

# **Standard Operating Procedures**

**for**

## **Streamlining Ethical Review of Multi-site Clinical Trials System in Victoria**

## **CONTENTS**

<b>SOP 01</b>	Scope of the Consultative Council for Human Research Ethics
<b>SOP 02</b>	Role and responsibilities of the Coordinating Principal Investigator and delegation
<b>SOP 03</b>	Online Human Research Ethics Application Forms Website
<b>SOP 04</b>	Procedure for allocating an application to a reviewing HREC
<b>SOP 05</b>	Submitting an HREC application for multi-site clinical trials
<b>SOP 06</b>	Use of ionising radiation submission requirements for HREC review
<b>SOP 07</b>	Submitting a site specific assessment for multi-site clinical trials
<b>SOP 08</b>	Validation of an HREC application
<b>SOP 09</b>	Ethical review of applications and the 30 working day clock
<b>SOP 10</b>	Clinical trials conducted under the Clinical Trials Notification (CTN) or Clinical Trials Exemption (CTX) Schemes
<b>SOP 11</b>	Clinical Trial Research Agreements (CTRA) for clinical trials
<b>SOP 12</b>	Review of Participant Information and Consent Form
<b>SOP 13</b>	Notification of the decision following HREC review
<b>SOP 14</b>	Amendment of an ethically approved research project
<b>SOP 15</b>	Monitoring of approved research
<b>SOP 16</b>	Reporting on approved research
<b>SOP 17</b>	Early termination of an approved research project
<b>SOP 18</b>	Adverse event (AE)/Serious Adverse Event (SAE) reporting for clinical trials
<b>SOP 19</b>	Withdrawal or suspension of ethical approval
<b>SOP 20</b>	Appeals concerning the ethical review and decision of a reviewing HREC
<b>SOP 21</b>	Complaints concerning the conduct of an ethically approved research project
<b>SOP 22</b>	Adding a new site to a project approved in the single ethical review system for multi-site clinical trials
<b>SOP 23</b>	Projects, approved before the establishment of the multi-site ethical review system, progressing to multi-site research

- SOP 24** Multi-site research approved prior to establishment of the multi-site ethical review system
- SOP 25** The Research Governance Officer
- SOP 26** Authorisation of site specific assessment
- SOP 27** Amendment of a site specific assessment at a study site
- SOP 28** Withdrawal or suspension of SSA authorisation

## **SOP 01 Scope of the Consultative Council for Human Research Ethics**

**Purpose** To outline the scope of the system for human research ethical and scientific review of multi-site research in Victoria.

### **Scope**

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 researchers affiliated with different organisations;
- A project conducted at an organisation where the researcher is affiliated with another organisation and where more than one organisation requires ethical review and approval of the same research project.

1.2 The central system for ethical and scientific review of multi-site research will apply only to research involving an interventional drug or device trial, radiation therapy, surgery, treatment and diagnostic procedure.

- Commercial sponsors;
- Collaborative groups/Consortiums, either supported or not supported by a commercial company;
- Investigator initiated groups, either supported or not supported by a commercial company.

The scope also includes research involving radiation therapy, surgery, treatment and diagnostic procedure. However at this stage it excludes research that involves supportive care and psycho-oncology only and these areas will be considered at a later stage.

1.3 The central system now includes interventional clinical trials involving **adults and children.**

*Note: Intake of HREC applications for interventional clinical trials involving **children** will occur from February 2011 (for March 2011 HREC meeting).*

1.4 **New:** The central system will apply to interventional clinical trials, as defined above, and studies associated with ongoing activities relating to trials that have been conducted. This may include observational research and evaluation of a trial, developing a registry and other post-marketing surveillance activities.

1.5 In time, consideration may be given to extending the scope of research reviewed through the central system to other types of human research, subject to available capacity in the system and budget for this purpose.

1.6 Organisations that participate in the system for single review of multi-site research must sign a Memorandum of Understanding with the Consultative Council for Human Research Ethics in order to become a Participating Organisation. Participating organisations must agree to the following:

- i. The participating organisation must accept the ethical and scientific review of a reviewing HREC and not undertake any further review by the organisation's HREC;

- ii. 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;
- iii. A multi-site research project must not commence at a site unless the following has been completed:
  - The project has received ethical approval from a reviewing HREC;
  - A site-specific assessment has been conducted at the site where the research is to be undertaken;
  - The Chief Executive or delegate has sighted the HREC approval and endorsed the SSA giving authorisation for the project to be conducted at the site.
- iv. Consistency of HREC review standards and processes, and ongoing participation in professional development of ethics committee members and related stakeholders.

1.7 The Consultative Council for Human Research Ethics will:

- Be responsible for accreditation and selection of the human research ethics committees that undertake review of multi-site studies;
- Have oversight of the secretariat that will provide administrative support to the Consultative Council and coordinate ethics review processes within the system;
- Report to the Minister for Health and the Department of Health on the operational effectiveness of the overall system that undertakes ethics review of the multi-site studies;
- Promote best practice ethical review of multi-site human research and provide advice to participating health services in Victoria where required;
- Provide timely and authoritative advice to the Minister for Health and the Department of Health on relevant human research ethics issues at a state and national level;
- Establish policies, procedures and requirements of the operation of the streamlined system and monitor compliance with the same;
- Promote consistency of HREC review processes and ongoing participation in professional development of ethics committee members and other stakeholders";
- Review the accreditation process and extend accreditation to other organisations as required or revoke accreditation;
- Provide consultative support in collaboration with other relevant bodies.

1.8 Research involving organisations and sites external to Victoria will require approval from the organisation's HREC in accordance with the external jurisdiction's requirements.

## **SOP 02 Role and responsibilities of the Coordinating Principal Investigator and delegation**

**Purpose** To describe the role and responsibilities of the Coordinating Principal Investigator/or delegate in relation to ethical review.

### **Scope**

- 2.1 A Coordinating Principal Investigator must be nominated for each individual research project.
- 2.2 The Coordinating Principal Investigator must be employed and professionally based in an Australian organisation.
- 2.3 For international studies with a co-ordinating investigator outside Australia, a health professional based in Australia must be nominated as the Co-ordinating Principal Investigator responsible for the conduct of the research in Australia.
- 2.4 The Coordinating Principal Investigator/or delegate for a multi-site research project is responsible for submission of an application to a reviewing Human Research Ethics Committee (HREC).
- 2.5 The Coordinating Principal Investigator/or delegate will be responsible for correspondence relating to the ethical review and the HREC in accordance with the *National Statement on Ethical Conduct in Human Research (2007)*, chapter 5.2. This function, in part, may be delegated to a person who will act as a contact person on behalf of the Coordinating Principal Investigator.
- 2.6 Subsequent standard operating procedures will refer to the specific responsibilities of the Coordinating Principal Investigator/or delegate.
- 2.7 Correspondence between the Coordinating Principal Investigator and the Principal Investigators at other organisations conducting the clinical trial may be delegated by the Coordinating Principal Investigator. The following arrangements could be made for a clinical trial with the agreement of the reviewing HREC Coordinator. The reviewing HREC Coordinator's role would be to:
  - o Forward the HREC application (NEAF) and any supporting documents (electronically) to the Principal Investigator(s) so they can upload the ethics application (NEAF and supporting documents) to their site's SSA Online Form. If any supporting document is hard copy only, then the document should, in most cases, be scanned and emailed to the Principal Investigator(s).
  - o Copy all letters relating to the HREC application to Principal Investigator(s), Research Governance Officer(s) and the sponsor and Trial Coordinator. (*This may be via email*);
  - o Forward any changes to the HREC application (NEAF) required by the reviewing HREC (*this would include the cover letter explaining the changes*).
  - o Forward any new version of the supporting documents (electronically) to the Principal Investigator(s) so they can upload the new/approved version of the supporting documents to their

site's SSA Online Form. If any supporting document is hard copy only, then the document should, in most cases, be scanned and emailed to the Principal Investigator(s). The printed documents must be submitted by the principal Investigator to the Research Governance Officer at the site. *(All supporting documents would therefore be the same version as the approved HREC application).*

- 2.8 If the Coordinating Principal Investigator is absent or unavailable for a significant period then another Investigator must be nominated.

