Standard Operating Procedures
for
Streamlining Ethical Review of Research Projects

in Victoria and as part of National Mutual Acceptance

Version: July 2015

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. Commencement of NMA superseded Interstate Mutual Acceptance (IMA) and these SOPs are applicable to multi-site research projects conducted under the NMA arrangements.

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 Trial Research website: www.health.vic.gov.au/clinicaltrials

Health and Medical Research website: www.health.vic.gov.au/healthandmedicalresearch

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Glossary	
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
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IMA	Interstate Mutual Acceptance (superseded by NMA)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
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

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.

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.

The introduction of NMA is a phased approach – currently New South Wales, Queensland, South Australia and Victoria are participating. NMA commenced on 1 November 2013 for clinical trials only.

Multi-centre clinical trials being submitted for ethical and scientific review, and taking place in one or more of the participating states, may be eligible for single ethical and scientific review.

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 has been 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 of research types eligible for NMA is: 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. This may include post-trial activities such as observational research and evaluation of a trial, developing a registry and other post-marketing surveillance activities.

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 www.health.vic.gov.au/clinicaltrials). 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 NSW and SA, 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 Completion of the Victorian-Specific Module (VSM) is mandatory when a NEAF is used. As part of the ethics application process, a completed VSM to address Victorian-specific legislation must be attached to the NEAF.

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 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 endorsement by the Victorian PI will suffice.

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 NEAF.

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 passing on any outcomes to the PIs, RGOs, sponsor/CRO and project coordinator.

3.2 One CPI must be nominated for each research project. The CPI must be employed and professionally based in an Australian 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 is responsible 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.

Principal Investigator (PI)

3.6 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.

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

3.8 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), who will then liaise with the reviewing HREC Coordinator. An exception to this is the urgent reporting of SAEs/SUSARs/USADEs, which may be done by the PI in extenuating circumstances (refer to SOP 22).

3.9 The CPI is also the PI for their own site.

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

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

Reviewing HREC Coordinator

3.10 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.

3.11 Following submission of the HREC application, the reviewing HREC Coordinator will perform a validation assessment prior to the application being reviewed by the HREC.

3.12 The HREC Coordinator's responsibilities include sending all letters and documentation relating to the HREC application to the CPI, who will then forward the information to all relevant parties. If there is an issue that requires urgent action at site(s), the HREC Coordinator must communicate directly with the site PI and RGO to avoid any delay.

3.13 *SOPs for Coordinators of Reviewing HRECs* are available from www.health.vic.gov.au/clinicaltrials and www.health.vic.gov.au/healthandmedicalresearch.

Research Governance Officer (RGO)

3.14 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).

3.15 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.

3.16 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.

3.17 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.

3.18 *SOPs for Research Governance Officers* and *Research Governance and Site Specific Assessment – Process and Practice* are available from www.health.vic.gov.au/clinicaltrials and www.health.vic.gov.au/healthandmedicalresearch.

SOP 04 Completing ethics and research governance application forms

Purpose To describe use of the Online Forms website for completion of the NEAF and SSA forms for ethics and governance applications respectively, or the LNR VIC and LNR VIC SSA for ethics and governance of low and negligible risk projects

4.1 The National Ethics Application Form (NEAF) 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 NEAF.

4.2 Victoria has a Low and Negligible Risk form (LNR VIC) for appropriate low risk research projects to be conducted in Victoria. The 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 NEAF.

If an applicant considers that their project may qualify as low and negligible risk, they must consult with the research office of the reviewing HREC prior to completing an application form. The designation of risk type is at the discretion of the research office.

4.3 The Online Forms website allows the applicant (CPI or delegate) to complete the NEAF 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.

4.4 In the streamlined ethical review system, research governance is administered by the process of site specific assessment (SSA). SSA forms are used to address research governance associated with a NEAF application; LNR VIC SSA forms are used to address research governance associated with a LNR VIC application.

SSA forms and LNR VIC SSA forms for research governance at participating sites are completed and submitted using Online Forms.

SSA forms **must** be created from the NEAF for that particular research project by the CPI (or delegate). Accordingly, LNR VIC SSA forms must be created from the LNR VIC for that particular research project by the CPI (or delegate). The forms should then be transferred to the participating sites' PIs for completion.

4.5 Following submission of the ethics application to the reviewing HREC, Online Forms allows applicants 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

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 NEAF or LNR VIC as required.
- Use the 'My Project' hyperlink to access the 'Email Notifications' tab. Nominate colleagues to receive communication about the project (NEAF **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 have read-only access to the application in their own Online Forms account.

Preparing a NEAF using Online Forms (CPI)

- To begin filling the form, select 'NEAF' below the 'My Project' icon on the left of the screen. Follow the instructions to fill in the form. Work across the form tabs from left to right.
- NEAF: Note that Section 2, Question 1 (details for the Chief Researcher/Investigator (CPI)) cannot be recorded until Section 5, Question 1 (type of research) has been recorded as 'Clinical Research'.
- All supporting documents must be uploaded. To determine the supporting documents required for the application, refer to the **CPI/PI Ethics Checklist** (available from www.health.vic.gov.au/clinicaltrials or www.health.vic.gov.au/healthandmedicalresearch). A VSM is required for all NEAF applications with a site in Victoria.
  To upload documents to the application:
  - Select the 'Documents' tab and a list of document types appears.
  - Choose the 'Upload' tab; select the 'Browse' or 'Choose Files' button and select multiple documents (hold down Ctrl key); fill in details and select 'Upload Files'.
  - If uploading more than one document of the same type, distinguish them by putting the specific detail in the 'Version' field.
- The 'Transfer' tab is used to transfer the NEAF to a colleague (either temporary transfer for collaboration, or permanent transfer which is a two step process under 'My Project').
- The 'Authorisation' tab allows electronic signature of the document (N.B. All signatories must have their own Online Forms account). Any changes made to the form **after** electronic signature will cause the authorisation to be invalidated.
- The 'Submission' tab is used for submitting an application to a reviewing public health organisation in Victoria. Answer the questions on the tab and select 'Submit your application electronically'. For a multi-site project, record the HREC Reference Number obtained from CAS.
  For a single-site project, the HREC Reference Number appears on the form after it has been uploaded in AU RED by the administrator.

