilities of the Coordinating Principal Investigator (CPI), Principal Investigator (PI), Reviewing HREC Coordinator and Research Governance Officer (RGO) in a research project

Coordinating Principal Investigator (CPI)

3.1 The CPI is the individual who takes overall responsibility for the research project and submits the project for ethical and scientific review. The CPI is responsible for ongoing communication with the HREC and communicating with the PIs, sponsor/CRO and project coordinator. The CPI is also the PI for their own site.

3.2 One CPI must be nominated for each research project. The CPI must be employed and professionally based in an Australian public health organisation. For international research projects with a co-ordinating investigator outside Australia, a health professional based in Australia must be nominated as the CPI responsible for the conduct of the research in Australia.

3.3 The CPI for a multi-site research project is responsible for submission of an application to a reviewing HREC. The CPI does not need to have any professional affiliation with the institution that hosts the reviewing HREC.

3.4 The CPI has responsibility for correspondence relating to the ethical review and the reviewing HREC in accordance with the *National Statement on Ethical Conduct in Human Research* (NHMRC, 2007), chapter 5.2. This responsibility may, in part, be delegated to a person who will act as a contact person on behalf of the CPI. Correspondence may be delegated by the CPI regarding contact with the PIs at other organisations conducting the research project.

3.5 If the CPI is absent or unavailable for a significant period then another Investigator must be nominated to replace them as the CPI. The reviewing HREC must be notified of this change via an HREC amendment process.

3.6 Further information on the role and responsibilities of the CPI is available from www2.health.vic.gov.au/about/clinical-trials-and-research.

Principal Investigator (PI)

3.7 The PI is the individual who takes responsibility for the overall conduct, management, monitoring and reporting of research conducted at a site and submits the research project for research governance/site specific assessment (SSA) authorisation.

3.8 The PI (or delegate) is responsible for corresponding with the site's RGO regarding all matters relating to the research project at that site.

3.9 The PI is not responsible for communication with the reviewing HREC. Any matters for attention of the HREC should be forwarded to the CPI (or delegate).

3.10 Further information on the role and responsibilities of the PI is available from www2.health.vic.gov.au/about/clinical-trials-and-research.

Every research project has one Coordinating Principal Investigator (CPI).

Every site in the research project has one Principal Investigator (PI).

Reviewing HREC Coordinator

3.11 The reviewing HREC Coordinator is an important intermediary between the CPI and the HREC. They are responsible for communicating with the CPI (or delegate) of the research project regarding the application for ethical and scientific review.

3.12 Following e-Submission of the HREC application, the reviewing HREC Coordinator will perform a validation assessment prior to the application being reviewed by the HREC.

3.13 The HREC Coordinator's responsibilities include sending letters and relevant documentation relating to the HREC application to the CPI, who will then forward the information to other parties as required.

3.14 *SOPs for Coordinators of Reviewing HRECs* are available from www2.health.vic.gov.au/about/clinical-trials-and-research.

Research Governance Officer (RGO)

3.15 Research Governance is a framework for institutions to use to ensure that research is conducted responsibly and safely and is scientifically and ethically sound. Research Governance considers legal compliance, financial management, accountability and risk management associated with research at a participating site. In the system for streamlined ethical review of multi-site research projects, research governance is administered by the process of site specific assessment (SSA).

3.16 The RGO is the individual appointed within an organisation who is responsible for the management of applications for site authorisation and administrative oversight of authorised research projects.

The RGO is responsible for reviewing the SSA form and making a recommendation to the Chief Executive (or delegate) to authorise or not authorise the conduct of the research project at that site.

3.17 It is a matter for the organisation to determine who will be responsible for research governance and site specific assessment, and any delegation of responsibility.

3.18 The RGO should liaise with the site PI to ensure timely SSA authorisation is achieved; they should provide assistance or advice to the PI as needed.

3.19 *SOPs for Research Governance Officers* and *Research Governance and Site Specific Assessment – Process and Practice* are available from www2.health.vic.gov.au/about/clinical-trials-and-research.

SOP 04 Completing Ethics and Research Governance Application Forms

Purpose To describe use of Online Forms to complete the HREA (or LNR VIC) and SSA (or LNR VIC SSA) forms for ethics and governance applications respectively.

Ethics Application

4.1 The Human Research Ethics Application (HREA) is a standard Australian form, created and owned by NHMRC, to be used for ethics applications for research projects involving human participants. The Online Forms website (https://au.ethicsform.org) contains a licensed copy of the HREA.

The HREA supersedes the National Ethics Application Form (NEAF). An application that was prepared on the Online Forms website using a NEAF may still be submitted to a reviewing HREC in Victoria.

4.2 Victoria has a Low and Negligible Risk form (LNR VIC) for appropriate Victorian single-site low risk research projects. **The LNR VIC must not be used for multi-site research projects**. All multi-site ethics applications, including those that are considered low risk, must be submitted using the HREA. Consult with the research office of the reviewing HREC prior to completing an ethics application form.

Guidance on projects that are low and negligible risk is in SOP 05.

4.3 The Online Forms website (https://au.ethicsform.org) allows the applicant (CPI or delegate) to complete the HREA or LNR VIC and submit it electronically. In order to use Online Forms, an applicant must first register for an account. Online Forms must be used for the completion of applications to a reviewing HREC.

Research Governance Application

4.4 Research governance is administered by the process of site specific assessment (SSA). SSA forms are used to address research governance associated with an ethics application.

A SSA form for research governance at a participating site is completed and submitted using the Online Forms website (https://au.ethicsform.org).

If an ethics application is being reviewed in ACT, NSW, QLD, SA or VIC, the SSA forms are created from the HREA for that particular research project. The CPI (or delegate) must create the Victorian SSA forms using the Online Forms website.

If an ethics application is being reviewed in WA, the CPI (or delegate) must create the SSA forms for Victoria using the Online Forms website; the Victorian SSA forms are created from the Minimal Dataset Form (MDF).

Once created by the CPI, the SSA forms should be transferred to each participating site's PI in Victoria.

4.5 Following submission of the ethics or research governance application to the reviewing HREC, Online Forms allows the applicant to view the progress of the application. The applicant can also nominate colleagues to have access to this information in their own Online Forms account (refer to the *Online Forms Handbook* p23 at www2.health.vic.gov.au/about/publications/policiesandguidelines/online-forms-handbook).

4.6 Online Forms is operated by Infonetica Ltd. The IT helpdesk assists users with technical problems. 10am - 4pm AEST Monday - Friday. Tel 02 9037 8408, email helpdesk@infonetica.net.

Getting started with Online Forms

- In order to use Online Forms, an applicant must first register for an account.
- Online Forms website: https://au.ethicsform.org
- The Online Forms welcome screen allows new users to create an account.
- Once the login (email address) and password are submitted, the 'My Projects' page appears. The blue navigation bar at the top of the page is used to access the main menu.
- Select 'My Projects' and 'Create new project', then indicate the jurisdiction in which the ethics application will be submitted
- Under 'Ethics Form Type', select HREA or LNR VIC or MDF as required.
- Use the 'My Project' hyperlink to access the 'Email Notifications' tab. Nominate colleagues to receive communication about the project (HREA **and** SSA, or LNR VIC **and** LNR VIC SSA). Select 'Send email' to include that person in email communication from the reviewing organisation; select 'Submission tab access' for them to have read-only access to the application in their own Online Forms account.
- *Online Forms Handbook* is available from www2.health.vic.gov.au/about/publications/policiesandguidelines/online-forms-handbook

SOP 05 Low and Negligible Risk Projects

Purpose Guidance on determining if a project is low and negligible risk or not, in consultation with the proposed reviewing organisation

5.1 The applicant must always discuss the project with the reviewing organisation's research office prior to creating an ethics application.

5.2 The LNR VIC application form may only be used for a single-site ethics application in Victoria, not for a multi-site application. Some reviewing HRECs may not accept the LNR VIC, and will request all ethics applications to be submitted on the HREA.

The choice of ethics application form (HREA or LNR VIC) is dependent on the level of risk and the policy of the reviewing HREC, and so it is important to communicate with the research office at an early stage.

Examples of Risk Types	
Physical harm	Includes injury, illness, pain
Psychological harms	Includes feelings of worthlessness, distress, guilt, anger or fear related, for example, to disclosure of sensitive or embarrassing information, or learning about a genetic possibility of developing an untreatable disease
Devaluation of personal worth	Includes being humiliated, manipulated or in other ways treated disrespectfully or unjustly
Social harm	Includes damage to social networks or relationships with others; discrimination in access to benefits, services, employment or insurance; social stigmatisation; and findings of previously unknown paternity status
Economic harm	Includes the imposition of direct or indirect costs on participants
Legal harm	Includes discovery and prosecution of criminal conduct

Definitions	
Risk	A potential for harm, discomfort or inconvenience. It involves (a) the likelihood that a harm (or discomfort or inconvenience) will occur; and (b) the severity of the harm, including its consequences.
Negligible Risk	Research where there is no foreseeable risk of harm or discomfort and any foreseeable risk is no more than inconvenience.
Low Risk	Research where the only foreseeable risk is one of discomfort.
High Risk	Research where the risk is more serious than discomfort.

5.2 For example use this checklist within the LNR VIC application form to assess the level of ethical review that may be required for a research project.