## **SOP 03 Online Human Research Ethics Application Forms Website**

**Purpose** To describe the online forms on the Online Forms website

### **AURED NEAF and SSA Online Forms**

- 3.1 The ethics application form (NEAF) must be accessed from the Online Forms website and used for all applications to a reviewing HREC.
- 3.2 The Online Forms website allows the applicant to complete the ethics application (NEAF) and site-specific assessment form (SSA) electronically.
- 3.4 The Online Forms can be accessed from [www.ethicsform.org/au](http://www.ethicsform.org/au) and an applicant must first register for an account. Once registered, an email with a user ID and password will be sent.
- 3.3 The **Victorian** forms must be used for all applications in Victoria.
- 3.5 The Online Forms website enables applicants to view updates on the status of their application.
- 3.6 A help desk will be available to assist users of the Online Forms website with technical problems. The online forms IT help desk can be accessed between 10am to 4pm AEST Monday to Friday on +61 2 903 78 404 or 02 9037 8408 or by email to [helpdesk@infonetica.net](mailto:helpdesk@infonetica.net).
- 3.7 For queries regarding the ethics application and any ethical issues, the Coordinating Office for Human Research Ethics may be contacted by phone on (03) 9092 1987 or by email to [Multisite.Ethics@health.vic.gov.au](mailto:Multisite.Ethics@health.vic.gov.au).

## **SOP 04 Procedure for allocating an application to a reviewing HREC**

**Purpose** To describe the procedure for bringing an ethics application into the system for single ethical review

- 4.1 Step by step details regarding the submission of an HREC application are provided on the Consultative Council for Human Research Ethics (CCHRE) website at [www.health.vic.gov.au/cchre](http://www.health.vic.gov.au/cchre).
- 4.2 To determine the reviewing HREC for a proposed ethics application the Coordinating Principal Investigator/or delegate should first contact the central Coordinating Office for Human Research Ethics by phone and speak to the coordinator of the Central Allocation System (CAS). *(This should be at the time the sponsor or investigator has identified the proposed sites to conduct the trial, and before the completion of the application. An application should be allocated to a reviewing HREC approximately two to four weeks before the ethics submission is made to a reviewing HREC).*
- 4.3 At the time of contact with the central Coordinating Office the applicant should be ready to submit the application within two to four weeks.
- 4.4 The caller will be asked to provide information regarding the application so that the application can be allocated to a reviewing HREC.
- 4.5 Once the questions have been answered, the CAS coordinator will allocate a reviewing HREC. An email will be sent to the Coordinating Principal Investigator, the caller *(if not the CPI)*, the reviewing HREC Coordinator and the Research Governance Officer. This will contain the following details:
  - the reviewing HREC name;
  - Booking Reference Number;
  - HREC Reference Number (unique identifier);
  - HREC meeting information;
  - some questions asked and the recorded answers which were provided.
- 4.6 Once the application has been allocated, the reviewing HREC Coordinator will automatically receive an email notification and the application details will appear on the AU RED Work Area under CAS allocation.
- 4.7 When the application is received, it must be validated by the reviewing HREC Coordinator.
- 4.8 It is important to note that the reviewing HREC Coordinator must assign the application to the allocated HREC meeting using AURED. Otherwise the application will not appear on the next reviewing HREC agenda.
- 4.9 The Coordinating Principal Investigator/or delegate must communicate with the reviewing HREC Coordinator regarding all subsequent matters relating to the application.

## **SOP 05 Submitting an HREC application for multi-site clinical trials**

**Purpose** To provide details of the process, the Coordinating Principal Investigator/or delegate should follow in submitting an application to a reviewing HREC

- 5.1 All new HREC applications are to be submitted using the National Ethics Application Form (NEAF) accessed via the Victorian portal of the Online Forms website <http://www.ethicsform.org.au>.
- 5.2 A completed Victorian-Specific Module to address Victorian-specific legislation must be attached to the NEAF application. This and other required documents must be uploaded on to the Online Forms website when completing the ethics application. Supporting documents should be attached and would include the Participant Information Consent Form, CTN form and other trial-related documents.
- 5.3 Once the ethics form is finally complete it must have a <sup>1</sup>'submission code' generated and printed on the form. The ethics form must be printed and signed by the Coordinating Principal Investigator (*other Principal Investigators are not required to sign the ethics application*). An Ethics Checklist for Coordinating Principal Investigators must be attached to an HREC Submission and available at [www.health.vic.gov.au/cchre](http://www.health.vic.gov.au/cchre).
- 5.4 The original application (*with original signature*) and the appropriate number of copies of the application with all supporting documents (*appearing on the checklist and others as required*) must be submitted to the reviewing HREC (*an application without a 'submission code' will not be accepted*).
- 5.5 Information on reviewing HREC details and meeting dates can be obtained from the CCHRE website ([www.health.vic.gov.au/cchre](http://www.health.vic.gov.au/cchre)) or the website of the organisation hosting the reviewing HREC.
- 5.6 If an application is withdrawn and the applicant wishes to re-submit it, then a new booking should be made and the application will be treated as a new application. A new HREC Reference Number will be issued.

**Navigation steps for preparing an application using the Online Forms website (*note these steps may change as the Online forms website is modified from time to time*).**

- Access the Victorian portal of the Online forms website at <http://www.ethicsform.org.au>.
- The Online Forms screen allows researchers/others to obtain a login password which will be sent by email on request.
- Once the login (email address) and password are submitted, the 'My Projects' page appears on the screen. There is a blue bar at the top of the page used to access the main menu.
- Select MY PROJECTS and 'create new project' and an HREC application form (NEAF) is created.

---

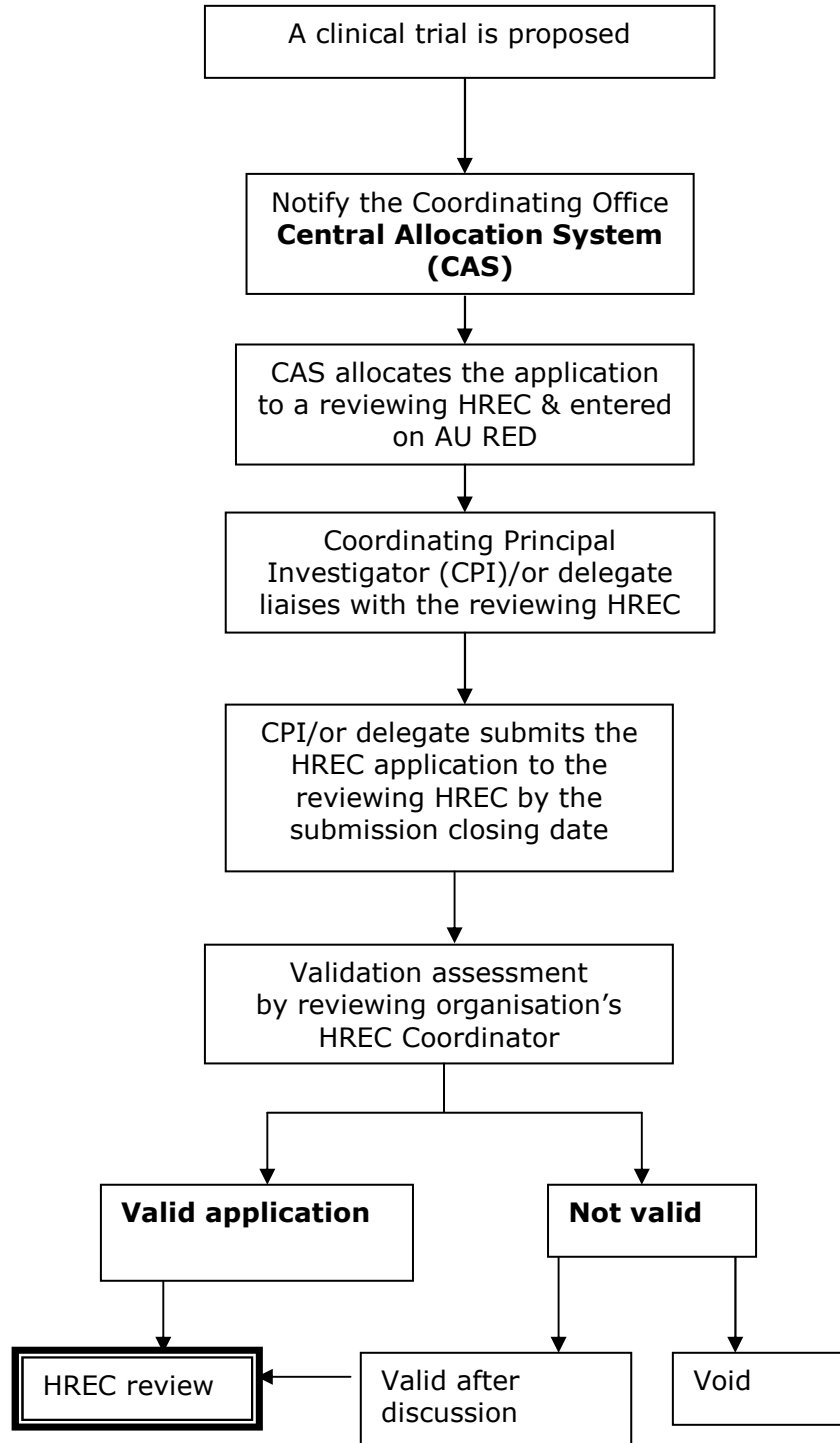
<sup>1</sup> If the Form (NEAF or SSA) is changed or revised after review/assessment, edit the Form and save the changes, request electronic authorisations (if required) and on the 'Submissions' tab generate a new submission code, print and submit to the administrator with the new submission code. This function now allows editing of NEAF and SSA Forms.