Preparing a LNR VIC using Online Forms (CPI)

- To begin filling the form, select 'LNR VIC' below the 'My Project' icon on the left of the screen. Follow the instructions to fill in the form. Work across the form tabs from left to right.
- All supporting documents must be uploaded. To determine the supporting documents required for the application, refer to the **CPI/PI Ethics Checklist** (available from www.health.vic.gov.au/clinicaltrials or www.health.vic.gov.au/healthandmedicalresearch). A VSM is **not** required for a LNR VIC application.
  To upload documents to the application:
  - Select the 'Documents' tab and a list of document types appears.
  - Choose the 'Upload' tab; select the 'Browse' or 'Choose Files' button and select multiple documents (hold down Ctrl key); fill in details and select 'Upload Files'.
  - If uploading more than one document of the same type, distinguish them by putting the specific detail in the 'Version' field.
- The 'Transfer' tab is used to transfer the LNR VIC to a colleague (either temporary transfer for collaboration, or permanent transfer which is a two step process under 'My Project').
- The 'Authorisation' tab allows electronic signature of the document (N.B. All signatories must have their own Online Forms account). Any changes made to the form **after** electronic signature will cause the authorisation to be invalidated.
- The 'Submission' tab is used for submitting an application to a reviewing public health organisation in Victoria. Answer the questions on the tab and select 'Submit your application electronically'. For a multi-site project, record the HREC Reference Number obtained from CAS.
  For a single-site project, the HREC Reference Number appears on the form after it has been uploaded in AU RED by the administrator.

Preparing a SSA form using Online Forms (CPI <u>and</u> PI)

- The CPI (or delegate) **<u>must</u>** generate the required number of SSA forms from the NEAF for that particular research project. This allows data flow from the NEAF to the SSA and creates an electronic link between the documents.
- In the NEAF, select the 'SSA' tab; enter the number of SSAs required and select 'Create a new SSA form' The new SSA(s) will appear in a list.

- Select each new SSA individually and nominate the jurisdiction in which the site is located. **SSA forms differ for jurisdictions**.
- The CPI (or delegate) must transfer each SSA form to the site's PI (or delegate) by using the SSA 'Transfer' tab and entering the email address of the PI/delegate. An email will be sent to the PI/delegate informing them that a SSA form is available for them to complete.
- All PIs/delegates must have Online Forms accounts in order to complete the SSA. When the PI logs into Online Forms, their SSA form is accessible.
- Supporting documents that were uploaded to the ethics application form by the CPI automatically transfer to the SSA. The PI should ensure that all supporting documents for an application are uploaded to the SSA (refer to instructions above regarding uploading supporting documents). Refer to the **Research Governance Checklist** (available from www.health.vic.gov.au/clinicaltrials or www.health.vic.gov.au/healthandmedicalresearch) to determine the supporting documents required.
- Some pages of the SSA form cannot be filled in by PIs (e.g. 'Declarations'); they may only be partially completed online and are designed to be authorised electronically.
- It is possible to obtain electronic signatures for 'Declaration' by authorities on the SSA form. Select the 'Authorisation' tab and choose the 'Authorisation type' to request a signature. If any changes are made to the form before submission, the authorisations will be invalidated; new authorisations will be required for submission of the SSA form.
- The 'Submission' tab is used for submitting an application to a reviewing public health organisation in Victoria. Answer the questions on the tab and record the HREC Reference Number for the associated ethics application. Select 'Submit your application electronically'.
  Note: The HREC Reference Number within the SSA form (on page 1) is automatically populated from the NEAF. It **must** be present on the NEAF in order for the SSA to be submitted.

Preparing a LNR VIC SSA form using Online Forms (CPI and PI)

- The CPI (or delegate) **must** generate the required number of LNR VIC SSA forms from the LNR VIC for that particular research project. This allows data flow from the LNR VIC to the LNR VIC SSA and creates an electronic link between the documents.
- In the NEAF, select the 'SSA' tab; enter the number of LNR VIC SSAs required and select 'Create a new SSA form' The new LNR VIC SSA(s) will appear in a list.
- The CPI (or delegate) must transfer each LNR VIC SSA form to the site's PI (or delegate) by using the SSA 'Transfer' tab and entering the email address of the PI/delegate. An email will be sent to the PI/delegate informing them that a LNR VIC SSA form is available for them to complete.
- All PIs/delegates must have Online Forms accounts in order to complete the LNR VIC SSA. When the PI logs into Online Forms, their LNR VIC SSA form is accessible.
- Supporting documents that were uploaded to the ethics application form by the CPI automatically transfer to the LNR VIC SSA. The PI should ensure that all supporting documents for an application are uploaded to the LNR VIC SSA (refer to instructions above regarding uploading supporting documents). Refer to the **Research Governance Checklist** (available from www.health.vic.gov.au/clinicaltrials or www.health.vic.gov.au/healthandmedicalresearch) to determine the supporting documents required.
- Some pages of the LNR VIC SSA form cannot be filled in by PIs (e.g. 'Declarations'); they may only be partially completed online and are designed to be authorised electronically.
- It is possible to obtain electronic signatures for 'Declaration' by authorities on the LNR VIC SSA form. Select the 'Authorisation' tab and choose the 'Authorisation type' to request a signature. If any changes in the form are made before submission, the authorisations will be invalidated; new authorisations will be required for submission of the LN VIC SSA form.
- The 'Submission' tab is used for submitting an application to a reviewing public health organisation in Victoria. Answer the questions on the tab and record the HREC Reference Number (multi-site project) or LNR Reference Number (single-site project) for the associated ethics application. Select 'Submit your application electronically'.
  Note: The HREC or LNR Reference Number within the SSA form (on page 1) is automatically populated from the LNR VIC. It **must** be present on the LNR VIC in order for the LNR VIC SSA to be submitted.