Type of Risk	**Negligible risk**	**Low risk**	**High risk**
Physical harm	☐	☐	☐
Psychological harm	☐	☐	☐
Devaluation of personal worth	☐	☐	☐
Social harm	☐	☐	☐
Economic harm	☐	☐	☐
Legal harm	☐	☐	☐
Discomfort	☐	☐	☐
Inconvenience	☐	☐	☐

- If any 'High risk' → **Full HREC Review** is required.
- If any 'Negligible risk' or 'Low risk' but no 'High risk' → **Low Risk Ethical Review** at a minimum. Discuss the level of review with the reviewing organisation's research office.
- If 'Negligible risk' only (which can only relate to 'inconvenience') → may be exempt from ethical

review but may require another type of review. Discuss the level of review with the reviewing organisation's research office.

- For Quality Assurance application, discuss the level of review with the reviewing organisation's research office.

5.3 Use the information below to determine the review process. Consult with the reviewing organisation's research office to confirm.

Low Risk research includes:

a. Questionnaire studies that **do not** involve:
   - Personally intrusive questions
   - A major time commitment from staff and/or patients
   - Plans to publish information that could potentially identify specific individuals

b. Most student projects involving data collection (by questionnaires or from records) from small numbers of patients

c. Some quality assurance projects – particularly those involving minor privacy concerns

d. Clinical research projects involving only patient record review

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Refer to the reviewing organisation's policy on the review process for Low risk research

High Risk research includes:

a. Clinical trials involving new therapies used for new indications

b. Involvement of vulnerable groups, see Chapter 4 *National Statement* (e.g. children/foster care, mental health, indigenous populations)

c. Major surveys or epidemiological studies involving extensive data collection from patients

d. Studies involving the extraction of personally sensitive information from records

e. Research involving invasive procedures

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Full HREC review

SOP 06 Allocating a Multi-site Research Project Ethics Application to a Reviewing HREC

Purpose To describe the process for selecting and allocating a HREC to review an application

6.1 For NMA applications, the CPI and colleagues should decide in which jurisdiction the application will be submitted for review. For applications in QLD, book through www.health.qld.gov.au/ohmr/html/regu/cen_coord_serv.asp. For applications in VIC, contact the Central Allocation System (CAS) on 03 9096 7395. In ACT, NSW, SA and WA, contact the research office of the proposed reviewing HREC.

6.2 Information on Victorian reviewing HRECs and meeting dates is available from www2.health.vic.gov.au/about/clinical-trials-and-research or the website of the organisation hosting the reviewing HREC.

6.3 To determine the reviewing HREC in Victoria, the CPI (or delegate) should contact CAS on 03 9096 7395. This should occur when the sponsor and/or CPI have identified the proposed sites to conduct the research project, and before the completion of the application. At the time of calling CAS, the applicant should be ready to submit the application within two to four weeks.

6.4 Some HRECs have a limited number of streamlined application slots for review at a meeting. If the applicant has a strong preference regarding their choice of reviewing committee, they should call CAS early to avoid disappointment or delay.

6.5 The CAS caller will be asked to provide information regarding the application so that it can be allocated to a suitable reviewing HREC. The names of all known participating sites are required, as well as details of the CPI.

6.6 Once the questions have been answered, the CAS operator will allocate the application to a reviewing HREC. An email will be sent to the CPI, the caller (if not the CPI) and the reviewing HREC Coordinator. The email contains the:
- **HREC Reference Number**
- Reviewing HREC name
- HREC meeting information

6.7 The **HREC Reference Number**, generated during the CAS process, is the unique identification number for the application. It **must** be entered on the HREA using Online Forms. All communication with the reviewing HREC and RGO(s) throughout the duration of the research project should clearly state the **HREC Reference Number**.

6.8 Once the application has been allocated, the reviewing HREC Coordinator will automatically receive an email notification and the application details will appear in the organisation's AU RED account.

6.9 The HREC Coordinator may override the CAS allocation to the selected meeting, should they have reason to do so. They must notify the CPI if this occurs

6.10 Once the application has been assigned to a reviewing HREC, the CPI (or delegate) should communicate with the reviewing HREC Coordinator to confirm the allocation, and regarding all subsequent matters relating to the application. The application is submitted electronically to the reviewing HREC research office (refer to SOP 07).

6.11 If it emerges that the application will not be submitted by the submission closing date, the CPI (or delegate) **must** contact the reviewing HREC Coordinator **and** CAS. Applications can be postponed until a later HREC meeting.

6.12 Note: For single-site applications the HREC Reference Number is generated when the HREC Coordinator uploads the e-submitted application into AU RED. The HREC Reference Number is auto-populated on the HREA or LNR VIC form.

SOP 07 Submitting an Ethics Application for a Multi-site Research Project

Purpose To detail the process for submitting an application to a reviewing HREC

7.1 For multi-site research projects, all ethics applications must be prepared using the HREA completed on the Online Forms website https://au.ethicsform.org (refer to SOP 04).

7.2 A completed VSM to address Victorian-specific legislation must be attached to the HREA. The VSM and other required documents must be uploaded to Online Forms when completing the ethics application (refer to SOP 04). To determine the supporting documents required for the application, refer to the **Ethics Cover Letter and Checklist** (available from www2.health.vic.gov.au/about/clinical-trials-and-research).

7.3 When the ethics application form is complete, it must be signed by the CPI using electronic authorisation available on Online Forms; other PIs are not required to sign. On Online Forms supporting documents must be uploaded to the application form and the whole application must be electronically submitted to the reviewing organisation.

7.4 A completed **Ethics Cover Letter and Checklist must** be attached to the application submitted to the reviewing HREC research office (available from the websites above in 7.2)

7.5 Contact the reviewing HREC research office if you have any queries regarding the documents required for submission.

Providing good quality documents to the HREC research office will enable a quicker HREC review process.

7.6 After the application is submitted to the HREC research office by the CPI (or delegate), it must be validated by the reviewing HREC Coordinator before progressing for HREC review.

7.7 The applicant (and any others whom they have nominated) can view real-time information on the progress of a submitted application on the Online Forms 'Project Progress' tab. Refer to the *Online Forms Handbook* (available from websites above) for information.

7.8 If an application is withdrawn and the applicant later wishes to re-submit, a new CAS booking must be made and it will be treated as a new application. A new HREC Reference Number will be issued.

7.9 A **HREC Radiation Notification Letter** (available from www2.health.vic.gov.au/about/clinical-trials-and-research) must be completed for each site where radiation exposure is **not** considered to be additional to normal clinical management/care at the particular site. A Medical Physicist's report must be submitted with the ethics application if the radiation exposure is considered to be additional to normal clinical management/care at the particular site.

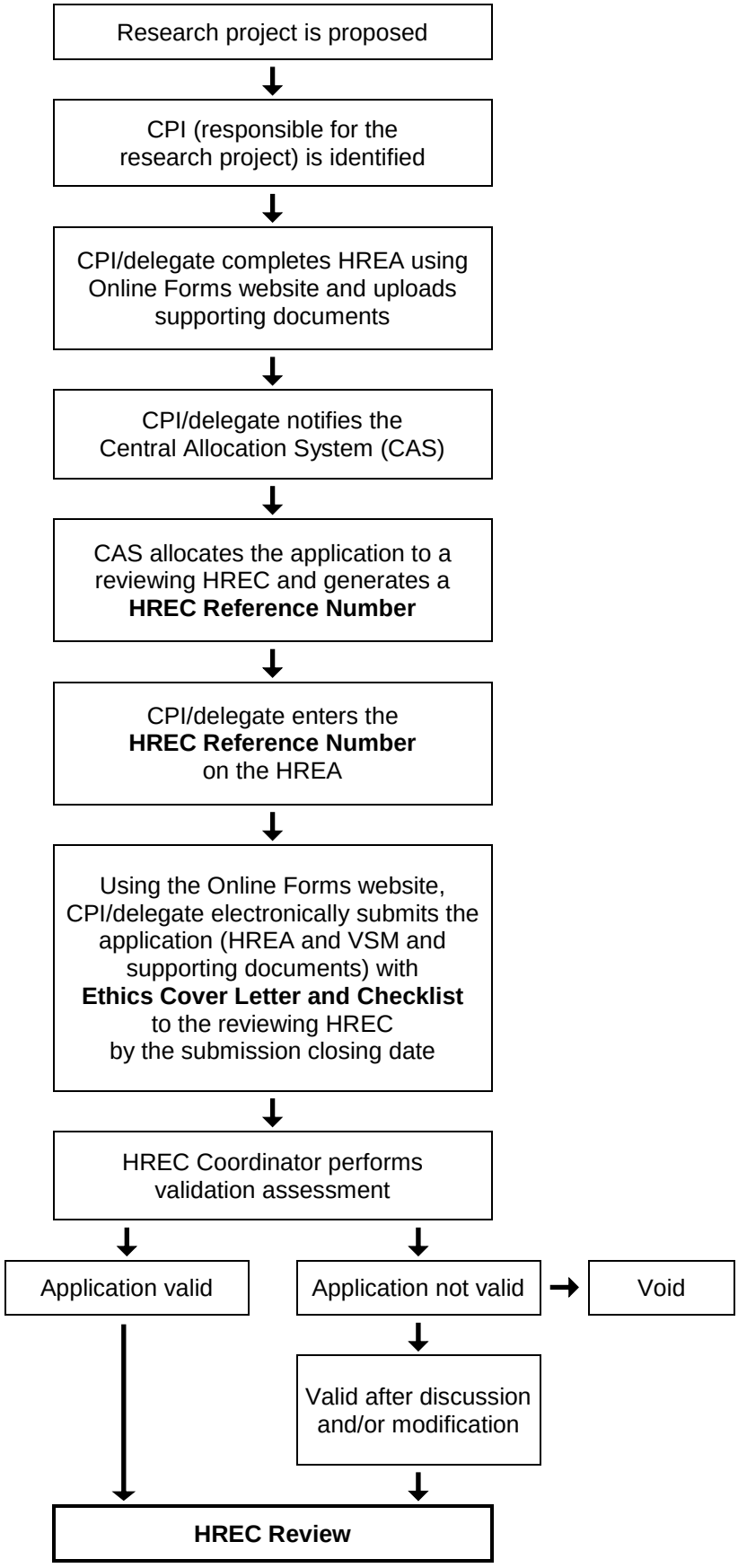
NMA submissions for review in Victoria

7.10 The above information also applies to NMA applications. A HREA must be used for all NMA applications (the LNR VIC is a single-site state-specific form and must **not** be used for NMA). Note: Ethics and research governance/SSA applications are linked across jurisdictions.