- The new HREC application form opens with the 'Navigation' page. Select Section 1 and commence filling out the form.
- Select 'Victoria' as the location of the research site.
- Proceed to fill out the NEAF. Note that the details for the Chief Researcher/Investigator or Coordinating Principal Investigator will not appear at the front of the form until 'Clinical Research' is selected in Section 5 PROJECT.
- When the NEAF is complete, all supporting documents must be attached to the NEAF.
- Select the **Document tab** and a 'List' of document-types appears.
- Choose the 'Upload' tab the document type dropdown list appears. Select the document type to upload, fill in details and browse to upload the document.  
TIP – If uploading more than one document of the same type, distinguish them by putting the specific detail in the 'Version' box e.g. CTN form can have the specific 'CTN site name' entered in the 'Version' box.
- Work across the tab. If you wish to transfer the NEAF to a colleague go to 'Transfer' tab, or to 'Authorisation' if you want to get a signature(s) electronically.
- The 'Submission' tab allows a 'submission code' to be generated, this is mandatory for submitting the NEAF to the reviewing HREC Coordinator.
- When the NEAF is complete and the 'submission code' has been generated the NEAF form must be printed for submission to the reviewing HREC Coordinator.
- To print the NEAF supporting documents, go to 'Documents' and select under 'Tools' the 'view/manage' option. Under 'History' (bottom of the page) select 'view uploaded file' and when it opens choose print the document.

#### Site Specific assessment (SSA) Form

- The Coordinating Principal Investigator must generate the required number of SSA Forms. Select the 'SSAs' tab and enter the number of SSAs required and select 'Create new SSA or PHA Form'. The new SSAs will appear under the 'SSA/PHA Form' list.
- A Site Specific Assessment (SSA) Form must be completed by the Coordinating Principal Investigator (see SOP 07) and all Principal Investigators at each study site.
- Select each new SSA form and when it opens nominate 'Victoria' as the site location for all Victorian sites.
- The Coordinating Principal Investigator must transfer an SSA form to each Principal Investigator by using the 'Transfer' tab and entering the email address of the Principal Investigator.
- An email will be sent to the Principal Investigator informing them that an SSA Form is available for them to complete.
- The Principal Investigator must register on the Online Forms website <https://www.ethicsform.org/au> and open an account.
- The SSA Form is now accessible for the study (*created by the Coordinating Principal Investigator*).
- The process is repeated for each site SSA Form that is required.

## SUBMITTING A NEW HREC APPLICATION



**SOP 06      Use of ionising radiation submission requirements for HREC review**

**Purpose**      To inform Investigators regarding the process for ethics review and Department of Health requirements for use of ionising radiation in a research study.

- 6.1 The reviewing HREC will be responsible for providing ethics approval for clinical trials involving ionising radiation, when the trial is conducted at multiple study sites.
- 6.2 The reviewing HREC will review all relevant documents relating to the HREC application, including the following that relate to use of ionising radiation:
  - Victorian Specific Module completed by the Coordinating Principal Investigator (CPI).
  - Section 4 - Use of Ionising Radiation. An individual Section 4 for all other study sites (not including the CPI site).
  - The Master PICF for the CPI site that has the radiation risk statement for that site.
  - A Site Master PICF (if required) with a radiation risk statement for that site.
  - A Medical Physicists Report for each participating site.

**If the Medical Physicist(s) report(s) advises the relevant PI that the trial needs to be submitted to the Department of Health Radiation Safety Section, the following steps should be taken:**

- 6.3 Following HREC approval of a project, the CPI should submit the following to the Radiation Safety Section, Department of Health (DoH):
  - A cover letter stating the study is multi-site and has been reviewed in the streamlined system, title of the project, HREC Application Reference Number and all sites approved by the reviewing HREC.
  - Copy of the HREC approval letter.
  - Victorian Specific Module – (which includes use of ionising radiation details) at the CPI's site only.
  - Medical Physicists Report for the CPI's site.
  - Master PICF – approved by the reviewing HREC.
  - Study Protocol.
- 6.4 Following HREC approval of a project, the Radiation Safety Section, DoH would require from each Principal Investigator (PI) at each of the other study sites:
  - A cover letter stating the study is multi-site and has been reviewed in the streamlined system, title of the project, HREC Application Reference Number and all sites approved by the reviewing HREC.
  - Section 4 Use of Ionising Radiation for the individual site.
  - Medical Physicist's Report for the individual site.
  - The Master or Site Master PICF with the site's radiation risk statement.
- 6.5 If the dose of radiation is below the dose constraint of the ARPANSA Code then the Radiation Safety Section, DoH will add the research project to the licence of the health service.
- 6.6 If the dose of radiation is above the dose constraint of the ARPANSA Code then the Radiation Advisory Committee will review the project.

- Before a trial can commence Radiation Advisory Committee must approve the project.
- The Radiation Safety Section, DoH will communicate the outcome of the Radiation Advisory Committee review to the Investigator(s) and if approved the trial can then commence.

**If the Medical Physicist(s) report(s) advises the relevant PI that the trial does not need to be submitted to the Department of Health Radiation Safety Section, no further action, beyond submitting the relevant report to the reviewing HREC as part of the HREC application, is required unless directed otherwise by the reviewing HREC.**

## **SOP 07 Submitting a site specific assessment for multi-site clinical trials**

**Purpose** To provide details of the process, Principal Investigators should follow to complete and submit a Site Specific Assessment (SSA) form to the Research Governance Officer.

- 7.1 The sponsor/CRO in consultation with Investigators will choose sites to conduct a clinical trial. Then sponsors/CROs should promptly organise delivery of study documentation to Principal Investigators (PIs) at all participating sites. Provision of study documentation should occur as soon as the participating sites are agreed, and WELL BEFORE the Coordinating Principal Investigator (CPI) is ready to complete and submit the ethics application to the reviewing HREC.
- 7.2 Site specific assessment should be conducted at sites in a **parallel timeframe** with the ethics review process and should commence as soon as possible.
- 7.3 The site specific assessment 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. It does not involve ethical review by a local HREC but is a research governance process.
- 7.4 Each PI at a site involved in a multi-site research project must complete an SSA form for that research study. The SSA form involves consideration of the following:
  - the facilities and resources required for the research to proceed at the site are appropriate and available;
  - whether the researchers 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 are made using the Online forms website [www.ethicsform.org/au](http://www.ethicsform.org/au).

**Navigation steps for preparing a Site Specific Assessment Form using the Online Forms website (*note these steps may change as the Online forms website is modified from time to time*).**

### **Completing the SSA Form**

- Access the Victorian portal of the Online forms website at <https://www.ethicsform.org/au>.
- The Online Forms screen allows investigators/others to obtain a login and password which will be sent by email on request;
- Once the login and password are submitted, the 'My Projects' page appears;
- Choose the SSA Form for the study (*the project title on the HREC Form will appear in the SSA project title*);
- The SSA Form must be completed;
- The SSA Form can be filled out online up to and including number 13 Biosafety, Chemical and Radiation Safety and the checklist;

- Some pages cannot be filled in by PIs, for example Declarations which may only be partially completed online and are designed to be either authorised electronically or signed in hard copy;
- <sup>2</sup> Select the 'Authorisation' tab and choose the 'Authorisation type' to 'Request' a signature. Note, if any changes to the SSA Form are made before submission, the authorisations will be invalidated. New authorisations will be required for submission of the SSA Form.

**Uploading the SSA supporting documents** (see SOP 2)

The reviewing HREC Coordinator will send to PIs the electronic copy of the NEAF and supporting documents for the HREC application.

Check that these supporting documents appear in the documents 'List' (automatically uploaded from the NEAF) and upload any further site documents to the Online SSA Form.