SOP 05 Allocating a Multi-site Research Project Ethics Application to a Reviewing HREC

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

5.1 For NMA applications, the CPI and colleagues should decide in which jurisdiction the application will be submitted for review. For applications in Queensland, book through www.health.qld.gov.au/ohmr/html/regu/cen_coord_serv.asp. For applications in Victoria, contact the Central Allocation System (CAS) on 03 9096 7395. In New South Wales and South Australia, contact the research office of the proposed reviewing HREC.

5.2 Information on Victorian reviewing HRECs and meeting dates is available from www.health.vic.gov.au/clinicaltrials or www.health.vic.gov.au/healthandmedicalresearch or the website of the organisation hosting the reviewing HREC.

5.3 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 trial, 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.

5.4 Each HREC can review a limited number of streamlined applications at their meetings. If the applicant has a strong preference regarding their choice of reviewing committee, they should call CAS early to avoid disappointment or delay.

5.5 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.

5.6 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), the reviewing HREC Coordinator and the RGO(s). This email will contain the:
- **HREC Reference Number**
- Reviewing HREC name
- HREC meeting information

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

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

5.9 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.

5.10 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 06).

5.11 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.

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

6.1 All ethics applications must be prepared using the NEAF or LNR VIC completed on the Online Forms website https://au.ethicsform.org (refer to SOP 04).

6.2 A completed VSM to address Victorian-specific legislation must be attached to the NEAF (VSM is not required for LNR VIC applications). 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 **CPI/PI Ethics Checklist** (available from www.health.vic.gov.au/clinicaltrials or www.health.vic.gov.au/healthandmedicalresearch).

6.3 If ionising radiation is involved in a research project, a **Section 4 – Use of Ionising Radiation** (available from www.health.vic.gov.au/clinicaltrials or www.health.vic.gov.au/healthandmedicalresearch) and a Medical Physicist's report must be submitted for each participating site. A separate **Section 4** is not required for the CPI's site, as the one within the VSM encompasses their site information.

6.4 When the ethics application form (NEAF or LNR VIC) is complete, it must be signed by the CPI (electronic authorisation is available on the Online Forms website); other PIs are not required to sign. On the Online Forms website, supporting documents must be uploaded to the application form and the whole application must be electronically submitted to the reviewing organisation.

6.5 A completed **CPI/PI Ethics Checklist** and **Cover Letter** (both available from www.health.vic.gov.au/clinicaltrials or www.health.vic.gov.au/healthandmedicalresearch) **must** be attached to the application submitted to the reviewing HREC research office.

6.6 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 facilitate an easier and quicker HREC review process.

6.7 After the application is submitted to the HREC research office by the CPI, it must be validated by the reviewing HREC Coordinator before progressing for HREC review.

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

NMA submissions for review in Victoria

6.9 The above information, with the exception of that relating to ionising radiation, applies to both Victoria-only and NMA applications.

Note: Direct electronic submission from Online Forms is not available in other states/territories. Ethics and research governance/SSA applications remain linked across jurisdictions.

A NEAF must be used for all NMA applications; the LNR VIC is a state-specific form and must **not** be used for a NMA application.

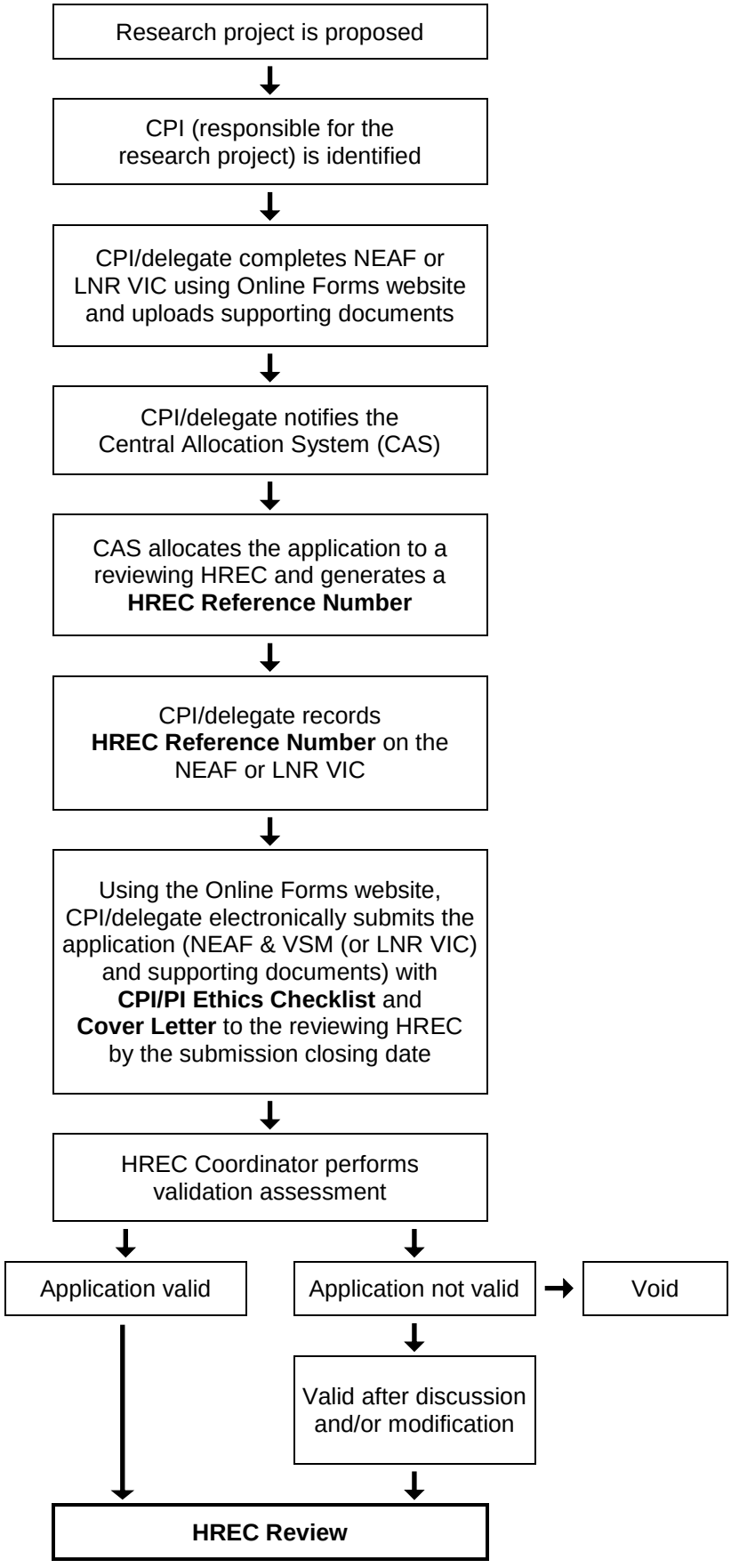
6.10 For research projects involving the use of ionising radiation at a Victorian site, with HREC review in Victoria, NSW, QLD or SA, the Victorian sites must submit a **Section 4 – Use of Ionising Radiation** (for VIC CPI site, the VSM must be completed).