7.11 If a New South Wales site is participating in a research project under NMA, applicants should be aware that in certain circumstances the *NSW Privacy Form* (available from www2.health.vic.gov.au/about/clinical-trials-and-research/clinical-trial-research/national-mutual-acceptance) may be required for the ethics submission to the reviewing HREC.

7.12 If a Western Australia site is participating in a research project under NMA, a Western Australian Specific Module (WASM) is required for the ethics submission to the reviewing HREC. Details are available from www2.health.vic.gov.au/about/clinical-trials-and-research/clinical-trial-research/national-mutual-acceptance.

Figure 1. Application process for ethical review in Victoria



SOP 08 Submitting a SSA for a Multi-site Research Project

Purpose To detail the process for submitting a Site Specific Assessment (SSA) research governance application to the site RGO

8.1 The research governance/SSA process is a mechanism to assess the suitability of a research project to be conducted at a particular site. It is a separate process to ethical review and does not involve a local HREC. It is a research governance assessment process. Early submission of a SSA and supporting documents will allow the RGO to assess the documents and obtain legal or other review without causing a delay to the overall governance process.

8.2 At the planning stage of the research project the sponsor/CRO, in consultation with Investigators, will choose the research sites. The sponsor/CRO should promptly organise delivery of project documentation to PIs at all participating sites. Provision of project documentation should occur as soon as the participating sites are agreed, and well before the CPI/delegate is ready to complete and submit the ethics application to the reviewing HREC.

8.3 The CPI/delegate should generate the ethics form using Online Forms and the required number of SSA forms, then transfer an SSA to each PI using the Online Forms **Transfer** tab.

8.4 Research governance/SSA should be conducted at sites in a parallel timeframe with the ethics review process and should commence **as soon as possible**. The site PI should submit the completed documents for research governance assessment as soon as they are available. The RGO may accept a completed SSA form with some supporting documents. The RGO can request further information from the applicant, which allows the PI to upload further supporting documents and re-submit.
Note: When submitting a SSA or LNR VIC SSA from the Online Forms website, it is a requirement to record the HREC Reference Number of the associated ethics application.

8.5 Each PI at a site involved in a multi-site research project must complete a SSA form for that project (refer to SOP 04). The form involves consideration of:
- whether the facilities and resources required for the research to proceed at the site are appropriate and available;
- whether the investigators involved in the project at the site have the necessary skills, experience, training and expertise to carry out their role in the research project;
- whether the organisation is prepared to conduct the research at that site considering the patient availability; and
- other compliance and policy aspects.

8.6 SSA applications are created using Online Forms https://au.ethicsform.org (refer to SOP 04). When the SSA is complete, it must be signed by the PI (electronic authorisation is available on Online Forms).

8.7 Supporting documents must be uploaded to the Online Forms SSA application. A **Research Governance Cover Letter and Checklist** with full details **must** be included (available from www2.health.vic.gov.au/about/clinical-trials-and-research/clinical-trial-research/how-to-make-an-hrec-application-for-clinical-trials or www2.health.vic.gov.au/about/clinical-trials-and-research/health-and-medical-research/how-to-make-an-hrec-application-and-reporting).

8.8 The SSA application (electronically authorised or signed by the PI) and all supporting documents must be electronically submitted to the site's RGO by the PI (or delegate) using Online Forms.

8.9 Once the complete research governance/SSA application is submitted to the RGO, it must be validated. After the RGO has been notified that HREC approval has been granted by the reviewing HREC (refer to SOP 14), the RGO can recommend research governance/SSA authorisation to the organisation's Chief Executive (or delegate). Once the Chief Executive (or delegate) authorises the SSA, the research project can commence **at that site**.

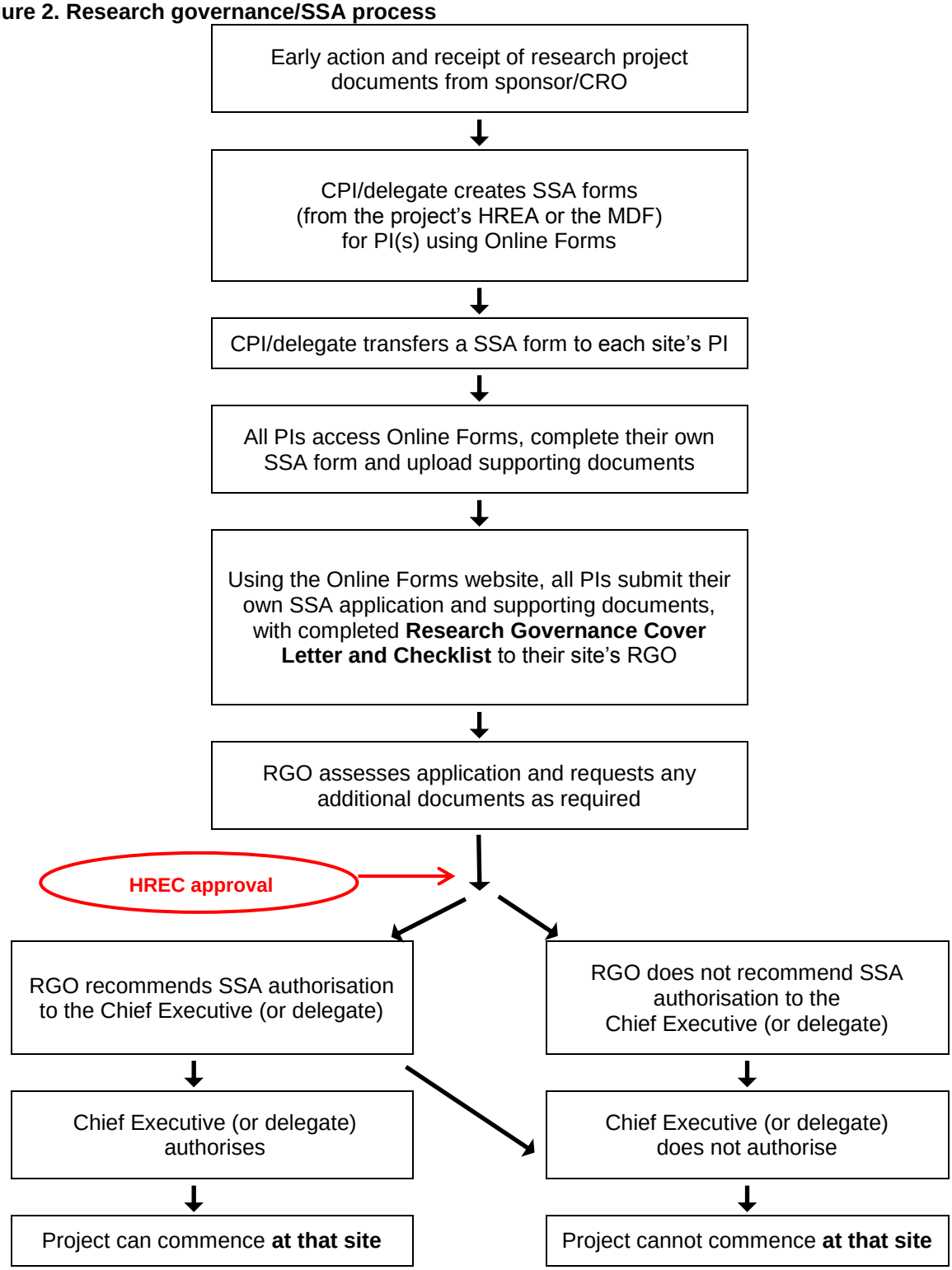
8.10 The applicant can view real-time information on the progress of a submitted application on the Online Forms 'Project Progress' tab. Refer to the *Online Forms Handbook* (available from websites above) for information.

8.11 Both HREC approval **and** research governance/SSA authorisation are required before a research project can commence at a site.