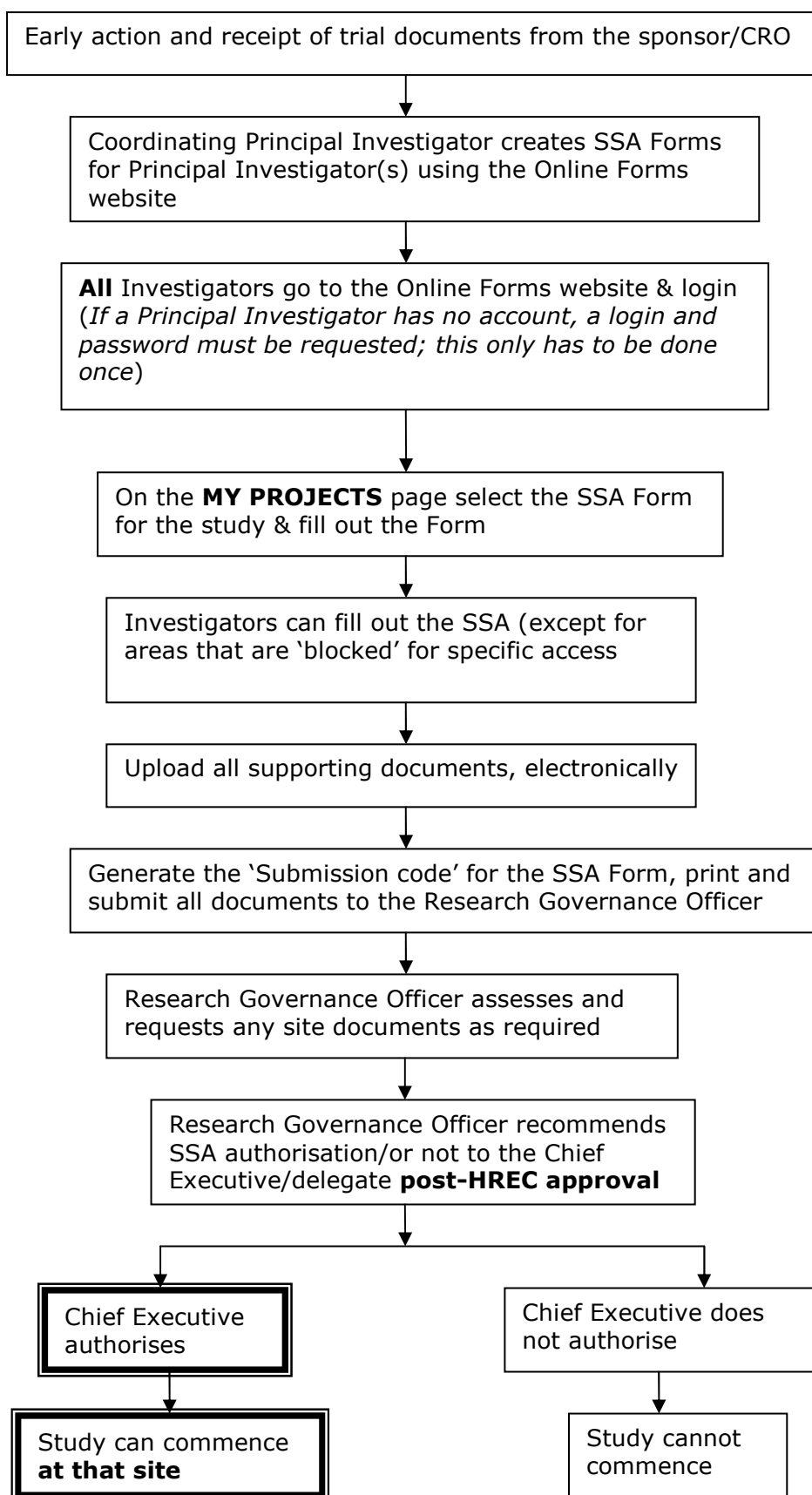
- Select the **Document tab** and a 'List' of document-types appears.
- Choose the 'Upload' tab' the document type dropdown list appears. Select the document type to upload, fill in details and browse to upload the document.  
TIP – If uploading more than one document of the same type, distinguish them by putting the specific detail in the 'Version' box e.g. enter the 'site name' for a document in the 'Version' box.

7.6 To 'submit' an SSA form select the '**Submissions**' tab. The 'Submission' tab allows a 'submission code' to be generated, this is mandatory for submitting the SSA Form. Then print the SSA Form and required supporting documents (located in 'Documents') for submission to the Research Governance Officer.

---

<sup>2</sup> It is now possible to obtain electronic signatures for 'Declaration' by authorities on the SSA Form.

## SUBMITTING A SITE SPECIFIC ASSESSMENT FORM



## **SOP 08 Validation of an HREC application**

**Purpose** To describe the process for the reviewing HREC Coordinator to validate an HREC application.

- 8.1 An Ethics Checklist for Coordinating Principal Investigators must be attached to an HREC Submission and is available at [www.health.vic.gov.au/cchre](http://www.health.vic.gov.au/cchre). A valid application is one that is deemed to be complete and accurate, by the reviewing HREC Coordinator.
- 8.2 Validation criteria include but are not limited to:
  - The HREC Reference Number for the application, obtained from the Central Allocation System (CAS). This must be entered on the application form prior to submission;
  - Submission of the NEAF form on the Victorian portal with a 'Submission code' and all required supporting documents marked with version number and date;
  - A research protocol and all supporting documents that have been submitted e.g. Master Participant Information Consent Form, Site Master Participant Information Consent Form (if applicable), CTN form for all sites, study Protocol, Investigator Brochure, etc.;
  - The NEAF form signed by the Co-ordinating Principal Investigator (*Principal Investigators at other sites do not need to sign*);
  - Any specific requirements of the reviewing organisation's HREC e.g. number of copies.
- 8.3 The reviewing HREC Coordinator has the responsibility of deciding whether or not an application is valid and will notify the applicant. Notification should be given within 5 working days of receiving the application submission closing date.
- 8.4 The reviewing HREC Coordinator must confirm the valid application with the meeting designated by the Central Allocation System (CAS). (*CAS indicates what meeting the HREC application must go to but the reviewing HREC Coordinator must complete the meeting arrangement in AU RED so the application appears on the HREC agenda*).
- 8.5 If the application is valid, the reviewing HREC Coordinator must notify the Coordinating Principal Investigator/or delegate using the AU RED standard acknowledgement for a valid application letter.
- 8.6 If an application is invalid, the reviewing HREC Coordinator should notify the Co-ordinating Principal Investigator/or delegate with the reasons why the application was invalid using the AU RED acknowledgement of an invalid application letter.
- 8.7 If after negotiation between the reviewing HREC Coordinator the applicant issues cannot be resolved, an application cannot be validated. The Coordinating Principal Investigator/or delegate may re-book the application with the CAS and re-submit the application, and it will be treated as a new application.

- 8.8 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.

## **SOP 09 Ethical review of applications and the 30 working day clock**

**Purpose** To explain the AU RED clock and the relevance it has to the 30 working day benchmark for the ethics application process.

- 9.1 The benchmark for the multi-site review system will be 30 working days and the AU RED clock (using calendar days) will monitor the time taken for the review process.
- 9.2 The AU RED clock will start on the submission closing date for the reviewing HREC.
- 9.3 The clock will be stopped on the day that a request for further information is sent to the Coordinating Principal Investigator/or delegate.
- 9.4 The clock will re-start when a complete response, addressing the issues raised by the reviewing HREC, has been received by the reviewing HREC Coordinator.
- 9.5 When the reviewing HREC has made a final decision on an application, a letter will be sent to the Coordinating Principal Investigator/delegate and copied to the Principal Investigator(s), Research Governance Officers, sponsor/CRO and Trial Coordinator. The clock will be stopped when this letter is sent.
- 9.6 The 30 working day clock is a benchmark for performance of the ethics review system. Expiration of the 30 working day clock does not entitle the investigators any remedies, such as an immediate decision from the reviewing HREC, or the return of an application fee.
- 9.7 A research study cannot commence at a study site, even if ethically approved, until the research governance process has been completed and site specific assessment has been authorised by the Chief Executive/delegate.

## **SOP 10 Clinical trials conducted under the Clinical Trials Notification (CTN) or Clinical Trials Exemption (CTX) Schemes**

**Purpose** To outline the requirements for conducting clinical trials under the CTN/CTX Scheme

- 10.1 For a trial study to be conducted under the CTX Scheme, the sponsor submits an application to the Therapeutic Goods Administration (TGA) for TGA-approval.
- 10.2 An HREC application involving clinical trials to be conducted under the CTN scheme should be accompanied by a separate '*Notification of Intent to Supply Unapproved Therapeutic Goods under the Clinical Trial Notification (CTN) Scheme*' form (obtained from the Therapeutic Goods Administration) for **each** site participating in the study.  
  