For sites in NSW, QLD and SA, **Section 4 – Use of Ionising Radiation** is **not** required. A **Notification to the Reviewing HREC** (available from www.health.vic.gov.au/clinicaltrials) must be

completed for each site in NSW, QLD and SA 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 if the radiation exposure is considered to be additional to normal clinical management/care at the particular site.

6.11 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 www.health.vic.gov.au/clinicaltrials) may be required for the ethics submission to the reviewing HREC.

Figure 1. Application process for ethical review in Victoria



SOP 07 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

7.1 At the planning stage of the research project, the sponsor/CRO in consultation with Investigators will choose sites at which to conduct it. Sponsors/CROs 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 is ready to complete and submit the ethics application to the reviewing HREC.

7.2 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 ethical review by a local HREC. It is a research governance process.

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

Note: When submitting a SSA or LNR VIC SSA from the Online Forms website, it is a requirement to record the HREC or LNR Reference Number for the associated ethics application. The HREC or LNR Reference Number **must** also be present on the NEAF or LNR VIC.

7.4 Each PI at a site involved in a multi-site research project must complete a SSA or LNR VIC 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; and
- other compliance and policy aspects.

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

7.6 Supporting documents must be uploaded to the application form. A **Research Governance Checklist** and **Cover Letter** (both available from www.health.vic.gov.au/clinicaltrials or www.health.vic.gov.au/healthandmedicalresearch) with full details **must** be included.

7.7 The SSA or LNR VIC 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 the Online Forms website.

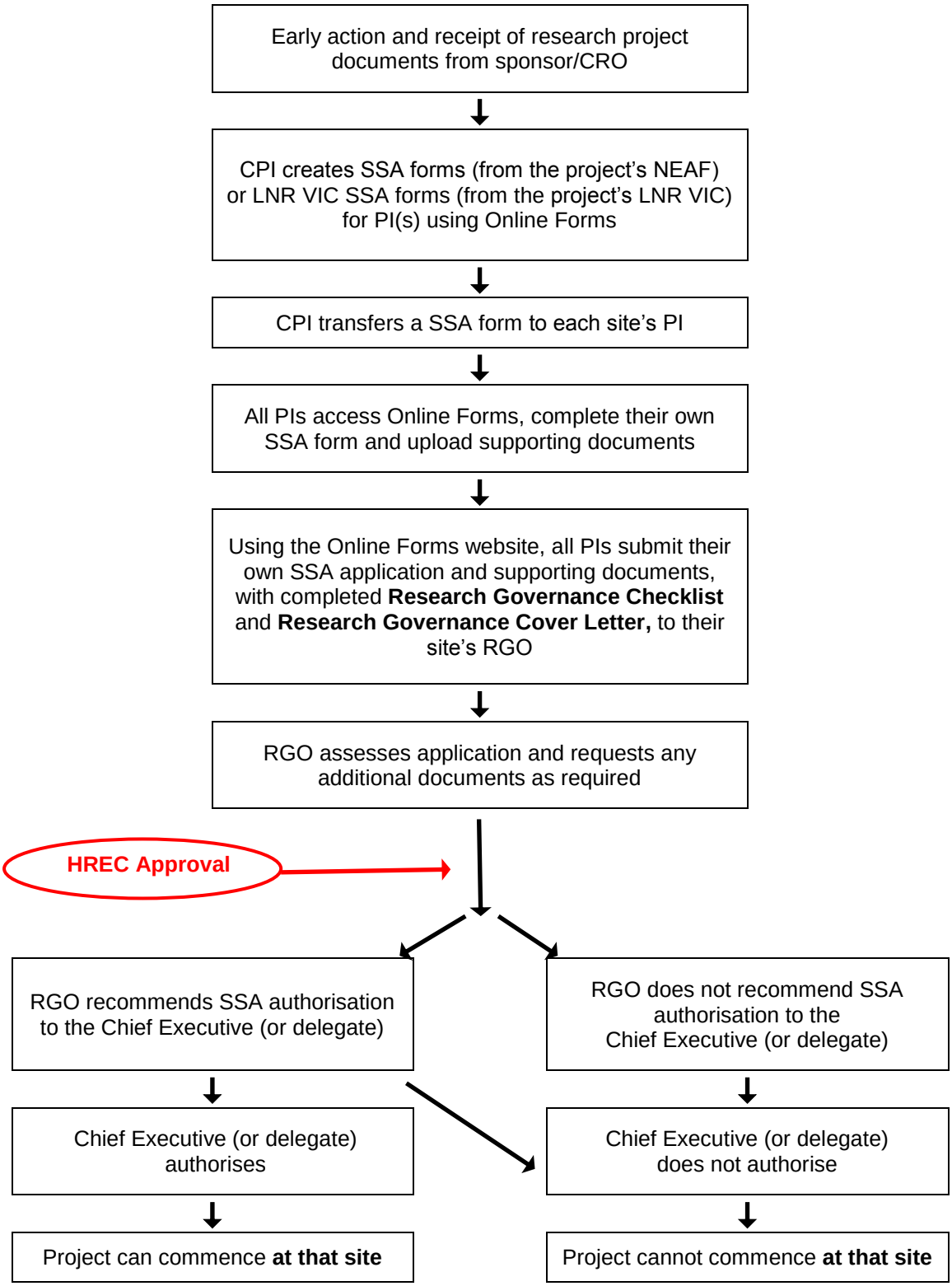
7.8 Once the complete research governance/SSA application is submitted to the RGO, it must be validated. After the RGO has been notified that HREC approval has been granted by the reviewing HREC (refer to SOP 13), the RGO can recommend research governance/SSA authorisation to the organisation's Chief executive (or delegate). Once the Chief Executive (or delegate) authorises the SSA, the research project can commence **at that site**.