> **Early submission of SSA documents allows early validation and timely SSA authorisation.**

8.12 For detailed guidance on research governance and SSA, refer to *Research Governance and Site Specific Assessment – Process and Practice* (available from www2.health.vic.gov.au/about/clinical-trials-and-research/clinical-trial-research/site-specific-assessment-and-research-governance-in-clinical-trials or www2.health.vic.gov.au/about/clinical-trials-and-research/health-and-medical-research/site-specific-assessment-and-research-governance).

Figure 2. Research governance/SSA process



SOP 09 Validation of an Ethics Application for a Research Project

Purpose To describe the process of the reviewing HREC Coordinator validating the application

9.1 After the application is submitted to the HREC research office by the CPI/delegate, it must be validated by the reviewing HREC Coordinator before progressing for HREC review. Validation should occur on the submission closing date of the HREC meeting, or as soon as possible after that date.

9.2 A completed **Ethics Cover Letter and Checklist** and must be attached to an HREC submission (available from www2.health.vic.gov.au/about/clinical-trials-and-research/clinical-trial-research/how-to-make-an-hrec-application-for-clinical-trials or www2.health.vic.gov.au/about/clinical-trials-and-research/health-and-medical-research/how-to-make-an-hrec-application-and-reporting).

A valid application is one that is deemed by the reviewing HREC Coordinator to be complete and accurate.

9.3 Validation criteria include ensuring the following are present:
- HREA or LNR VIC with all required supporting documents uploaded to the Online Forms application (refer to **Ethics Cover Letter and Checklist** for a list of relevant documents)
- HREC Reference Number (if a multi-site project) (assigned by CAS and entered on the HREA by the CPI or delegate)
- Signature (or electronic authorisation) of the CPI on the ethics application form
- Any specific requirements of the reviewing HREC.

Timeline: The reviewing HREC Coordinator notifies the CPI of validation within 5 working days after the submission closing date.

9.4 The reviewing HREC Coordinator determines whether or not an application is valid, and notifies the CPI/delegate. If an application is invalid, the reviewing HREC Coordinator should specify the reasons why it is invalid.

9.5 If an application is invalid, the CPI (or delegate) should discuss the issues with the reviewing HREC Coordinator. On Online Forms the application form can be modified and/or new/revised supporting documents uploaded and electronically submitted.

If the application's issues cannot be resolved, it cannot be validated. The HREC Coordinator may allow the application to be postponed until a later HREC meeting, allowing the CPI/delegate more time to resolve the issues; this should be discussed with the reviewing HREC Coordinator.

9.6 Revisions must not be made and will not be accepted once an application has been validated. If the applicant requests to make major revisions to the application or attach additional documentation prior to HREC review, the application may be withdrawn by the applicant. This should be discussed with the reviewing HREC Coordinator.

9.7 The applicant (and any others whom they have nominated) can view real-time information on the progress of a submitted application on the Online Forms 'Project Progress' tab. Refer to the Online Forms Handbook (available from websites above) for information.

SOP 10 Requirements for a Multi-site Research Project Involving the Use of Ionising Radiation

Purpose To describe the process for ethics review and special requirements for research projects involving the use of ionising radiation

10.1 The reviewing HREC is responsible for providing ethics approval for a research project involving ionising radiation when the trial is conducted at multiple sites.

10.2 The reviewing HREC will review the following documents that relate to use of ionising radiation:
- Medical Physicist's report for each participating site, if treatment is above standard of care
- The Master PICF including, as appropriate, a statement to include a radiation risk statement prepared by the medical physicist for each site. Once approved, each site's PICF retains its relevant wording and that of other sites is deleted.

Under exceptional circumstances, a Site Master PICF may be used (refer to SOP 13). It should include a statement instructing the PI to include a radiation risk statement, if required (as determined by the site medical physicist's report).

10.3 If the dose of radiation is above the dose constraint of Table 1 of the ARPANSA Code, a second medical physicist's confirmation of the dose calculation is required. This should be recorded in the report provided to the reviewing HREC by the medical physicist.

10.4 If the dose of radiation is above the dose constraint of Table 1 of the ARPANSA Code and approval has been given by the HREC, then the organisation (licence holder) providing research governance/SSA authorisation must notify the Radiation Team, DHHS, within 14 days of research governance/SSA authorisation. The project may commence prior to notification being submitted to DHHS.

If the dose of radiation is below the dose constraint of Table 1 of the ARPANSA Code, approval has been given by the reviewing HREC and research governance/SSA authorisation has been given, no DHHS notification is required.

10.5 For further information, refer to www2.health.vic.gov.au/public-health/radiation or email radiation.safety@dhhs.vic.gov.au.

SOP 11 A Clinical Trial Conducted under the CTN or CTX Scheme

Purpose To outline the requirements for conducting a clinical trial under the CTN or CTX scheme

11.1 There are two schemes under which clinical trials involving therapeutic goods may be conducted in Australia: the Clinical Trial Exemption (CTX) Scheme and the Clinical Trial Notification (CTN) Scheme. For a clinical trial to be conducted under either of these schemes, the sponsor must submit an application to the Therapeutic Goods Administration (TGA) for approval. Information on the online CTN notification process is available from www.tga.gov.au/completing-online-ctn-form.

11.2 An HREC application involving a clinical trial to be conducted under the CTN scheme should comply with TGA instructions for the online CTN form.

11.3 If adding a new site to an approved research project (refer to SOP 19), a CTN form must be generated for the additional site.

SOP 12 Clinical Trial Research Agreement for a Multi-site Clinical Trial

Purpose To describe the use of a Clinical Trial Research Agreement (CTRA) for multi-site clinical trials

Clinical trials

12.1 For reasons of timeliness and cost, and compliance with insurance requirements, it is recommended that the standard CTRAs are used as appropriate. Any modifications to an agreement can be submitted to the Southern Eastern Border states (SEBS) inter-jurisdictional panel for consideration. Further information is available from https://medicinesaustralia.com.au/policy/clinical-trials/clinical-trials-research-agreements.

Standard clinical trial agreement are available from:
- For commercially sponsored clinical trials - the Medicines Australia website https://medicinesaustralia.com.au/policy/clinical-trials/clinical-trials-research-agreements;
- For device clinical trials - Medical Technology Association of Australia website www.mtaa.org.au/clinical-investigations;
- For investigator-initiated (non-commercial) clinical trials - the Clinical Trial Research website www2.health.vic.gov.au/about/clinical-trials-and-research/clinical-trial-research/site-specific-assessment-and-research-governance-in-clinical-trials

A standard agreement is currently under development for investigator-initiated clinical trials with part commercial involvement.

12.2 In the event that a sponsor submits a CTRA that has not been prepared using a Medicines Australia or a Medical Technology Association of Australia (Medical Device) template, RGOs should review the agreement in accordance with their usual practice and seek legal advice (through in-house or external legal counsel) at the sponsor's expense, as deemed necessary and in accordance with their own institution's policies and practices. Institutions may choose not to accept a "non-standard" agreement and may request the sponsor to prepare a new agreement using the appropriate template.

12.3 Schedule 7 of the Commercially sponsored CTRAs and Schedule 4 of the CRG/CRO and Phase 4 CTRAs may be used to incorporate unique requirements that are required by a party to the agreement to facilitate the conduct of the clinical trial. They are not to be used to substantially amend the CTRA or to introduce provisions that contradict or otherwise undermine the substantive provisions or intent of the CTRA. The VMIA policy document regarding agreements is available from www.vmia.vic.gov.au/learn/clinical-trials.

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12.4 A listing of commercial and non-commercial clinical trial standard Schedule 7 and 4 Special Conditions for Sponsors is provided to public hospitals by the Coordinating Office. Four States participate in agreeing standard Schedules using the SEBS panel and details are on the Medicines Australia website (https://medicinesaustralia.com.au/policy/clinical-trials/clinical-trials-research-agreements/).

12.5 RGOs should check the submitted Schedule 7 and 4 Special Conditions in CTRAs from sponsors against the agreed conditions. Where a sponsored CTRA contains a Schedule 7 or 4 that differs from the agreed version for that particular company, or where there is no agreed Schedule 7 or 4 for a given company, the RGO should review the Schedule and seek legal advice (through in-house or external legal counsel) at the sponsor's expense, as deemed necessary and in accordance with their own institution's policies and practices.

Non-clinical trials

12.6 Agreements for non-clinical trials are in development (e.g. for registries). In the interim an agreement can be adapted for use using the Medicines Australia CRG CTRA template with appropriate standard Special Conditions, Schedule 4 that meet the requirements of the project.

SOP 13 Participant Information and Consent Form for a Research Project

Purpose To describe the use of template Participant Information and Consent Forms (PICFs) for a research project

13.1 The standard national templates for PICFs, which have been endorsed by NHMRC, should be used to create the specific PICF(s) for a research project. The templates are available from www2.health.vic.gov.au/about/clinical-trials-and-research/clinical-trial-research/how-to-make-an-hrec-application-for-clinical-trials or www2.health.vic.gov.au/about/clinical-trials-and-research/health-and-medical-research/how-to-make-an-hrec-application-and-reporting.

13.2 Where the PICF is identical (except for local contact information) for each site, the CPI (or delegate) must submit a Master PICF to the reviewing HREC.

There may be more than one Master PICF if special consent requirements apply (e.g. consent forms for parents/guardians of children, persons responsible). Separate templates are available from the website listed above.