*A CTN form for **each** site must be provided by the sponsor. The Coordinating Principal Investigator should receive an **original** CTN for all participating sites to send to the reviewing HREC as part of the ethics application.*
- 10.3 The CTN forms should be submitted to the reviewing HREC by the Coordinating Principal Investigator.
- 10.4 The signature of the site Principal Investigator in Section 2 is not required before submission to the reviewing HREC.
- 10.5 Following HREC approval of an ethics application, an HREC member will sign Section 3 of each CTN form.
- 10.6 A CTN form for each site should be sent to the Research Governance Office at each relevant site. Each individual site must ensure the Principal Investigator signs Section 2.
- 10.7 Completion of the CTN form requires the Research Governance Office, as part of site-specific assessment, to ensure that the site's approving authority signs Section 4 and that the TGA is notified accordingly.
- 10.8 The Victorian Managed Insurance Authority (VMIA) has a policy on clinical trial notification requirements for public health care organisations. The conditions and details for approval from VMIA are available from the '*Guidelines for Clinical trials for Victorian Public Hospitals*' on the VMIA website <http://www.vmia.vic.gov.au>. Conditions relating to the CTN/CTX Schemes and special requirements for clinical trials are explained in the VMIA guidelines.
- 10.9 If adding a new trial site, a CTN form must be signed by the reviewing HREC, Principal Investigator, the site's approving authority and the TGA notified by the sponsor.

## **SOP 11 Clinical Trial Research Agreements (CTRA) for clinical trials**

**Purpose** To outline the process for administrative review of CTRAs

- 11.1 VMIA and Medicines Australia have developed a suite of templates for CTRAs. For reasons of timeliness and cost, and to ensure that institutions do not jeopardise their entitlements to indemnity under the policies arranged by the VMIA, it is recommended that the following templates are used as appropriate:
- Commercially Sponsored CTRA
  - Collaborative Research Group (CRG) CTRA
  - Contract Research Organisation (CRO) CTRA
  - Investigator Initiated CTRA
  - Clinical Investigation Research Agreement – Medical Technology Association of Australia (Medical Device)
- 11.2 In the event that a sponsor submits a CTRA that has not been prepared using a VMIA approved Medicines Australia or a Medical Technology Association of Australia (Medical Device) template, Research Governance Officers (RGOs) should review the agreement in accordance with their usual practice and seek legal advice (through in-house legal counsel or external legal counsel) 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 request the sponsor to prepare a new agreement using the appropriate VMIA approved template.
- 11.3 Schedule 7 of the Commercially Sponsored CTRA and Schedule 4 of the CRG/CRO and Investigator-initiated CTRA may be used to incorporate any unique operational 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 VMIA/Medicines Australia CTRA, risk compromising insurance cover under VMIA policy.
- 11.4 VMIA has negotiated a set of standard Schedule 7 Special Conditions with a number of commercial clinical trial sponsors. These have been distributed to institutions insured by VMIA. RGOs should check the Schedule 7 Special Conditions in CTRAs from commercial sponsors against the pre-approved conditions provided by VMIA. Where a commercially sponsored CTRA contains a Schedule 7 that differs from the VMIA-approved version for that particular company, or where there is no pre-approved Schedule 7 for a given company, the RGO should review this Schedule 7 in accordance with their usual practice. The RGO may seek legal advice (through in-house legal counsel or external legal counsel) as deemed necessary and in accordance with their own institution's policies and practices.
- 11.5 For Collaborative Research Group, Investigator-Initiated CTRAs and Medical Device agreements there are not, at this time, a set of VMIA pre-approved Special Conditions. In the case of these CTRAs, RGOs should review the agreement and any schedules that may be enclosed in accordance with their usual practice and seek legal advice (through in-

house legal counsel or external legal counsel) as deemed necessary and in accordance with their own institution's policies and practices.

## **SOP 12 Review of Participant Information and Consent Form**

**Purpose** To outline the requirements for HREC review of the Participant Information, Consent Form and related documents for multi-site studies

12.1 It is advisable that the Department of Health Participant Information and Consent Form (PICF) template for Clinical Drug/Device Research Projects is used.

### **12.2 Master PICF**

Where the PICF is identical (except for local contact information) for each site, the Co-ordinating Principal Investigator/delegate must submit a Master PICF to the reviewing HREC.

A **Master PICF** which contains the required wording (applicable to all study sites) and the details relating to the **Coordinating Principal Investigator**

Including:

- Letterhead, organisation/site where recruitment will occur, Investigator name and contact details, details for complaints, name and contact details of the reviewing HREC
- The version number and date must appear in the footer of each page

*Note: There may be more than 1 Master PICF if special consent requirements apply (e.g. Parents/Guardians of Children, Person Responsible, Participant Continuation)*

Following HREC approval, the Master PICF(s) must be used for all study sites and ONLY modified to reflect the details of individual sites.

This includes:

- Printing on institutional letterhead
- Stating the organisation/site where recruitment is occurring
- Showing the site PI name and contact details
- Naming the person dealing with complaints and their contact details

### **12.3 Site Master PICF**

Where there is specific site policy and standard wording required by one or more organisations, for studies on children, religious or other reasons, the Co-ordinating Principal Investigator/delegate may submit:

- A **Master PICF** without the site-specific wording with version date in the footer of each page;
- A **Site Master PICF**, based on the Master PICF with the special site-specific wording inserted and the site name, version date in the footer of each page.

The Master PICF must:

- be on the letterhead of the Coordinating Principal Investigator's organisation (*if a participating study site, otherwise do not use letterhead*);
- state the site where recruitment is to occur;
- show the Coordinating Principal Investigator's name and contact details;
- show the name of the person dealing with complaints and their contact details;
- show the name and contact details of the reviewing HREC;
- show the current version date in the footer on each page.

The Site Master PICF with the special site-specific wording must:

- On the front page, have a statement such as "**Based on the [project title] [HREC Reference Number] Master Consent Document Version [number] and date**
- be on the letterhead of the site that has the special policy requirements;
- show the name of the site where recruitment is to occur;
- show the site Principal Investigator's name and contact details;
- show the name and contact details of the person dealing with complaints at the site;
- show the name and contact details of the reviewing HREC;
- indicate the Master PICF version date (*on which the site specific master PICF is based*);
- show the special Site Master PICF version date.

12.6 Both the Master PICF and the Site Master PICF must be approved by the reviewing HREC.

12.7 Where changes are required on the Master PICF (and Site Master PICF), as a condition of HREC approval, then the PICF(s) must be updated with the latest version date and uploaded on to the Online Forms website. For the relevant NEAF application, go to 'Documents' and 'Upload' tab then upload the selected documents. Indicate the document type, version (notate re update), browse and click on 'Upload'. The new document will appear in the checklist below.

12.8 The approved Master PICF version must be sent to all Principal Investigators at participating sites.

12.9 The approved Site Master PICF must be sent to the relevant Principal Investigator(s).

12.10 Catholic institutions in Victoria have standard wording for the site-specific PICF when addressing the issues below. This wording must be inserted in to a PICF and approved by a reviewing HREC.

**Standard Catholic Hospital clause for a PICF**

**It is acceptable within Catholic teaching to counsel a woman and/or her partner to avoid becoming pregnant when either the woman or partner is undergoing treatment that might affect an embryo/foetus. It is not acceptable to counsel a woman or her partner to use a contraceptive for the express intention of making intercourse infertile. Do not include any statements in the application (e.g. participant information sheet, scientific description etc) to the effect that participants must practise methods of contraception or avoiding pregnancy.**

**Women must have a pregnancy test prior to entering the study and women and/or partners must be given the following information in the PICF.**

The following paragraphs are proposed for inclusion in the template PICF:

**"Section #. Pregnancy**

**You must avoid becoming pregnant during the course of this trial. If you become pregnant you will have to withdraw from the trial and you will be medically followed up carefully until delivery. Should you become pregnant you should notify your family doctor and the study doctor as soon as possible. These precautions are necessary because the information on the effects on the unborn or newborn baby of drugs like [drug name(s)] is still very limited.**

*Only if needed, the following wording may be added to the above pregnancy clause:*

**Sexually active women who are potentially fertile will be excluded unless they are using a medically reliable method of preventing conception.**

*(Examples of medically reliable methods of preventing conception are not to be included).*

*This clause may also include 'You may wish to discuss this with you doctor.'*

*The PICF may also include the following paragraph if relevant.*

**Section #. Fathering a child**

**If you are the partner of a sexually active woman who is potentially fertile, you will be excluded from the study unless you are using a medically reliable method of preventing conception for the duration of the study."**

### **SOP 13 Notification of the decision following HREC review**

**Purpose** To outline the notification process for the HREC review decision on a research application

- 13.1 The reviewing HREC Coordinator must notify the Coordinating Principal Investigator, Principal Investigator(s), Research Governance Officers, sponsor/CRO and Trial Coordinator of the outcome of the HREC review meeting. A written letter should be sent, and copied to the above, within 5 working days of the HREC meeting, by the reviewing HREC Coordinator.
- 13.2 The AU RED clock should be stopped on the date of the correspondence indicating the final decision of the HREC for an application.