7.9 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.

7.10 For detailed guidance on research governance and site specific assessment (SSA), refer to *Research Governance and Site Specific Assessment – Process and Practice* (available from www.health.vic.gov.au/clinicaltrials or www.health.vic.gov.au/healthandmedicalresearch).

Figure 2. Research governance/SSA process



SOP 08 Validation of an Ethics Application for a Research Project

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

8.1 After the application is submitted to the HREC research office by the CPI, 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.

8.2 A completed **CPI/PI Ethics Checklist** and **Cover Letter** must be attached to an HREC submission (both documents are available from www.health.vic.gov.au/clinicaltrials or www.health.vic.gov.au/healthandmedicalresearch). A valid application is one that is deemed by the reviewing HREC Coordinator to be complete and accurate.

8.3 Validation criteria include ensuring the following are present:
- NEAF with all required supporting documents uploaded to Online Forms website (refer to **CPI/PI Ethics Checklist** for a list of relevant documents)
- HREC Reference Number (assigned by CAS and entered on the NEAF or LNR VIC by the CPI or delegate)
- Signature (or electronic authorisation) of the CPI on the NEAF or LNR VIC
- Any specific requirements of the reviewing HREC.

8.4 The reviewing HREC Coordinator determines whether or not an application is valid, and notifies the CPI. Notification should be given within 5 working days of the submission closing date. If an application is invalid, the reviewing HREC Coordinator should specify the reasons why it is invalid.

8.5 If an application is invalid, the CPI (or delegate) should discuss the issues with the reviewing HREC Coordinator. On the Online Forms website, the application form can be modified and/or new/revised supporting documents uploaded; these can then be 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 meeting, allowing the CPI more time to resolve the issues; this should be discussed with the reviewing HREC Coordinator.

8.6 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.

SOP 09 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

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

9.2 The reviewing HREC will review the following documents that relate to use of ionising radiation:
- VSM, including Section 4, completed by the CPI (or a Victorian PI, if the CPI is based outside Victoria)
- Additional VSM Section 4 *Use of Ionising Radiation* for all other participating Victorian sites (not including the CPI site)
- 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 12). 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).

9.3 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.

9.4 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 and approval has been given by the reviewing HREC, and research governance/SSA authorisation no DHHS notification is required.

9.5 For further information, refer to www.health.vic.gov.au/radiation.

SOP 10 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

10.1 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 is available on www.tga.gov.au.

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

10.3 If adding a new site to an approved research project (refer to SOP 18), a CTN form must be generated for the additional site.

SOP 11 Clinical Trial Research Agreement for a Multi-site Clinical Trial

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

11.1 Standard clinical trial agreements are available on the Medicines Australia website www.medicinesaustralia.com.au and Medical Technology Association of Australia website www.mtaa.org.au. For reasons of timeliness and cost, and compliance with insurance requirements, it is recommended that the standard CTRAs are used as appropriate.

11.2 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.

11.3 Schedule 7 of the Commercially Sponsored CTRA and Schedule 4 of the CRG/CRO and Phase 4 CTRA 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. Organisations that allow sponsored clinical trials to operate under agreements that do not adhere to the conditions stipulated in a standard CTRA, risk compromising insurance cover under VMIA policy.

11.4 A set of standard Schedule 7 and 4 Special Conditions with a number of commercial and non-commercial clinical trial sponsors is provided to public hospitals by the Coordinating Office. Four States participate in agreeing standard Schedules using the Southern Eastern Border States panel and details for applications are on the Medicines Australia website (www.medicinesaustralia.com.au). 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.

SOP 12 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

12.1 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 www.health.vic.gov.au/clinicaltrials or www.health.vic.gov.au/healthandmedicalresearch.

12.2 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 at 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. Permissable 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.

12.3 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.

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

12.5 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).

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

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

12.8 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 13 Notification of an HREC Decision following Ethics Review of a Research Project

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

13.1 The reviewing HREC Coordinator must notify the CPI of the outcome of the HREC review meeting in writing within 5 working days of the HREC meeting.

Provisional approval of application, with a request for further information

13.2 The reviewing HREC may decide to request further information from the CPI. A standard letter detailing the information required will be sent to the CPI. When the HREC Coordinator records the further information request, the Online Forms application form becomes available for modification.

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.

13.3 The CPI must provide the requested information to the reviewing HREC Coordinator **as soon as possible**. The HREC review process and approval cannot continue until the reviewing HREC Coordinator has received a satisfactory response from the CPI.

A prompt response from the CPI to any information requests is essential in order to facilitate the HREC review process.

Application approved

13.4 A HREC approval letter specifying the conditions of HREC approval will be sent to the CPI, who must forward it to the PI(s), RGO(s), sponsor/CRO and project coordinator. The date of the decision is the date on which the correspondence is sent.

13.5 The research project cannot commence at a site until authorisation of research governance/SSA at that site is granted (refer to SOP 14). Completion of the CTN regulatory requirement and any other licence/regulatory requirements are necessary before SSA authorisation can occur.

13.6 For clinical trials there should be a CTN form for each site involved (refer to SOP 10).

13.7 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

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

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

Appeals concerning ethical review and decision

13.10 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 14 Authorisation of Research Governance/SSA

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

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

14.2 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.

14.3 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.

14.4 For clinical trials conducted under the CTN scheme, the TGA acknowledgement is issued once the CTN form has been processed by the TGA. The sponsor's insurance does not take effect until the TGA acknowledgement is issued.

14.5 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.

14.6 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.

14.7 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.

14.8 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).

14.9 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.

