Department of Health

health

Research governance and Site specific assessment

Process and practice

State Government Victoria

Research governance and Site specific assessment

Process and practice

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Contents

Definitions

ABN	Australian Business Number
AE	Adverse Event
ABR	Australian Business Register
AU RED	Australian Research Ethics Database
AUD	Australian Dollar
CAS	Central Allocation System
Cc	Carbon copy
CEO	Chief Executive Officer
CIRA	Clinical Investigation Research Agreement (devices)
CPI	Coordinating Principal Investigator
CRA	Contract Research Associate (use of CRA is interchangeable with trial monitor)
CRO	Contract Research Organisation
CTN	Clinical Trial Notification
CTRA	Clinical Trial Research Agreement
CTX	Clinical Trial Exemption
CV	Curriculum Vitae
DSUR	Development Safety Update Report
FDA	Federal Drug Administration (USA)
GCP	Good Clinical Practice
GST	Goods and Services Tax
HREC	Human Research Ethics Committee
IB	Investigator Brochure
ICH-GCP	International Conference on Harmonisation – Good Clinical Practice
IFU	Instruction for Use
IND	Investigational New Drug
MTAA	Medical Technology Association of Australia
NEAF	National Ethics Application Form
NHMRC	National Health Medical Research Council
NMA	National Mutual Acceptance (of ethical and scientific review)
NSW	New South Wales

OH & S	Occupational Health and Safety
PI	Principal Investigator
PICF	Participant Information Consent Form
PSRI	Periodic Safety Reports for Investigators
RGO	Research Governance Officer
RSO	Radiation Safety Officer
SAE	Serious Adverse Event
SEBS	Southern Eastern Border States
SOP	Standard Operating Procedures
SSA	Site Specific Assessment
SUSAR	Suspected Unexpected Serious Adverse Reaction
TGA	Therapeutic Goods Administration
USADE	Unanticipated Serious Adverse Device Effect
VMIA	Victorian Managed Insurance Authority
VSM	Victorian Specific Module

Introduction

The purpose of this document is to provide guidance to assist all sectors involved in clinical trials to understand the processes used to meet the regulatory requirements for clinical trial research in Australia.

This document will refer to research governance / site-specific assessment (SSA), as it is site assessment that is central to governance of the regulatory aspects of research.

The emphasis of this document is on multi-site clinical trials, but the content can be applied equally to other human health and medical research, although some requirements will not apply.

Process and practice

There are a number of ways to approach the practical aspects to meet the required process, and there are defined responsibilities outlined in policies and operating procedures. However, the actual process, steps and timing will be particular to each institution's management.

This document has been developed from experience over the past four years in the relatively new research governance process for SSA that is required to conduct a clinical trial at a particular institution.

This document also addresses the interface between research ethics and governance. Ethics and research governance/SSA are separate in that decision making is distinctly different. The research governance officer (RGO) will base an assessment on some of the same documents that are reviewed by a human research ethics committee (HREC). The deliberation in each case is different; one is ethical and the other considers risk, the law and management of issues around research at the institution.

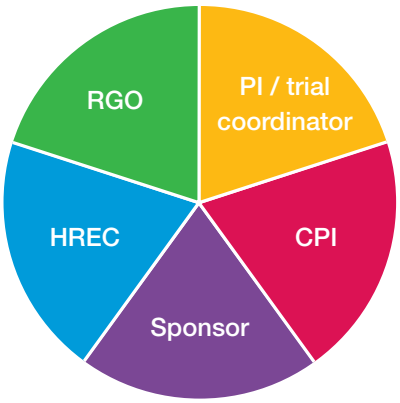
Timely responses to queries between the coordinating principal investigator (CPI) / trial coordinator (on behalf of participating sites) and the reviewing HREC is crucial to avoid delay in commencing research. Clinical trial advancement requires assured processes and understanding at the CPI (lead) and participating sites. Consistency within the research governance process is important, and establishing uniform practices will enable timely processing.

Communication

Both before and after approval and authorisation, it is essential to ensure good communication among parties. All parties involved need to establish open lines of communication from the inception of the research proposal. If the processes are not discussed and coordinated correctly at the beginning, then the streamlined system will not operate to its full potential.

All those who participate in the regulatory steps required for research should familiarise themselves with the processes and practices outlined in this document, and a unified approach among relevant parties is encouraged.

Figure I.1: Key stakeholders in research governance/SSA



Good communication will underpin resolution of any issues that may arise in the complexity of SSA requirements.

- The principal investigator (PI) / trial coordinator is advised to work collaboratively with both the industry sponsor and/or contract research organisation (sponsor/CRO) and the RGO.
- The RGO is strongly advised to liaise with relevant stakeholders and to agree on roles and what additional information is provided by the site PI.
- The sponsor/CRO is advised to communicate with site clinical and study-related personnel concerning the local site requirements for research governance/SSA.

Collaboration is paramount among all parties, and this booklet provides information for investigators / trial coordinators, RGOs and sponsors/CROs. All parties should review all relevant sections for a complete understanding of each other's roles and responsibilities.