#### **Application approval**

- 13.3 The standard HREC approval letter specifying the conditions of HREC approval will be sent to the Coordinating Principal Investigator, Principal Investigator(s), sponsor/CRO and Research Governance Officers. The reviewing HREC Coordinator will record the decision of the HREC in AU RED as soon as practicable (no later than 5 working days) from the date of the meeting at which the decision was made. The date of the decision is the date on which the correspondence is sent.

***The research cannot commence at a site until authorisation of site-specific assessment at a study site is granted. Completion of the CTN regulatory requirement and any other licence/regulatory requirements are necessary before SSA authorisation can be granted.***

- 13.4 For clinical trials there should be a CTN form for each site (signed by the reviewing HREC) involved in the clinical trial. The CTN forms and the HREC approval notification should be sent to each Principal Investigator and site Research Governance Office by the reviewing HREC Coordinator. Subsequently the sponsor/CRO must sign the CTN and send it to TGA.
- 13.5 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 study 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. PIs are responsible for having the study notified to the Radiation Safety Section, Department of Health and added to their institution's "Research with Human Volunteers" licence before commencing the research. See SOP 06 regarding use of ionising radiation.

#### **Provisional approval with a request for further information**

- 13.6 The reviewing HREC may decide to request further information from the Coordinating Principal Investigator. A standard letter detailing the information required will be sent to the Coordinating Principal Investigator.
- 13.7 The AU RED clock for this application will stop on the date the correspondence is sent to the Coordinating Principal Investigator requesting further information. The clock will re-start when the response is received by the reviewing HREC Coordinator.

### **An application is rejected**



- 13.8 A standard letter signed by the reviewing HREC Chair (or Deputy Chair) will be sent to the Coordinating Principal Investigator informing the non approval of the research project with reasons for the HREC decision.
- 13.9 In the interest of efficiency, it is recommended that the reviewing HREC Coordinator sends an email or printed notification of the HREC's decision letter to the Coordinating Principal Investigator, Principal Investigator(s), Research Governance Officers, sponsor/CRO and trial Coordinator as soon as possible.
- 13.10 Appropriate action should be taken to discontinue any site-specific assessment that is underway.

## **SOP 14 Amendment of an ethically approved research project**

**Purpose** To describe the process for an amendment of an ethically approved project.

- 14.1 An amendment is broadly defined as a change made either to the terms of the ethics application, the protocol or any other supporting documentation after the study has started which may affect the ethical and/or scientific acceptability of the research project.
- 14.2 If a study requires an amendment to the research project 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.
- 14.3 The Coordinating Principal Investigator/or delegate should access the CCHRE website [www.health.vic.gov.au/cchre](http://www.health.vic.gov.au/cchre) to obtain standard forms and specific requirements for amendments. The Coordinating Principal Investigator/delegate will be responsible for submitting an amendment to the reviewing HREC.
- 14.4 If necessary, the Coordinating Principal Investigator/delegate should communicate with the reviewing HREC Coordinator regarding the amendment.
- 14.5 The reviewing HREC Coordinator will send a letter acknowledging that an amendment has been validated or not validated.
- 14.6 The Coordinating Principal Investigator/delegate should communicate with the sponsor and Principal Investigators, regarding the amendment process.

### **Amendments requiring a change to the HREC application (NEAF)**

- 14.7 The NEAF Form may be revised or changed following submission to the reviewing HREC. Text changes can be tracked by using the 'hourglass' symbol  on the right hand side of a text box. Select  and a new window opens. Deleted text appears as strike-through, added text is highlighted and original text remains. When submitting the NEAF to the reviewing HREC choose the text option to print the 'last 3 text changes' relating to the last three submission codes.
- 14.8 If any supporting documents require change, go to the relevant NEAF application select the 'Documents' tab and indicate the document type, version, browse and 'Upload'. The document will appear in the checklist below.
- 14.9 If electronic signature authorisation is required, go to the 'Authorisation' tab and request signature(s).
- 14.10 A cover letter carefully explaining the sections in the NEAF requiring change should be sent to the reviewing HREC.
- 14.11 A new 'submission code' for the NEAF should be generated by selecting 'Submission' and then a paper copy of the amended application and/or supporting documents must be submitted to the reviewing HREC

Coordinator. Amendments should be assigned to the next available meeting and entered on AU RED.

- 14.12 The decision of the reviewing HREC should be notified, by the reviewing HREC Coordinator, using a standard letter in AU RED to the Coordinating Principal Investigator and copied to Principal Investigator(s), Research Governance Officers, sponsor/CRO and Trial Coordinator.

### **Site Specific Assessment**

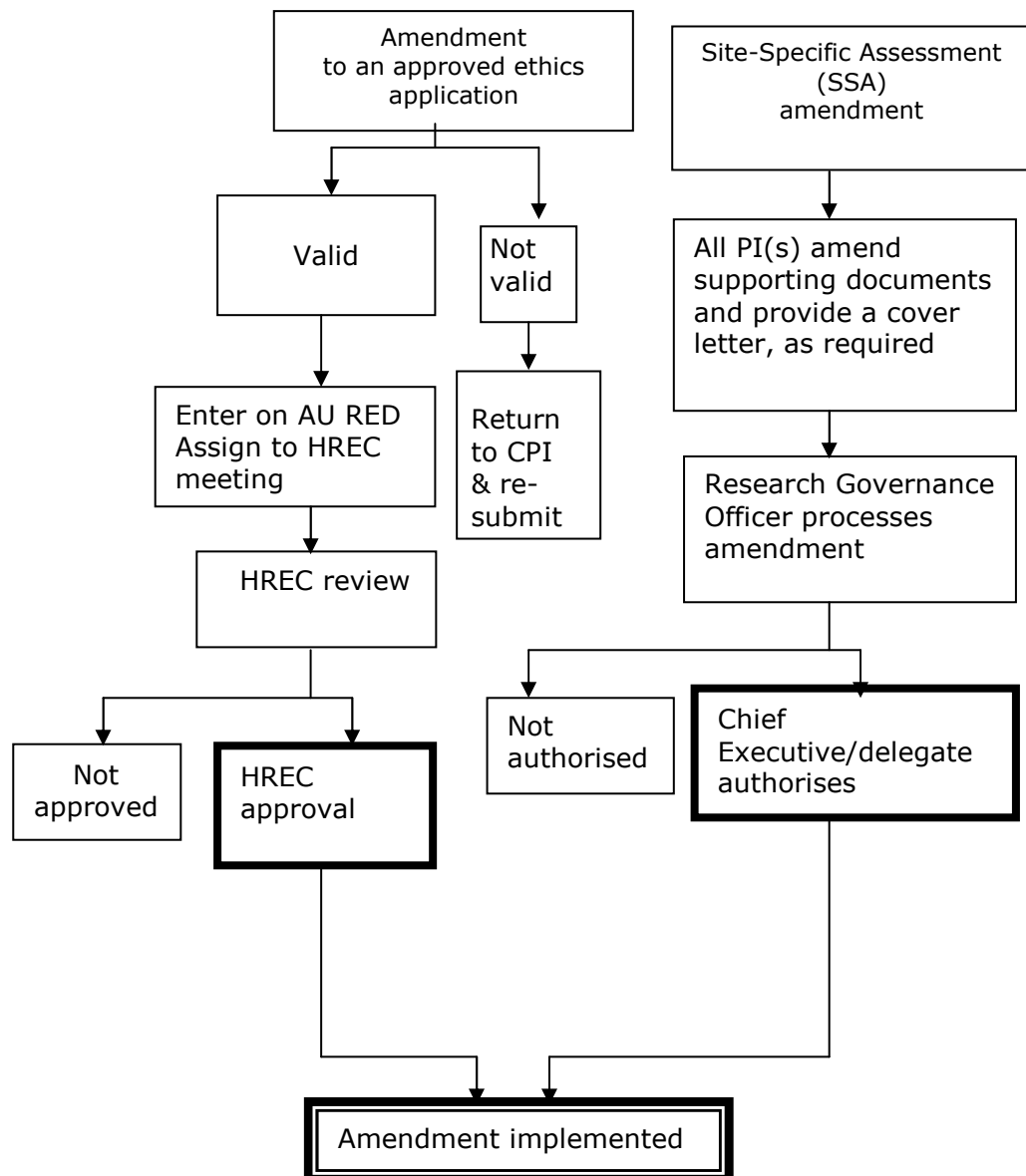
- 14.13 When it is intended to make an amendment to a research project, the Principal Investigators must liaise with their respective Research Governance Officers to determine whether or not SSA authorisation is required for the amendment to be implemented at a site(s).
- 14.14 If the Research Governance Officer believes SSA authorisation *is NOT* required then the Research Governance Officer must notify the Principal Investigator in writing via a letter or an email and the Principal Investigator may implement the amendment upon HREC approval being granted.
- 14.15 If an amendment has an impact on site specific assessment this must be considered by the Research Governance Officer at each site and authorisation sought from the Chief Executive (or delegate).
- 14.16 Any changes to the SSA Form may be made subsequent to initial authorisation of the SSA. Text changes can be tracked by using the 'hourglass' symbol ⌚ on the right hand side of a text box. Select ⌚ and a new window opens. Deleted text appears as strike-through, added text is highlighted and original text remains. When submitting the SSA choose the text option to print the 'last 3 text changes' relating to the last three submission codes.
- 14.17 Sections in the SSA requiring change, should be explained in a cover letter to the Research Governance Officer.
- 14.18 If any supporting documents require change, access the relevant SSA go to the 'Documents' tab and indicate the document type, version, browse and 'Upload'. The new document will appear in the checklist below.
- 14.19 A new 'submission code' for the SSA should be generated by selecting 'Submission' and then a paper copy of the amended SSA and/or supporting documents must be submitted to the Research Governance Officer at the study site. When submitting the SSA, with changes choose the text option to print the 'last 3 text changes'.
- 14.20 The Research Governance officer will assess the SSA and recommend authorisation by the Chief Executive/delegate, or not recommend authorisation.
- 14.21 The Chief Executive/delegate must authorise the SSA before an amendment can be implemented.