A Master PICF contains the required wording applicable to all sites and includes the name and contact details of the reviewing HREC. It should be a generic form for multi-centre research (i.e. no site letterhead).

Following HREC approval, the Master PICF(s) must be used for all sites the HREC has approved. The approved document may **only** be modified to reflect individual sites' details. Permissible changes are:

- Letterhead of the site
- Name of the site where recruitment is to occur
- Name and contact details of the site PI
- Name and contact details of the person dealing with complaints at the PI's organisation

If specific wording is required for religious reasons at any site, the relevant wording should be included in the Master PICF. This text may be removed at sites where it is not applicable.

13.3 A site master PICF should only be used in exceptional circumstances. It should be based on the master PICF and be formatted with the specific site details.

13.4 All PICFs **must** be approved by the reviewing HREC.

13.5 Where changes are required to the Master PICF as a condition of HREC approval, the PICF(s) must be updated with the latest version date and uploaded to Online Forms as a supporting document (refer to SOP 04).

13.6 The HREC-approved version of the Master PICF must be sent by the reviewing HREC Coordinator to the CPI/delegate, along with all other approved documents. The CPI/delegate must forward the approved documents to all PIs at participating sites, and to RGOs, sponsor/CRO and project coordinator as applicable.

13.7 The HREC-approved Site Master PICF (if applicable) will also be sent by the reviewing HREC Coordinator to the CPI/delegate, who will then forward it to the relevant PI(s).

13.8 A statement has been recommended for use in PICFs to be used at Catholic hospitals and institutions. The following statement was developed through the deliberations of the Catholic Health Australia working group representing Catholic hospital ethicists and clinicians. This is recommended for use by any human research ethics committee seeking to provide clear communication to potential research participants of child-bearing age and is consistent with Catholic teaching. This wording may be inserted into a PICF but consult with the site regarding their specific requirements.

Patient Information and Consent Form Statement where pregnancy must be avoided: Recommended Template for Catholic Institutions

The effects of [Name of investigational product] on the unborn child and on the newborn baby are not known. Because of this, it is important that research project participants are not pregnant or breast-feeding and do not become pregnant during the course of the research project. You must not participate in the research if you are pregnant or trying to become pregnant, or breast-feeding. If you are female and child-bearing is a possibility, you will be required to undergo a pregnancy test prior to commencing the research project. If you are male, you should not father a child or donate sperm for at least [number] months after the last dose of study medication.

Both male and female participants must avoid pregnancy during the course of the research and for a period of [number] months after completion of the research project. You should discuss effective methods of avoiding pregnancy with your study doctor.

For female participants: If you do become pregnant whilst participating in the research project, you should advise your study doctor immediately. Your study doctor will withdraw you from the research project and advise on further medical attention should this be necessary. You must not continue in the research if you become pregnant.

For male participants: You should advise your study doctor if you father a child while participating in the research project. Your study doctor will advise on medical attention for your partner should this be necessary.

SOP 14 Notification of an HREC Decision following Ethics Review of a Research Project

Purpose To describe the process for HREC review decision and its notification

Timeline: The CPI/delegate must be notified of the HREC review meeting outcome in writing within 5 working days of that meeting.

14.1 The applicant (and any others whom they have nominated) can view real-time information on the progress of a submitted application on the Online Forms 'Project Progress' tab. Refer to the *Online Forms Handbook* (available from www2.health.vic.gov.au/about/publications/policiesandguidelines/online-forms-handbook) for information.

Provisional approval of application, with a request for further information

14.2 The reviewing HREC may decide to request further information from the CPI/delegate. A standard letter detailing the information required will be sent to the CPI/delegate. When the HREC Coordinator records the further information request, the Online Forms application form can be modified.

On the Online Forms website, the application form can be modified and/or new/revised supporting documents uploaded; this can then be electronically re-submitted. Re-submission can include **either** (a) the revised application form with or without new/revised supporting documents **or** (b) new/revised supporting documents only.

Timeline: The CPI/delegate must provide the requested information to the reviewing HREC Coordinator within 2 weeks or as soon as possible after the request

14.3 The HREC review and approval process cannot continue until the reviewing HREC Coordinator has received a satisfactory response from the CPI/delegate.

A prompt response from the CPI/delegate to any information request is essential for timeliness of the HREC review process.

Application approved

Timeline: A HREC approval letter specifying the conditions of HREC approval should be sent to the CPI/delegate within 5 working days of the meeting decision.

14.4 The CPI/delegate must inform the PI(s) and relevant parties. The date on the approval letter is the date of HREC approval or as specified in the letter. The approval letter can be directly communicated via AU RED by the HREC Coordinator using the Email tab and the ethics form owner can share this information with those to be notified by setting up access in the Online Forms **Email - History** tab and **Project - Progress** tab. Refer to the *Online Forms Handbook* page 23 (available from www2.health.vic.gov.au/about/publications/policiesandguidelines/online-forms-handbook).

14.5 The research project cannot commence at a site until authorisation of research governance/SSA at that site is granted (refer to SOP 15). Completion of the CTN notification and any other agreement/regulatory requirements are necessary before SSA authorisation can occur.

14.6 For clinical trials there should be a CTN form for each site involved (refer to SOP 11).

14.7 Radiation safety in research involving the exposure of human volunteers to ionising radiation is the responsibility of the institution at which the research is being undertaken. The PI at each site is responsible for ensuring that any advice provided by a Radiation Safety Officer (RSO) in relation to a particular research project is complied with in full.

Application not approved

14.8 A standard letter signed by the reviewing HREC Chair (or Deputy Chair) will be sent to the CPI/delegate informing them of the non-approval of the research project, with reasons for the HREC decision. The CPI/delegate must then forward the letter to the PI(s) and relevant parties.

14.9 Appropriate action should be taken to discontinue any site specific assessment that is underway.

Appeals concerning ethical review and decision

14.10 The policy concerning appeals regarding review of a research project should be available from the website of the organisation hosting the HREC or by contacting the organisation directly.

SOP 15 Authorisation of Research Governance/SSA

Purpose To describe the process for Site Specific Assessment (SSA) authorisation to be obtained at a site

15.1 Both HREC approval **and** authorisation of research governance/SSA are required before a research project can commence at a site.

15.2 Authorisation of research governance/SSA must be granted by the Chief Executive (or delegate) for a research project to commence at a site. Only the Chief Executive (or delegate) has the authority to grant/not grant authorisation for a research project.

15.3 In making a determination, the Chief Executive (or delegate) must consider the SSA form or LNR VIC SSA form submitted by the PI to the RGO and must have seen the HREC approval letter.

15.4 For clinical trials conducted under the CTN scheme, the TGA acknowledgement is issued once the CTN form has been processed by the TGA and an acknowledgement provided (emailed letter).

15.5 The RGO is responsible for notifying the site's PI of the Chief Executive's (or delegate's) decision. This notification must be in writing, accompanied by all authorised documents.

15.6 Only when research governance/SSA has been authorised by the Chief Executive (or delegate) and all regulatory compliance has been completed, can the research project commence at that site.

15.7 The RGO and PI must both keep a copy of all documentation relating to research governance/SSA, including evidence of ethical approval and all supporting documentation for the SSA form or LNR VIC SSA form. These documents must be maintained in a secure and confidential manner and may be hard copy or electronic (e.g. in AU RED and Online Forms).

15.8 Neither the RGO nor the PI are required to notify the reviewing HREC of the research governance/SSA outcome. The reviewing HREC Coordinator is able to access this information from AU RED (the information management system used by research offices).

15.9 The Chief Executive (or delegate) may choose not to authorise research governance/SSA for the conduct of the research at a site, even though the project has HREC approval. This means that the project cannot proceed at that site. Refer to Figure 2 for an overview of the research governance/SSA process.

15.10 The applicant can view real-time information on the progress of a submitted application on the Online Forms 'Project Progress' tab. Refer to the *Online Forms Handbook* (available from www2.health.vic.gov.au/about/publications/policiesandguidelines/online-forms-handbook) for information.

SOP 16 Timeliness of Regulatory Processes for a Multi-site Research Project

Purpose To describe the benchmark time for ethical review and the process for timely research governance/SSA authorisation

Ethical Review

Timeline: The benchmark time for streamlined ethical review (HREC) in Victoria is 30 working days.

16.1 The Victorian benchmark is calculated using the clock stop-start feature in AU RED (the information management system used by research offices) and is calculated from the ethics Submission Closing Date (SCD) for the reviewing HREC meeting to the date that an HREC decision is made.
It **excludes** time taken for the CPI/delegate to respond to information requests from the HREC.

16.2 If the reviewing HREC requests further information from the CPI/delegate, the AU RED clock must be stopped on the day that the request for further information is sent to the CPI/delegate. The clock will re-start once a complete response has been received and entered on AU RED by the reviewing HREC Coordinator. If the response from the CPI/delegate does not sufficiently address the HREC's requirements, the reviewing HREC Coordinator may make further requests for information from the CPI/delegate. Each time a request is made and response received, the clock will stop and start accordingly.

A prompt response from the CPI/delegate for information is essential in order for a timely HREC review process.

16.3 When the reviewing HREC has made a final decision on an application, the AU RED clock must be stopped. A letter/certificate will be sent to the CPI/delegate. This can be sent by AU RED email directly to the applicant's Online Forms account; it will appear in 'Email History' tab.