SOP 15 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

15.1 The benchmark time for streamlined ethical review by an HREC in Victoria is 30 working days. This is calculated using the clock stop-start feature in AU RED (the information management system used by research offices).

15.2 The time for review 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 to respond to information requests from the HREC.

15.3 If the reviewing HREC requests further information from the CPI, the AU RED clock must be stopped on the day that the request for further information is sent to the CPI (or 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 does not sufficiently satisfy the HREC's requirements, the reviewing HREC Coordinator may make further requests for information from the CPI. Each time a request is made and response received, the clock will stop and start accordingly.

A prompt response from the CPI to any information requests is essential in order to facilitate the HREC review process.

15.4 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 (or delegate).

15.5 A 30 working day benchmark for performance of ethics review has been set in Victoria. Expiration of this 30 working day period does not entitle the investigator or sponsor to any redress (e.g. immediate decision from the reviewing HREC or refund of an application fee).

15.6 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

15.7 A research project cannot commence at a site, even if ethically approved, until the research governance process has been completed and SSA or LNR VIC SSA has been authorised by the Chief Executive (or delegate) (refer to SOP 14).

15.8 Whilst authorisation of the SSA or LNR VIC 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. The RGO can request further information from the applicant, which allows the PI to upload further supporting documents and re-submit electronically. The RGO can assess the documents and obtain legal or other review without causing a delay to the overall governance process. The SSA or LNR VIC SSA can therefore 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, which leads to timely SSA authorisation and project start-up.

SOP 16 Amendment to an Ethically Approved Research Project

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

16.1 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 research.

16.2 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 is responsible for submitting an amendment to the reviewing HREC; they must complete a **HREC Amendment Form** (available from www.health.vic.gov.au/clinicaltrials for clinical trials and www.health.vic.gov.au/healthandmedicalresearch for health and medical research).

16.3 If necessary, the CPI (or delegate) should communicate with the reviewing HREC Coordinator regarding the amendment. The CPI (or delegate) must communicate with the sponsor/CRO, PI(s) and RGO(s) regarding the amendment process.

16.4 On the Online Forms website, new/revised supporting documents (including **HREC Amendment Form**) can be uploaded to the original application; these can be electronically submitted to the reviewing HREC Coordinator.

16.5 The reviewing HREC Coordinator must send a letter to the CPI acknowledging whether an amendment has been validated or not validated.

16.6 The reviewing HREC Coordinator must communicate the decision of the reviewing HREC by letter to the CPI, who will then forward it to PI(s), RGO(s), sponsor/CRO and project coordinator.

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

16.8 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 19).

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

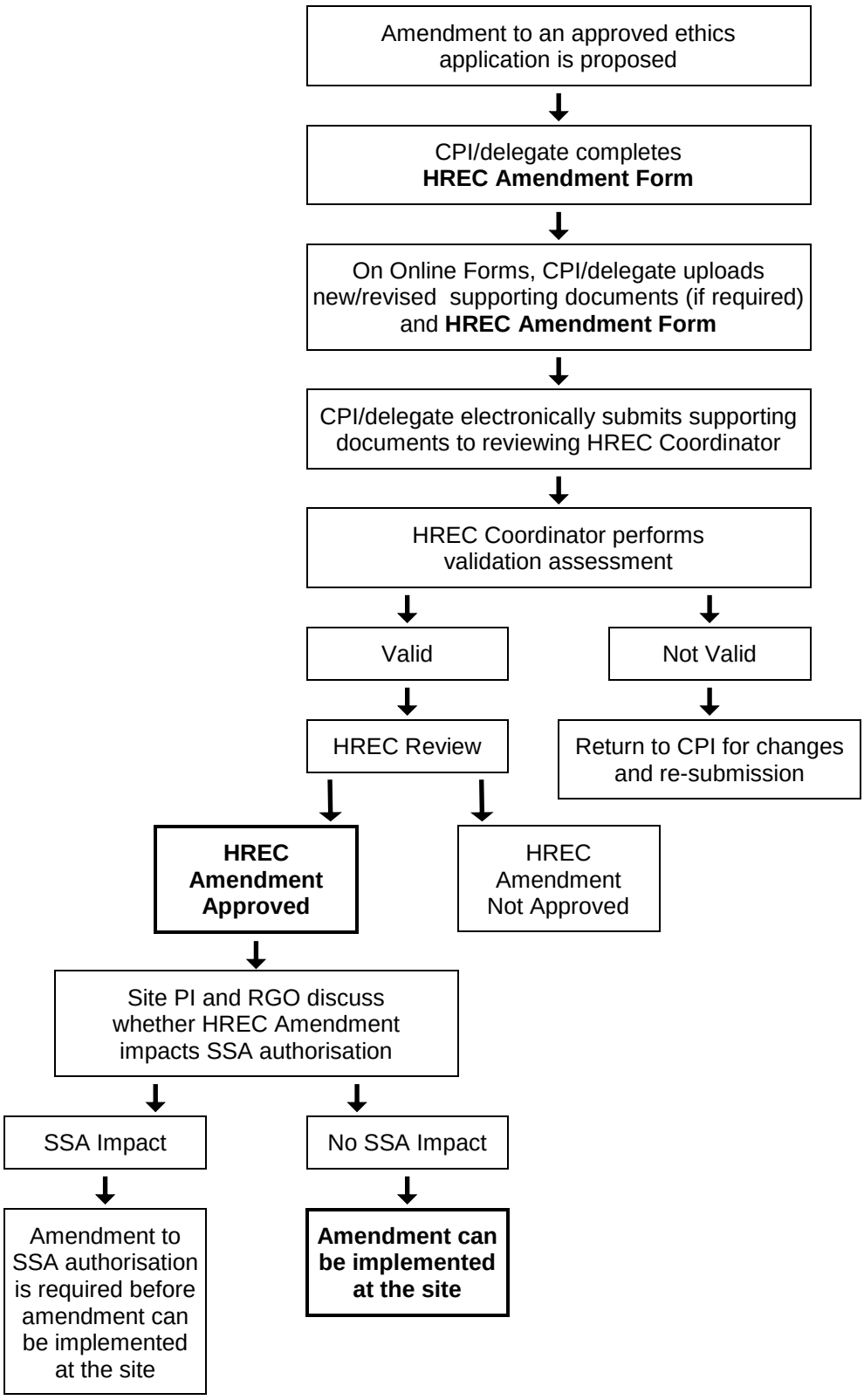
Implementation of an amendment

16.10 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 (if applicable) has been authorised by the Chief Executive (or delegate).