### **Implementation of an amendment**

- 14.22 An amendment cannot be implemented at individual sites until the reviewing HREC has given approval and the Chief Executive/delegate at a site(s) has authorised SSA.

- 14.23 If an amendment does not require ethics approval, Investigators may implement the amendment to the SSA once the SSA is authorised and notified in writing by the Research Governance Officer.
- 14.24 Exceptions to the amendment process may be made in circumstances where there is a serious threat to the health and safety of participants. The Coordinating Principal Investigator/or delegate should notify the reviewing HREC Coordinator and ensure that Principal Investigators notify the Research Governance Officer at each relevant site.

## HREC AMENDMENT TO AN APPROVED RESEARCH PROJECT



## **SOP 15 Monitoring of approved research**

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

15.1 According to the National Statement (2007), monitoring of research refers to the process of verifying that the conduct of research conforms to the approved research proposal.

15.2 According to the National Statement (2007), the responsibility for ensuring that research is monitored adequately lies with institution under which the research is conducted.

Mechanisms for monitoring can include:

- Reports from researchers;
- Reports from independent agencies (e.g. data and safety monitoring board);
- Review of adverse event reports;
- Random inspection of research sites, data, or consent documentation; and
- Interviews with research participants or other forms of feedback from them.

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

## **SOP 16 Reporting on approved research**

**Purpose** To describe the procedure for reporting on an approved research project.

### **Annual progress report**

- 16.1 The Coordinating Principal Investigator is responsible for communicating with the reviewing HREC regarding reports on research projects being conducted.
- 16.2 The report to the reviewing HREC should contain information about the project from Principal Investigators at all sites. This should be prepared as a collection of individual site reports and submitted by the CPI with an HREC progress report CPI cover sheet.
- 16.3 Principal Investigators should send a copy of their site report to the Research Governance Officer at their site.
- 16.4 Progress of research should be reported annually or as required by the reviewing HREC. Reports must be submitted on the recommended template. Templates are available from the CCHRE website [www.health.vic.gov.au/cchre](http://www.health.vic.gov.au/cchre).
- 16.5 The Coordinating Principal Investigator must upload the report electronically under the 'Documents' tab on the Online Forms website. Hard copies should be sent to the reviewing HREC Coordinator with the required number of copies.
- 16.6 AU RED must be updated by the reviewing HREC Coordinator when reports are received.
- 16.7 The reviewing HREC Coordinator will send a reminder letter for an annual/progress report if the report is not received within 12 months of the project being approved.
- 16.8 Once a report has been received by the reviewing HREC Coordinator a letter of acknowledgement will be sent.

***Continuation of ethical approval for a research project will be dependent on timely submission of annual/progress reports.***

### **Final report**

- 16.9 At the conclusion of a research project at one or more sites, the Coordinating Principal Investigator/or delegate must notify the reviewing HREC Coordinator and submit a final report. The template for the final report/close of study is available from the CCHRE website [www.health.vic.gov.au/cchre](http://www.health.vic.gov.au/cchre). See the reviewing organisation's HREC website for the specific requirements and the procedure to follow for submission of a final report.
- 16.10 AU RED must be updated by the reviewing HREC Coordinator when a final report is received.
- 16.11 Once a final report has been received by the reviewing HREC Coordinator a letter of acknowledgement of the report will be sent.

16.12 Principal Investigators at each site must also provide the Research Governance Officer at their site, with a copy of a site final report.

## **SOP 17 Early termination of an approved research project**

**Purpose** To describe the communication required when a research project is terminated before the intended completion date.

- 17.1 Where a research project is terminated or suspended by the Coordinating Principal Investigator and/or Principal Investigator(s) before the expected date of completion, the reviewing HREC, Research Governance Office, sponsor/CRO and Trial Coordinator must be promptly notified.
- 17.2 A detailed written explanation of the reasons why a research project has been terminated must be submitted to the reviewing HREC Coordinator and the Research Governance Office at each site.

### **Study completion**

- 17.3 On completion of a clinical trial, the Coordinating Principal Investigator/delegate must notify the reviewing HREC Coordinator that the study has been completed.
- 17.4 AU RED must be updated by the reviewing HREC Coordinator when a study completion report is received.
- 17.5 Once a study completion report has been received by the reviewing HREC Coordinator, a letter of acknowledgement will be sent to the Coordinating Principal Investigator. A copy of the letter and report should be emailed to the Principal Investigator(s), Research Governance Officers, sponsor/CRO and Trial Coordinator.

## **SOP 18 Adverse Event (AE)/Serious Adverse Event (AE/SAE) reporting for clinical trials**

**Purpose** To describe the procedure for reporting AE/SAEs to a reviewing HREC.

- 18.1 Reporting of AE/SAEs to the reviewing HREC must meet the requirements of the *National Statement on Ethical Conduct in Human Research (2007) (the National Statement)* and the National Health and Medical Research Council Australian Health Ethics Committee (AHEC) Position Statement "*Monitoring and reporting of safety for clinical trials involving therapeutic products*", May 2009 or any other document that supersedes this document.
- 18.2 A standard template for AE/SAE reporting is available from the CCHRE website at [www.health.vic.gov.au/cchre](http://www.health.vic.gov.au/cchre). Reporting requirements for AE/SAEs in a clinical trial 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 clinical trials depending on the perceived risk of the research to the participants.
- 18.3 It is the responsibility of the Coordinating Principal Investigator/or delegate to provide appropriate AE/SAE reports to the reviewing HREC. The Principal Investigator's must notify the Coordinating Principal Investigator/delegate of an AE/SAE report where there is a material impact on the continued ethical acceptability or the AE/SAE indicates a need for a change to the trial protocol. The CPI must then submit AE/SAE reports to the reviewing HREC in a prompt manner (within 24 hours). Note that the local Research Governance Officer and VMIA should also be notified. *(To avoid delay the PI may contact the CPI and decide to forward the AE/SAE directly to the reviewing HREC.*
- 18.4 Upon receipt of an AE/SAE report, the reviewing HREC will review the report and take appropriate action.
- 18.5 Where the reviewing HREC considers that the report requires immediate suspension or discontinuation of the ethical approval of the clinical trial, the reviewing HREC must immediately notify the:
  - Coordinating Principal Investigator;
  - Principal Investigator(s) and;
  - Research Governance Officer
  - Sponsor/CRO;
  - Trial Coordinator.

This should be promptly followed by a notice in writing.

## **SOP 19    Withdrawal or suspension of ethical approval**

**Purpose**    The conditions for withdrawal or suspension of ethical approval for a research project are described.

- 19.1    A reviewing HREC may have reason to withdraw or suspend a research project that may relate to the welfare of the participant or the conduct of research that is not in accordance with ethical approval.
- 19.2    Where ethical approval for a research project is withdrawn by the reviewing HREC, the Principal Investigator(s) (including the Coordinating Principal Investigator,), the institution(s) and where possible the participants should be informed of the withdrawal of HREC approval in writing.
- 19.3    The institution must ensure the Investigators suspend the research once ethical approval has been withdrawn and that arrangements are made to meet the needs of the participants.
- 19.4    The Principal Investigators (including the Coordinating Principal Investigator) must notify the Research Governance Officer at the study site of the withdrawal or suspension.
- 19.5    The research may not be resumed unless either:
  - The investigator subsequently establishes that continuance will not compromise participant's welfare; or
  - The research is modified to provide sufficient protection for participants and the modification is ethically reviewed and approved.