16.4 The applicant (and any others whom they have nominated) can view real-time information on the progress of a submitted application on the Online Forms 'Project Progress' tab and 'Email-History' tab. Refer to the *Online Forms Handbook* (available from www2.health.vic.gov.au/about/publications/policiesandguidelines/online-forms-handbook) for information.

16.5 If the HREC approval timeline exceeds the 30 working day benchmark set in Victoria it does not entitle the investigator or sponsor to any redress (e.g. immediate decision from the reviewing HREC or refund of an application fee).

16.6 A 60 calendar day benchmark for performance of ethics review has been set for NMA. Expiration of this period does not entitle the investigator or sponsor to any redress.

Research Governance/SSA Authorisation

16.7 A research project cannot commence at a site, even if ethically approved, until the research governance process has been completed and SSA has been authorised by the Chief Executive (or delegate) (refer to SOP 15).

16.8 Whilst authorisation of the SSA is dependent on HREC approval, the research governance/SSA process can be expedited by submitting all relevant documents to the site's RGO as early as possible, so that the process proceeds in parallel with the HREC review.

The site PI should submit the completed documents for research governance assessment as soon as they are available. The RGO may accept a completed SSA form with some supporting documents: note all supporting documents uploaded to an ethics application are available on Online Forms and will be available to the RGO once the SSA form is uploaded in to AU RED. The

RGO should assess the documents and obtain legal or other review without causing a delay to the overall governance process.

16.9 The RGO can request further information from the applicant, which allows the PI to upload further supporting documents and re-submit electronically. The SSA should be validated by the RGO in advance of HREC approval; it can then be recommended for authorisation promptly following the RGO's receipt of the HREC approval and documentation.

Early submission of SSA documents allows early validation, and more timely SSA authorisation and project start-up

SOP 17 Amendment to an Ethically Approved Research Project

Purpose To describe the process for making an amendment to an ethically approved research project

17.1 An amendment is broadly defined as a change or addition made to the terms of the ethics application, the protocol, or any other supporting documentation after the research project has started which may affect the ethical and/or scientific acceptability of the research project.

Changes to the personnel on an approved HREC application (e.g. change of CPI or addition of a new investigator) should be notified to the reviewing HREC as an amendment to the approved research.

17.2 If a research project requires an amendment that may affect its ongoing ethical and/or scientific acceptability, then a request for an amendment, in writing, should be made to the reviewing HREC. The CPI/delegate and PIs should be consulted by the sponsor before the sponsor submits an amendment to the reviewing HREC; they must complete an **Amendment Request Form** (available from www2.health.vic.gov.au/about/clinical-trials-and-research/clinical-trial-research/monitoring-reporting).

17.3 If necessary, the sponsor should communicate with the reviewing HREC Coordinator regarding the amendment.

17.4 On Online Forms the new/revised supporting documents (including **Amendment Request Form**) should be uploaded to the original application and electronically submitted to the reviewing HREC Coordinator.

17.5 The reviewing HREC Coordinator must send a letter acknowledging whether an amendment has been validated or not validated.

17.6 The reviewing HREC Coordinator must communicate the decision of the reviewing HREC by letter to the sponsor/delegate who will then inform relevant parties.

17.7 An amendment to a research project will require the site PI to inform their RGO to determine whether or not research governance/SSA amendment authorisation is required before the amendment is implemented at the site.

17.8 If an amendment impacts the SSA or LNR VIC SSA, this must be considered by the RGO at each site and authorisation sought from the Chief Executive (or delegate) (refer to SOP 20).

17.9 If the RGO believes research governance/SSA authorisation is **not** required then they must notify the PI in writing indicating the PI may implement the amendment upon HREC amendment approval being granted.

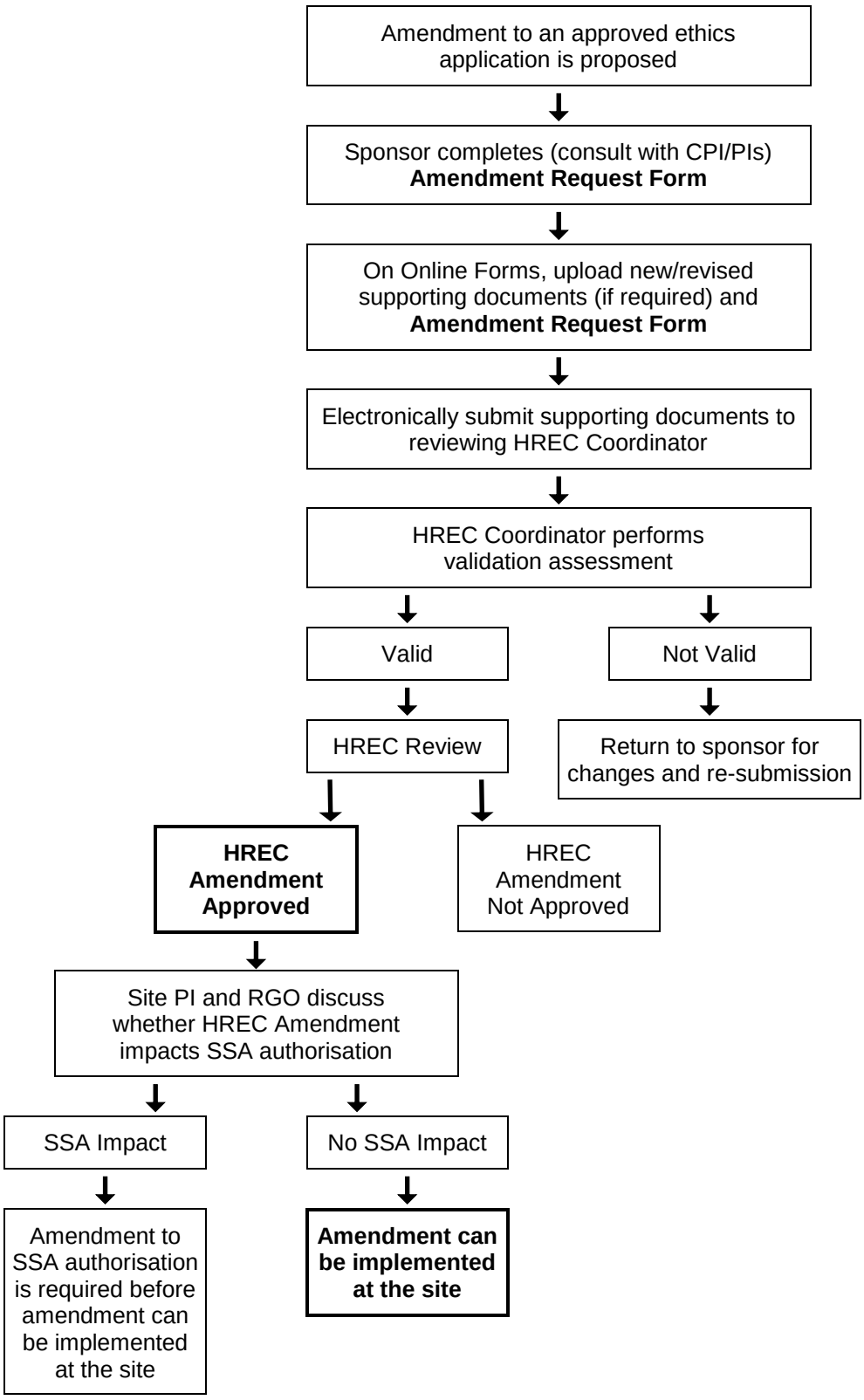
Implementation of an amendment at a site

17.10 An amendment must not be implemented at a site until the HREC amendment has been approved by the reviewing HREC **and** a research governance/SSA amendment (if applicable) has been authorised by the Chief Executive (or delegate).

17.11 If an amendment only affects site authorisation and does not require ethics approval, the PI may implement the research governance/SSA amendment once it has been authorised by the site's Chief Executive (or delegate) and notified in writing by the RGO.

17.12 Exceptions to the amendment process may be made in circumstances where there is a serious threat to the health and safety of participants. The sponsor should notify the reviewing HREC Coordinator and ensure that CPI/PIs notify the RGO at each relevant site.

Figure 3. HREC Amendment to an Approved Research Project



SOP 18 Expanding an Ethically Approved Single-site Research Project to a Multi-site Project

Purpose To describe the process in the event that an ethically approved single-site research project is expanded to include additional sites

18.1 Details of policy and documents to guide or submit through National Mutual Acceptance (NMA) are available from www2.health.vic.gov.au/about/clinical-trials-and-research.

18.2 Applicants are advised to undertake careful planning before deciding whether a project is likely to be conducted at a single site or multiple sites. If, at the planning stage of the research project, it is considered likely that multiple sites will be involved, a multi-site application should be submitted (refer to SOP 07), even if there is only one site confirmed at the time of the HREC application.

18.3 If the streamlined system was not utilised and HREC approval has been given for a single-site application, this can be amended to include additional sites. This is only permissible with the agreement of the HREC Coordinator, notification to CAS, and the reviewing HREC is accredited to review in the streamlined system. The date of HREC approval must fall within the appropriate timeframe.