16.11 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 they have been notified in writing by the RGO.

16.12 Exceptions to the amendment process may be made in circumstances where there is a serious threat to the health and safety of participants. The CPI (or delegate) should notify the reviewing HREC Coordinator and ensure that PIs notify the RGO at each relevant site as soon as possible.

Figure 3. HREC Amendment to an Approved Research Project



SOP 17 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

17.1 Details of policy and documents to guide or submit through National Mutual Acceptance (NMA) are available at www.health.vic.gov.au/clinicaltrials.

17.2 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 06), even if there is only one site confirmed at the time of the HREC application.

17.3 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 with the agreement of the HREC Coordinator, notification to CAS, the reviewing HREC is NHMRC certified and the date of HREC approval falls within the appropriate timeframe.

17.4 If a single-site clinical trial has been approved by an HREC that is accredited to review in the streamlined system or certified with NHMRC (for interjurisdictional review), then the original approval can be expanded to a multi-site approval, with agreement of the reviewing HREC Coordinator. This can only be applied for research projects that would have qualified for the streamlined system that was in place at the time of their original approval. The start dates for the streamlined systems are detailed in the tables below. The project must qualify under the scope of the streamlined system (refer to SOP 01), and IMA or NMA applications must meet the relevant criteria (refer to SOP 02).

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
IMA	Clinical trials	NSW, QLD, VIC	February 2012
NMA	Clinical trials	NSW, QLD, SA, VIC	November 2013

17.5 If the HREC Coordinator agrees that a single site approval will be expanded to multi-site, the applicant must contact CAS (refer to SOP 05).

The process should be followed for adding an additional site to an existing approval (refer to SOP 18) and the SSA process carried out accordingly.

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

17.7 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.

17.8 A research project that was originally submitted and approved with a LNR VIC application cannot be expanded to include sites in other states/territories. LNR forms are state-specific. All NMA applications, including those that are considered low risk, must be submitted using the NEAF.

SOP 18 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

18.1 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 process. An **HREC Amendment Form** is available from www.health.vic.gov.au/clinicaltrials for clinical trials and www.health.vic.gov.au/healthandmedicalresearch for health and medical research. The CPI (or delegate) must also submit to the reviewing HREC the contact details and curriculum vitae of the PI at the new site.

18.2 Under the IMA and NMA initiatives, if the original HREC application was for a single state and the proposed additional site is in another state (therefore changing the HREC review to a NMA one), this should be made clear to the reviewing HREC and notified to CAS. HREC approvals can only be expanded to interstate sites if the research project meets the eligibility criteria for IMA or NMA (whichever was in place at the time of the HREC approval), and if the original HREC application was submitted after the relevant initiative commenced (refer to tables below for details and dates). This will require an HREC amendment process.

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
IMA	Clinical trials	NSW, QLD, VIC	February 2012
NMA	Clinical trials	NSW, QLD, SA, VIC	November 2013

If additional sites are to be added to an existing approved IMA or NMA multi-site research project, the CPI 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. LNR forms are state-specific. All NMA applications, including those that are considered low risk, must be submitted using the NEAF.

18.3 The CPI (or delegate) must generate a SSA form (or LNR VIC SSA form for eligible Victoria-only application) using the Online Forms website (refer to SOP 04) and transfer it to the new site's PI (or delegate). The SSA or LNR VIC SSA **must** be generated from the NEAF or LNR VIC that was submitted to and approved by the HREC.

18.4 The CPI must send the new site's PI and RGO a copy of all documents previously approved by the HREC.

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

18.6 For an eligible research project, a CTN form (if applicable) is required for the new site (refer to SOP 10).

18.7 The reviewing HREC will review the new PI's competence and qualifications and other relevant details as per the *National Statement on Ethical Conduct in Human Research* (NHMRC, 2007) and, if approved, issue a HREC approval for the research project listing the new site. This

approval should be sent by the HREC Coordinator to the CPI, who will forward it to all PIs and RGOs, the sponsor/CRO and project coordinator.

18.8 The SSA or LNR VIC 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 at the new site, the trial can commence at that site.

SOP 19 Amendment to Research Governance/SSA

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

19.1 A research governance/SSA amendment may be necessary as a result of an HREC amendment (refer to SOP 16), or may be due to an issue affecting that site only.

19.2 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 arrangements.

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

19.4 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.

19.5 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 RGO at the site. The RGO will send acknowledgement of the research governance/SSA amendment submission, indicating whether it is valid.

19.6 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.

19.7 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

19.8 Where new or amended documentation has been submitted to the reviewing HREC for ethical review, the approved documents must be sent by the CPI to each site's PI and RGO.

19.9 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 20 Monitoring of an Ethically Approved Research Project

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

20.1 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.

20.2 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 adverse 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.

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

20.4 Reporting forms are available from www.health.vic.gov.au/clinicaltrials for clinical trials and www.health.vic.gov.au/healthandmedicalresearch for health and medical research.

SOP 21 Reporting on an Ethically Approved Research Project

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

Annual progress report

21.1 Progress of research should be reported annually (at a minimum) or as required by the reviewing HREC.

21.2 Continuation of ethical approval for a research project is dependent on timely submission of annual progress reports.

21.3 The CPI is responsible for communicating with the reviewing HREC Coordinator regarding reports on research projects being conducted. Reports must be submitted on the recommended template.

21.4 The report to the reviewing HREC should contain information about the project from PIs at all sites. A **HREC Progress Report – Site Report** (available from www.health.vic.gov.au/clinicaltrials for clinical trials and www.health.vic.gov.au/healthandmedicalresearch for health and medical research) must be completed by each PI; one copy must be forwarded to the site's RGO and one copy sent to the CPI for collation.