**SOP 20 Appeals concerning the ethical review and decision of a reviewing HREC**

**Purpose** To explain the procedure for appeals, concerning the review of a research project by an HREC.

- 20.1 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 21 Complaints concerning the conduct of an ethically approved research project**

**Purpose** To describe the procedure to follow when a complaint about the conduct of a research project at a study site is received.

- 21.1 In accordance with the *National Statement*, institutions conducting research must have a policy regarding the procedure for handling complaints about the conduct of a research project.
- 21.2 The Participant Information and Consent Form informs the participant of the nominated person at the institution to which complaints concerning the research can be directed.
- 21.3 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* (2007).
- 21.4 The nominated person to receive complaints regarding the researchers or the conduct of the research should provide information regarding the complaint to the local site Research Governance Officer. The institution should deal with the complaint in a prompt manner.
- 21.5 If not already submitted, the Research Governance Officer should contact the responsible Investigator and request that a 'Complaints Report to HREC – Site Report' template is completed (available at <http://www.health.vic.gov.au/cchre/>).
- 21.6 The site Investigator should provide a copy of the completed 'Complaints Report to HREC – Site Report' form to the:
  - o The Coordinating Principal Investigator who will forward it to the reviewing HREC; and
  - o Research Governance Officer at the site where the complaint has arisen.

## **SOP 22 Adding a new site to a project approved in the single ethical review system for multi-site clinical trials**

**Purpose** To explain the process of adding a new site to a project approved in the single review system for clinical trials.

- 22.1 The reviewing HREC must be notified in accordance with the National Statement, Chapter 1.1(e) of the intent to add a new site to the previously approved multi-site trial. It is the decision of the reviewing HREC as to what mechanism of notification is required, either by a letter with relevant attached documents or via an amendment process. The Coordinating Principle Investigator (CPI) must also send to the reviewing HREC the contact details and curriculum vitae of the Principal Investigator (PI) at the new site.
- 22.2 The CPI will be required to generate a Site Specific Assessment Form (SSA) for the new site's PI using the Online Forms website. An email alert will be sent to this PI when the SSA is transferred to them by the CPI.
- 22.3 The Principal Investigator at the new site will be required to access the Online Forms website to open the SSA Form. If the PI has not been to this website before they will need to create an account. This action needs to occur once only.
- 22.4 The reviewing HREC Coordinator will send an email to the new site's Research Governance Officer (RGO) and the new Principal Investigator with a copy of the previously approved ethics documents. The PI should initiate site specific research governance, fill in the SSA Form and upload the NEAF application and other site specific documents to the Online Forms website. These documents should be printed and submitted to the RGO.
- 22.5 The reviewing HREC will review the new PI's competence and qualifications and other relevant details as per the National Statement and if approved, issue a HREC approval for the study listing the new site. This approval should be sent to the CPI, all PI's and RGO's, as well as the Sponsor and Trial Coordinator.
- 22.6 When the SSA authorisation has been obtained at the new site the trial can commence at that site.

**SOP 23 Single site projects, approved before the establishment of the multi-site ethical review system, progressing to multi-site research**

**Purpose** To explain the procedure for handling single-site projects that progress to multi-site research projects.

23.1 Applicants are advised to undertake careful planning before deciding whether the project is likely to be conducted at a single-site or at multiple sites.

23.2 If a single-site clinical trial has been approved by an HREC other than a reviewing HREC and the trial is to be extended to more than one additional site, an application may be made to a reviewing HREC for single ethical review. A full review will be conducted and the approval would include all sites.

23.3 If modifications or conditions are imposed by a reviewing HREC, then these will apply to all sites, no matter whether another HREC originally approved the project.

23.4 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.

**SOP 24 Multi-site research approved prior to establishment of the multi-site ethical review system**

**Purpose** To outline ongoing responsibilities of HRECs that have approved multi-site research projects prior to the establishment of the multi-site ethical review system in Victoria.

24.1 Institutional HRECs should continue to operate in accordance with previous arrangements for HREC review of a multi-site study.

## **SOP 25 The Research Governance Officer**

**Purpose** To describe the role of the Research Governance Officer

- 25.1 The Research Governance Officer is the person responsible for reviewing the Site Specific Assessment Form and for making a recommendation to the Chief Executive/or delegate to authorise or not authorise the conduct of the research project at that site.
- 25.2 It is a matter for the organisation to determine who will be responsible for research governance and site specific assessment.

## **SOP 26 Authorisation of site specific assessment**

**Purpose** To describe the process for gaining site specific assessment authorisation at a research site

- 26.2 HREC approval and authorisation of site specific assessment are required before a research project can commence at a site.
- 26.2 Authorisation of site specific assessment must be granted by the Chief Executive/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.
- 26.3 In making a determination, the Chief Executive/delegate will consider the SSA Form submitted by the Research Governance Officer and sight the HREC approval letter.
- 26.4 For clinical trials conducted under the CTN schemes, the Chief Executive/ delegate will also be required to sign the CTN form at Section 4 and return this to the Research Governance Officer.
- 26.5 The Research Governance Officer is responsible for notifying the local Principal Investigator of the Chief Executive's/delegate's decision. This must be in writing and in the form of a standard letter in AU RED, accompanied by the signed CTN form.
- 26.6 Only when the site specific assessment authorisation by the Chief Executive/delegate and all regulatory compliance has been completed, can the research project commence at that site.
- 26.7 The Research Governance Officer must enter the Chief Executive/delegate's decision to authorise the SSA in AU RED (*that is authorised or not authorised*), and **stop the AU RED SSA clock**. The date the Principal Investigator was notified of authorisation of SSA should also be noted.
- 26.8 All documentation relating to the site specific assessment for each research project must be kept on file in a secure and confidential manner. This would include evidence of ethical approval and all documentation attached to the SSA Form.
- 26.9 Neither the Research Governance Officer nor the local Principal Investigator are required to notify the reviewing HREC of the site specific assessment outcome (*the reviewing HREC Coordinator will be able to access this information from AU RED*).
- 26.10 The Chief Executive/delegate may choose not to authorise the site specific assessment 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.

## **SOP 27 Amendment of a site specific assessment at a study site**

**Purpose** To describe the process for gaining authorisation of an amendment for an individual study site.

27.1 Changes requiring new site-specific assessment authorisation could include:

- A significant change to the study at the research site;
- Appointing a new Co-ordinating Principal Investigator or Principal Investigator at a site;
- Change to the insurance and indemnity arrangements;
- Adding a new research site - an SSA Form must be completed for the new site.

27.2 If an amendment is required to an SSA Form the PI can make changes to the original SSA Form as required. The SSA Form will have a new 'submission code' and the SSA will still be linked to the NEAF.

### **An amendment involving review by the reviewing HREC**

27.3 Where new or amended documentation has been submitted to the reviewing HREC for ethical review, these documents must also be sent to each site's Research Governance Office and the Principal Investigator. The HREC Reference Number must be quoted.

27.4 The Research Governance Officer and the Principal Investigator should consider whether or not new site specific assessment authorisation is necessary for the amendment.

27.5 If site specific assessment changes are required, the Principal Investigator must access the Online Forms website SSA Form and upload all new supporting documents relating to the amendment (this includes HREC documents received from the HRE Coordinator and site documents) with correct version numbers.

27.6 If an amendment to the SSA is submitted, the Research Governance Officer will send a letter to the Principal Investigator acknowledging the SSA amendment submission indicating whether it is valid.

27.7 An amendment must not be implemented until:

- The amendment has been approved by the reviewing HREC; and
- The SSA has been authorised (if applicable).

27.8 The Chief Executive or delegate will be responsible for authorising SSA amendments that impact upon the institution.

27.9 A standard letter authorising the amended SSA will be sent by the Research Governance Officer to the site's Principal Investigator indicating that the amendment can be implemented.

**An SSA amendment only**

- 27.10 If an SSA amendment applies to a single site only and does not require ethical approval, the Principal Investigator at that site should submit the amendment to the site's Research Governance Officer to gain authorisation from the Chief Executive/delegate.
- 27.11 The Research Governance Officer should inform the Principal Investigator in writing once the SSA amendment has been authorised.

## **SOP 28    Withdrawal or suspension of SSA authorisation**

**Purpose**    Informing the reviewing HREC and Principal Investigator of withdrawal or suspension of SSA authorisation at a site.

- 28.1    Where a Chief Executive/delegate decides that the site cannot continue to conduct the research project, then SSA authorisation should be suspended or withdrawn.
- 28.2    The Research Governance Officer should notify the reviewing HREC and the Principal Investigator of the decision to withdraw SSA authorisation at that site as soon as possible.

***Research cannot continue at a site if SSA authorisation has been withdrawn or suspended by the Chief Executive/delegate.***