18.4 If a single-site clinical trial has been approved by an HREC that is accredited to review in the streamlined system or NMA, the original approval can be expanded to a multi-site approval, with agreement of the reviewing HREC Coordinator. The project must qualify under the scope of the streamlined system (refer to SOP 01), and NMA applications must meet the relevant criteria (refer to SOP 02). The start dates for the streamlined systems are detailed in the tables below.

If a project's ethical approval was obtained in a state/territory prior to that jurisdiction joining NMA, the existing approval **cannot** be expanded to include sites in other jurisdictions.

For applications in Victoria only:

Research Type	Start Date
Clinical trials	November 2009
Clinical trials and health/medical research	February 2015

For applications in Victoria and other states/territories:

Streamlined System	Research Type	States/Territories	Start Date
IMA	Clinical trials	QLD, VIC	October 2011
		NSW, QLD, VIC	February 2012
NMA	Clinical trials	NSW, QLD, SA, VIC	November 2013
	All human research	NSW, QLD, SA, VIC	December 2015
		ACT, NSW, QLD, SA, VIC	August 2016
		ACT, NSW, QLD, SA, VIC, WA	31 August 2017

18.5 If the HREC Coordinator agrees that a single-site approval will be expanded to multi-site, the applicant must contact CAS (refer to SOP 06). The process should be followed for adding an additional site to an existing approval (refer to SOP 19) and the SSA process carried out accordingly.

18.6 If modifications or conditions are imposed by a reviewing HREC, then these will apply to all approved sites.

18.7 Sites that gain ethical approval from a reviewing HREC will be required to comply with the ongoing monitoring and reporting requirements of the reviewing HREC.

18.8 A research project that was originally submitted and approved with a LNR VIC application cannot be expanded to include sites in other states/territories. All NMA applications, including those that are considered low risk, must use the HREA (or NEAF).

SOP 19 Adding Additional Site(s) to an Ethically Approved Multi-site Research Project

Purpose To describe the process in the event that an ethically approved multi-site research project is expanded to include additional sites

19.1 The reviewing HREC must be notified in accordance with the *National Statement on Ethical Conduct in Human Research* (NHMRC, 2007), Chapter 1.1(e) of the intent to add a new site to the previously approved multi-site research project. This will require an HREC amendment including the curriculum vitae and employment details of the PI at the new site. An **Amendment Request Form** is available from www2.health.vic.gov.au/about/clinical-trials-and-research/clinical-trial-research/monitoring-reporting.

19.2 A project with ethical approval from a Victorian or NMA reviewing HREC can add a site through an HREC amendment process (refer to SOP 17), with agreement of the reviewing HREC Coordinator.

If a project's ethical approval was obtained in a state/territory prior to that jurisdiction joining NMA, the existing approval **cannot** be expanded to include sites in other jurisdictions.

The start dates for the streamlined systems are detailed in the tables below.

For applications in Victoria only:

Research Type	Start Date
Clinical trials	November 2009
Clinical trials and health/medical research	February 2015

For applications in Victoria and other states/territories:

Streamlined System	Research Type	States/Territories	Start Date
IMA	Clinical trials	QLD, VIC	October 2011
		NSW, QLD, VIC	February 2012
NMA	Clinical trials	NSW, QLD, SA, VIC	November 2013
	All human research	NSW, QLD, SA, VIC	December 2015
		ACT, NSW, QLD, SA, VIC	August 2016
		ACT, NSW, QLD, SA, VIC, WA	31 August 2017

If additional sites are to be added to an existing approved NMA multi-site research project, the sponsor/delegate should communicate with the reviewing HREC and undertake an HREC amendment process.

A research project that was originally submitted and approved with a LNR VIC application cannot be expanded to include sites in other states/territories. All NMA applications, including those that are considered low risk, must use the HREA (or NEAF).

19.3 A SSA form must be created using Online Forms (refer to SOP 04). The SSA must be transferred to the new site's PI (or delegate). The SSA **must** be generated from the HREA that was submitted to, and approved by, the HREC (or a MDF, where applicable).

19.4 The PI (or delegate) must complete the SSA form using Online Forms (refer to SOP 04), upload supporting documents and electronically submit to the site RGO.

19.5 For an eligible research project, a CTN form (if applicable) is required for the new site (refer to SOP 11).

19.6 The reviewing HREC will review the new PI's competence and qualifications and other relevant details according to the *National Statement on Ethical Conduct in Human Research* (NHMRC, 2007). If approved, a HREC approval for the research project listing the new site will be issued.

This approval should be sent by the HREC Coordinator to the sponsor, who will forward it to all relevant parties. This can be received by email from AU RED directly to the applicant's Online Forms account and will appear in 'Email History' tab. Also actions taken by the HREC Coordinator in AU RED are tracked in the 'Project Progress' tab. Access to both tabs can be shared with colleagues (see *Online Forms Handbook*, page 23 at www2.health.vic.gov.au/about/publications/policiesandguidelines/online-forms-handbook).

19.7 The SSA will be processed by the RGO in the usual manner. When HREC approval has been given and research governance/SSA authorisation has been obtained the research can commence at the new site.

SOP 20 Amendment to Research Governance/SSA

Purpose To describe the process for an amendment to research governance/SSA authorisation

20.1 A research governance/SSA amendment may be necessary as a result of an HREC amendment (refer to SOP 17), or may be due to an issue affecting a site only.

20.2 Changes requiring new site specific assessment authorisation include:
- A significant change to the research project at the research site
- Appointing a new PI at a site
- A change to the insurance and indemnity and/or contractual arrangements.

20.3 When it is intended to make an amendment to a research project, the site PI must liaise with the RGO to determine whether or not research governance/SSA authorisation is required for the amendment to be implemented at the site.

20.4 If an amendment only affects site authorisation and does not require ethics approval, the PI may implement the research governance/SSA amendment once it has been authorised by the Chief Executive (or delegate) and they have been notified of research governance/SSA authorisation in writing by the RGO.

20.5 On the Online Forms website, new/revised supporting documents (including amendments) can be uploaded to the original application; these can be electronically submitted to the site RGO. The RGO will send acknowledgement of the research governance/SSA amendment submission, indicating whether it is valid.

20.6 The RGO must assess the amendment request and should recommend authorisation by the Chief Executive (or delegate) or not. The Chief Executive (or delegate) **must** authorise the amendment before it can be implemented. The Chief Executive (or delegate) is responsible for authorising research governance/SSA amendments that impact upon the institution.

20.7 A notification letter authorising the research governance/SSA amendment will be sent by the RGO to the site's PI indicating that the amendment can be implemented.

An amendment involving review by the reviewing HREC

20.8 Where new or amended documentation has been submitted to the reviewing HREC for ethical review, the approved documents must be available to each site's PI.

20.9 An amendment must not be implemented at a site until the HREC amendment has been approved by the reviewing HREC **and** the research governance/SSA amendment has been authorised at that site.

SOP 21 Monitoring of an Ethically Approved Research Project

Purpose To describe the responsibilities for monitoring the conduct of an ethically approved research project

21.1 According to the *National Statement on Ethical Conduct in Human Research* (NHMRC, 2007), monitoring of research refers to the process of verifying that the conduct of research conforms to the approved research proposal. The responsibility for ensuring that research is monitored adequately lies with the institution under which the research is conducted and the reviewing HREC.

21.2 Mechanisms for monitoring can include:
- Reports from investigators to the HREC
- Reports from independent agencies (e.g. data and safety monitoring board) to the HREC
- Review of safety event reports to the HREC
- Random inspection or audit of research sites, data, or consent documentation by the research office and/or RGO, or regulatory authorities
- Interviews with research participants or other forms of feedback from them.

21.3 The frequency and type of monitoring should be consistent with the degree of risk to the research participants.

21.4 Reporting forms are available from www2.health.vic.gov.au/about/clinical-trials-and-research/clinical-trial-research/monitoring-reporting.

SOP 22 Progress/annual Reporting on an Ethically Approved Research Project

Purpose To outline the ongoing progress reporting responsibilities for an ethically approved research project

Annual progress report

22.1 The sponsor is responsible for providing progress/annual reports on the research project to the responsible HREC; this includes information from all sites participating in the project. Reports must be submitted on the recommended template.

22.2 Progress/annual reports should contain information about the project at all sites. A **Progress Report – Project Form** (available from www2.health.vic.gov.au/about/clinical-trials-and-research/clinical-trial-research/monitoring-reporting).

22.3 The **Progress Report – Project Form** must be uploaded to Online Forms as a supporting document to the HREA or LNR VIC in Online Forms application 'Documents' tab then electronically submitted to the HREC using the 'Submissions' tab (see *Online Forms Handbook*, pages 66-69 www2.health.vic.gov.au/about/publications/policiesandguidelines/online-forms-handbook).

22.4 The HREC Coordinator will send a reminder letter to the sponsor for an annual progress report if the report is not received within 12 months of the project being approved (or the previous annual reporting date).

22.5 An acknowledgement of the report should be made available to the sponsor. If the HREC Coordinator uses the AU RED Email functionality the HREA owner can allow the sponsor and/or other parties to access the Online Forms application 'Email-History' and 'Project-Progress' tabs. Access to both tabs can be shared with any colleagues (see *Online Forms Handbook*, page 23).

Completion of a research project or closure of a site

22.6 Upon completion of an approved research project or closure of some but not all sites in a multi-site project, the sponsor must complete the **Project Final Report/Site Closure Report** and submit to the HREC (available from www2.health.vic.gov.au/about/clinical-trials-and-research/clinical-trial-research/monitoring-reporting).