21.5 The CPI must collate the Site Reports from participating sites, complete a **HREC Progress Report – CPI Cover Sheet** (available from www.health.vic.gov.au/clinicaltrials for clinical trials and www.health.vic.gov.au/healthandmedicalresearch for health and medical research), and submit them to the reviewing HREC Coordinator. The number of copies required is determined by the HREC Coordinator. If a site does not provide the CPI with the requested report that site may have ethical approval suspended until receipt of the report.

21.6 On the Online Forms website, the CPI must upload the Progress Report as a supporting document to the NEAF or LNR VIC under the 'Documents' tab, and then electronically submit.

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

An acknowledgement of the report will be sent to the CPI.

Final report

21.8 At the conclusion of a research project at one or more sites, the CPI (or delegate) must notify the reviewing HREC.

21.9 If a single site is being closed, that site's PI must complete a **HREC Final Report** (available from www.health.vic.gov.au/clinicaltrials for clinical trials and www.health.vic.gov.au/healthandmedicalresearch for health and medical research). One copy must be forwarded to the site's RGO and one copy sent to the CPI for forwarding to the reviewing HREC.

21.10 If the research project is completed at all sites, the CPI must complete a **HREC Final Report** (available from www.health.vic.gov.au/clinicaltrials for clinical trials and www.health.vic.gov.au/healthandmedicalresearch for health and medical research), submit it to the reviewing HREC Coordinator, and send a copy to all sites' PIs and RGOs. Contact the reviewing HREC Coordinator or refer to their website for specific requirements and the procedure to follow for submission of a final report.

21.11 An acknowledgement of the report will be sent to the CPI.

SOP 22 AE, SAE, SUSAR and USADE Reporting for a Research Project

Purpose To describe the requirements for reporting to the reviewing HREC regarding Adverse Events (AEs), Serious Adverse Events (SAEs), Suspected Unexpected Serious Adverse Reactions (SUSARs) and Unanticipated Serious Adverse Device Effects (USADEs) that occur during an ethically approved research project

22.1 Reporting of safety events (AEs, SAEs, SUSARs and USADEs) to the reviewing HREC must meet the requirements of the *National Statement on Ethical Conduct in Human Research* (NHMRC, 2007) and the AHEC *Position Statement: Monitoring and reporting of safety for clinical trials involving therapeutic products* (NHMRC, 2009) or any other document that supersedes this document.

22.2 A standard **AE and SAE Report** and a standard **SUSAR/USADE Site Report** are both available from www.health.vic.gov.au/clinicaltrials for clinical trials and a **AE and SAE Report** for health and medical research is available from www.health.vic.gov.au/healthandmedicalresearch. Reporting requirements for safety events in a research project will be found on the website of the reviewing HREC. The reviewing HREC may, as part of ethical approval, require more detailed and/or frequent reporting for research projects depending on the perceived risk of the research to the participants. It is the responsibility of the CPI (or delegate) to provide appropriate AE/SAE/SUSAR/USADE reports to the reviewing HREC

22.3 The PI must notify the CPI (or delegate) of an AE/SAE/SUSAR/USADE where there is a **material impact** on the continued ethical acceptability, or the AE/SAE/SUSAR/USADE indicates a need for a change to the protocol. The CPI must submit the relevant safety reports to the reviewing HREC in a prompt manner (**within 24 hours**). The site RGO should be notified by the PI.

22.4 Refer to the VMIA website www.vmia.vic.gov.au for information regarding SUSAR and USADE reporting.

22.5 To avoid delay, the PI may contact the CPI and forward details of the AE/SAE/SUSAR/USADE directly to the reviewing HREC. This is an exception to the general rule that the PI must always communicate with the reviewing HREC via the CPI.

22.6 Upon receipt of an **AE and SAE Report** or a **SUSAR/USADE Site Report,** the reviewing HREC will review the report and take appropriate action. The CPI will be notified of the review outcome.

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

22.8 If the PI considers that an event has **no material impact** on the research project, the PI should:
- Notify their RGO and ask if a copy of the AE/SAE report is required
- Determine whether the reviewing HREC has a local policy that requires the AE/SAE report to be forwarded to the HREC Coordinator.

If the reviewing HREC does not require a copy of the AE/SAE report, it should be filed securely according to local practice.

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

SOP 23 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

23.1 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.

23.2 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).

23.3 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.

23.4 The nominated person to receive complaints should provide information regarding the complaint to the site RGO, who 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.

23.5 If the complaint requires notification to the reviewing HREC, the site PI must complete a **Complaints Report to HREC – Site Report** (available from www.health.vic.gov.au/clinicaltrials for clinical trials and www.health.vic.gov.au/healthandmedicalresearch for health and medical research), and send one copy to the CPI (who will forward it to the reviewing HREC) and one copy to the RGO at their own site where the complaint arose.

SOP 24 Withdrawal or Suspension of Ethical Approval or SSA Authorisation for a Research Project

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

Withdrawal or suspension of ethical approval

24.1 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.

24.2 Where ethical approval for a research project is withdrawn or suspended by the reviewing HREC, the CPI, PI(s), RGO(s), sponsor and project coordinator must be notified **immediately** of the withdrawal/suspension of HREC approval. Notification in writing should be provided as soon as possible thereafter.

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

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

24.4 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

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

24.6 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.

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

SOP 25 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

25.1 On completion of a research project, the CPI (or delegate) must notify the reviewing HREC Coordinator that the research project has been completed by submitting an **HREC Final Report** (available from www.health.vic.gov.au/clinicaltrials for clinical trials and www.health.vic.gov.au/healthandmedicalresearch for health and medical research).

25.2 Once an **HREC Final Report** has been received by the reviewing HREC Coordinator, a letter of acknowledgement will be sent to the CPI who will forward it to the PI(s), RGO(s), sponsor and project coordinator.

Early termination of a research project

25.3 If a research project is terminated or suspended by the sponsor or CPI before the expected date of completion, the reviewing HREC, RGO(s), sponsor and project coordinator must be promptly notified.

25.4 A detailed written explanation, in the **HREC Final Report**, of the reasons why a research project has been terminated must be submitted to the reviewing HREC Coordinator and the RGO at each site.