22.7 The **Project Final Report/Site Closure Report** should be uploaded to the Online Forms application 'Documents' tab then electronically submit to the HREC using the 'Submissions' tab (see *Online Forms Handbook*, pages 66-69).

22.8 If the research project is completed at all sites, the sponsor must complete a **Project Final Report/Site Closure Report** (available as above) and ensure the report is uploaded to Online Forms application 'Documents' tab then electronically submitted to the HREC using the 'Submissions' tab (see *Online Forms Handbook*, pages 66-69).

22.9 An acknowledgement of the report should be sent by the HREC Coordinator to the sponsor/delegate using AU RED email; this will appear in the Online Forms application 'Email History' tab. Access can be shared with colleagues (see *Online Forms Handbook*, page 23).

SOP 23 Safety Reporting for an approved Research Project

Purpose To describe the requirements for reporting to the reviewing HREC regarding safety events that occur during an ethically approved research project

23.1 Reporting of safety events to the reviewing HREC must meet the requirements of the *National Statement on Ethical Conduct in Human Research* (NHMRC, 2007). For therapeutic goods requirements are set out in the *Safety Monitoring and Reporting in Clinical Trials Involving Therapeutic Goods* (NHMRC, 2016).

23.2 The sponsor has the primary responsibility for monitoring ongoing safety of investigational products/therapeutic goods. Some requirements and time lines for the sponsor to communicate safety information to the HREC are as follows (for more detail refer to *Safety Monitoring and Reporting in Clinical Trials Involving Therapeutic Goods*):

- Provide the HREC with an annual safety report;
- Notify the HREC and TGA of all significant safety issues and those that materially impact on the continued ethical conduct of a trial;
- Ensure the significant safety issue meets the definition of urgent safety measure and if so notify the HREC and TGA within 72 hours and all other significant safety issues should be notified within 15 days of the sponsor instigating or being aware of the issue;
- Other significant safety issues (not a SUSAR) that require action or an amendment should be submitted to the HREC without undue delay or a temporary halt of the trial should be submitted to the HREC within 15 days of the temporary halt; and
- An early termination of a trial should be notified without undue delay and not later than 15 days of the sponsor's decision to terminate the trial. Ethical review for related action should also be within 15 days.

23.3 The responsibility of the PI includes the following (for more detail refer to *Safety Monitoring and Reporting in Clinical Trials Involving Therapeutic Goods*):

- Capture and assess all adverse events at the site in accordance with the protocol within 24 hours of becoming aware of the event;
- Report to the sponsor as specified in the protocol; and
- Report to the institution within 72 hours of becoming aware of the event (all significant safety issues and SUSARs) arising at the local site.

23.4 If an urgent safety issue arises at a participating site, the PI must submit a completed **Safety Report** within 24 hours to the sponsor and the HREC for review if the event is possibly, probably or definitely related to participation in a research project within Australia. The participating institution should receive a report within 72 hours, from the PI. The report is available from www2.health.vic.gov.au/about/clinical-trials-and-research/clinical-trial-research/monitoring-reporting.

23.5 If the sponsor decides an amendment is required to an approved project, based on the degree of seriousness of the safety occurrence, a request for an amendment should be made (using the standard **Amendment Request Form** (available from www2.health.vic.gov.au/about/clinical-trials-and-research/clinical-trial-research/monitoring-reporting) and submitted to the reviewing HREC together with the safety event report.

22.6 Once the sponsor provides the reporting document it should be uploaded in the Online Forms application 'Documents' tab then electronically submitted to the HREC using the 'Submissions' tab (see *Online Forms Handbook*, pages 66-69 www2.health.vic.gov.au/about/publications/policiesandguidelines/online-forms-handbook).

23.7 Refer to the VMIA website www.vmia.vic.gov.au/learn/clinical-trials for information regarding SUSAR and USADE reporting.

23.8 In some cases, to avoid delay the PI may contact the sponsor and forward details of the safety report directly to the reviewing HREC.

23.9 Upon receipt of a **Safety Report** the reviewing HREC will review the report and take appropriate action. To communicate the outcome, the HREC Coordinator should use the AU RED email

functionality. The email is sent directly to the applicant's Online Forms account; it will appear in 'Email History' tab. Access can be shared with colleagues (see *Online Forms Handbook*, page 23).

23.10 Where the reviewing HREC considers that the report requires immediate suspension or discontinuation of the ethical approval of the research project, the sponsor must **immediately** notify the CPI/PI(s) at all sites. This should be promptly followed by a notice in writing.

23.11 If the PI considers that an event has **no material impact** on their research site, the PI should notify the site RGO and ask if a copy of the safety report is required.

For reports not requiring HREC review, a copy of the safety report should be filed securely at the site according to required practice.

This applies to Victorian sites and for NMA research projects conducted in Victoria.

SOP 24 Complaints Concerning an Ethically Approved Research Project

Purpose To outline the process in the event that a complaint is received about an ethically approved research project

24.1 In accordance with the *National Statement on Ethical Conduct in Human Research* (NHMRC, 2007), institutions conducting research must have a policy regarding the procedure for handling complaints about the conduct of a research project.

24.2 The institution conducting the research **must** have processes for dealing with research misconduct as described in the *Australian Code for the Responsible Conduct of Research* (NHMRC, 2007).

24.3 The PICF **must** inform the participants of the nominated person to whom complaints concerning the research can be directed. PICFs based on the national template should provide separate complaint contact details for matters relating to the site and matters relating to an aspect of the research or the conduct of the research project.

24.4 The nominated person to receive complaints should provide to the site RGO any information regarding the complaint. The RGO may liaise with the reviewing HREC Coordinator, depending on the nature of the complaint. The institution should deal with the complaint in a prompt manner.

24.5 If the complaint requires notification to the reviewing HREC, the site PI with the sponsor must complete a **Complaint Report.** The sponsor should submit the report to the reviewing HREC and a copy to the RGO at their own site where the complaint arose. The report should be uploaded in the Online Forms application 'Documents' tab then electronically submitted to the HREC using the 'Submissions' tab (see *Online Forms Handbook*, pages 66-69). The standard template is available from www2.health.vic.gov.au/about/clinical-trials-and-research/clinical-trial-research/monitoring-reporting.

SOP 25 Withdrawal or Suspension of Ethical Approval or SSA Authorisation for a Research Project

Purpose To describe the process for withdrawal or suspension of ethical approval or research governance/SSA authorisation

Withdrawal or suspension of ethical approval

25.1 A reviewing HREC may have reason to withdraw or suspend a research project that may relate to the welfare of the participants or the conduct of research that is not in accordance with ethical approval.

25.2 Where ethical approval for a research project is withdrawn or suspended by the HREC, the sponsor must be notified **immediately** of the withdrawal/suspension of HREC approval. Notification in writing should be provided as soon as possible to the sponsor to communicate with the CPI/ PIs and trial coordinators. The PIs should inform the site RGO.

Where possible, the research project participants should also be notified of the withdrawal or suspension of HREC approval

25.3 The institution, through the RGO, must ensure the research is suspended once ethical approval has been withdrawn and that arrangements are made to meet the needs of the participants.

25.4 The research may not be resumed unless either:
- The investigator subsequently establishes that continuance will not compromise participants' welfare; or
- The research is modified to provide sufficient protection for participants and an amendment is ethically reviewed and approved.

Withdrawal or suspension of research governance/SSA authorisation

25.5 Where a Chief Executive (or delegate) decides that the site cannot continue to conduct the research project, SSA authorisation **must** be suspended or withdrawn.

25.6 The RGO must notify the reviewing HREC and the PI of the decision to withdraw research governance/SSA authorisation at that site as soon as possible. The PI must notify the sponsor.

25.7 Research **must not continue** at a site if research governance/SSA authorisation has been withdrawn or suspended.

SOP 26 Completion or Early Termination/Abandonment of a Research Project

Purpose To describe the process at the completion or early termination of an ethically approved research project

Completion of a research project

26.1 Upon completion, early termination or abandonment of an approved research project, the sponsor must submit a **Project Final Report/Site Closure Report** form to the HREC (available from www2.health.vic.gov.au/about/clinical-trials-and-research/clinical-trial-research/monitoring-reporting). The report should be uploaded in the Online Forms application 'Documents' tab then electronically submitted to the reviewing HREC using the 'Submissions' tab (see *Online Forms Handbook*, pages 66-69 www2.health.vic.gov.au/about/publications/policiesandguidelines/online-forms-handbook).

26.2 Once a **Project Final Report/Site Closure Report** has been received by the reviewing HREC Coordinator, a letter of acknowledgement will be sent to the applicant. To communicate the outcome, the HREC Coordinator should use the AU RED email functionality. The email is sent directly to the applicant's Online Forms account; it will appear in 'Email History' tab. Access can be shared with colleagues (see *Online Forms Handbook*, page 23).

Early termination of a research project

26.3 If a research project is terminated or suspended by the sponsor or project sites before the expected date of completion, the HREC must be promptly notified (as above).

26.4 The **Project Final Report/Site Closure Report** must be prepared by the sponsor and submitted to the HREC Coordinator. Each site PI should ensure the site RGO receives a copy.