Research governance

Research governance can be defined as the broad range of regulations, principles and standards of good practice that exist to achieve, and continuously improve, research quality across all aspects of healthcare. In relation to this booklet, it refers to how the research is to be conducted at a site and, as such, covers a wide range of considerations.

- **Ethical protection of participants** – dignity, rights, safety and wellbeing
- **Scientific integrity** – high-quality, valid research
- **Health and safety** – occupational health and safety and physical, legal and social issues, such as where the research is undertaken and the experience of the research team
- **Information** – public access to information and findings; the role of the complaints contact person and whether they are suitable and have sufficient time
- **Business** – accountabilities and responsibilities, such as compliance with legal requirements and correct contractual arrangements and robust budget management
- **Quality research culture** – promotion of excellence

Streamlining clinical trial regulation

The separation of ethics from research governance has required the RGO role to be identified at health service institutions. The research governance process involving SSA takes into account the appropriateness of the research and whether the institution has the resources and facilities to conduct the research project.

The primary focus is to achieve timely and efficient research governance authorisation for multi-site clinical trials so that trials can commence as soon as possible following HREC approval. Introduction of the streamlined system is aimed at improving competitiveness and attracting global clinical trials to benefit patients by receiving new treatments sooner.

Streamlined ethical review of multi-site clinical trials in Victoria was extended to allow single ethical and scientific review among the eastern seaboard states (Interstate Mutual Acceptance) in 2011. Transition to acceptance of ethical review by other states and territories to National Mutual Acceptance (NMA) has applied from 1 November 2013 and will be a phased approach with some jurisdictions joining at a later date.

Considerable experience has been gained with the introduction of streamlining ethical and scientific review of multi-site clinical trials in Victoria. Under the streamlined system all participating sites obtain one HREC approval. This requires one ethics submission, and the reviewing HREC is responsible for the ethical and scientific review of the study for all participating sites.

A parallel process of research governance/SSA must be completed as the trial cannot commence until both HREC approval and SSA authorisation are obtained at a site.

Commercially sponsored clinical trials

The sponsor/CRO will be referred to together throughout this booklet and will encompass related study personnel.

Following feasibility and site selection for a clinical trial there are specific tasks required of the sponsor/CRO, and negotiation of additional assistance may be agreed for the trial. As a sponsor/CRO, communication with clinical trial site personnel is essential to ascertain local site requirements for research governance/SSA. This booklet provides information to ensure a streamlined approach is achieved among all parties.

The SSA form is the core document to manage site assessment requirements. The SSA form holds the information on how the project will be conducted at the site, including mandatory signatures and related supporting documentation.

The SSA form, along with the supporting documents, is the vehicle for transferring all essential clinical trial documents from the PI / trial coordinator to the RGO.

References and useful information

Online forms for CPIs and PIs

This website has online application forms for ethics and SSA and must be used for all applications: <www.ethicsform.org/au/>.

The following advice refers to existing documents on Victoria's Clinical Trial Research website. This may be updated from time to time and it is advised to check the website regularly.

Standard operating procedures for streamlining ethical review of clinical trials

This sets out the framework for the streamlined system, and is available at <www.health.vic.gov.au/clinicaltrials/streamlining>.

Standard operating procedures for research governance officers

The most recent version can be found at <www.health.vic.gov.au/clinicaltrials>.

Research governance checklist for all principal investigators **(research governance/SSA checklist)**

The checklist is used by the PI / trial coordinator and can be found at <www.health.vic.gov.au/clinicaltrials/site-specific>.

Cover letter for research governance applicatio**n (research governance/SSA cover letter)**

It is important for PIs to use this cover letter as it is also used for confirmation of an SSA submission by the RGO. It can be found at <www.health.vic.gov.au/clinicaltrials/site-specific>.

CPI and PI responsibilities

These summary documents give a snapshot of the responsibilities for clinical trials and can be found at <www.health.vic.gov.au/clinicaltrials/application-instructions>.

Other resources can be found at:

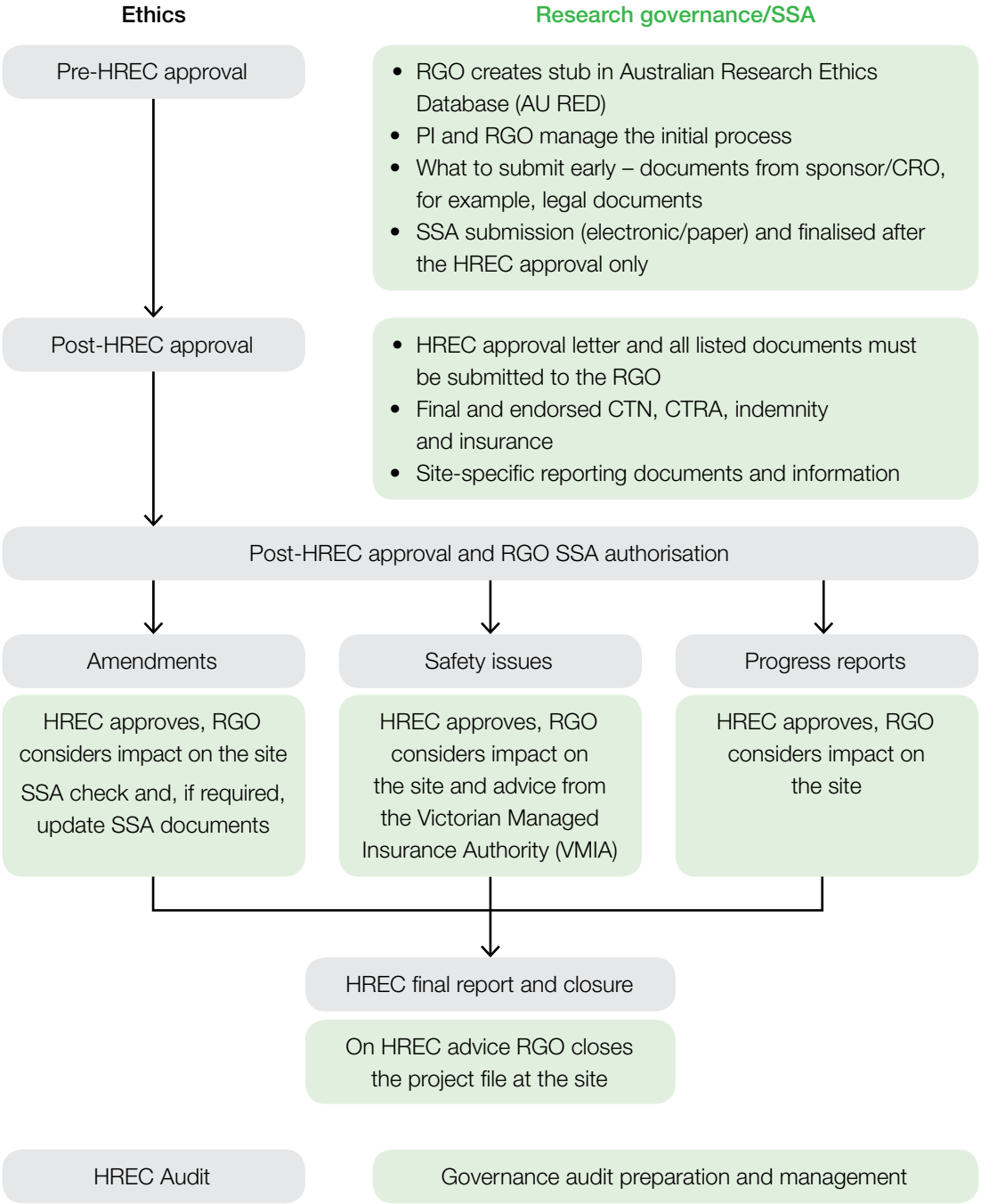
www.health.vic.gov.au/clinicaltrials

www.health.qld.gov.au/ohmr/documents/regu/rsrch_guide_com.pdf

hrep.nhmrc.gov.au/_uploads/files/HoMER-RolesandResponsibilitiesv3.0.pdf

hrep.nhmrc.gov.au

Figure I.2: Summary of the processes



Section 1:
Investigators / trial coordinators

Getting started

CPI (lead) site preparation

Once site selection has occurred the CPI / trial coordinator must first identify key personnel involved in research governance for the trial, and these would include:

- the PI / trial coordinator for the study at each participating site
- the local RGO
- the study monitor.

A meeting with each of the parties should be held so all are informed of the requirements for the SSA submission.

Important reference documents are available at <www.health.vic.gov.au/clinicaltrials/site-specific>.

- The *Standard operating procedures for streamlining ethical review of clinical trials* is an essential reference.
- The research governance/SSA cover letter provides consistent information to the RGO and highlights any special considerations.
- The research governance/SSA checklist lists the documents that may be included with every new research governance/SSA application submitted to the site's research governance office.

Early action

The research governance early action checklist is in three parts – A, B and C – and is based on the concept of starting the process as soon as site selection occurs. It is recommended that documents be submitted as they become available, and in parallel with the ethics review process. Therefore, not all documents need to be submitted at the one time, and this is preferred rather than having all governance documents provided later. In order to expedite research governance/SSA it is imperative that each participating site make contact with their institution's RGO to establish the preferred process at their site.

CPI study correspondence

The communication between the CPI (applicant) and the HREC needs to be timely so that HREC approval and SSA authorisation processes can occur with minimal delay.

It is planned that an electronic submission system will operate between Online Forms and AU RED that will provide direct interconnection and document flow between Online Forms investigator accounts and AU RED users for both ethics and SSA administration.

Currently many HRECs use email as a primary method of correspondence. In this case it is recommended that the CPI copies the correspondence to the participating sites.

CPI communications

The CPI for a multi-site clinical trial may use a contact template (Appendix 1.1) to record relevant clinical trial details and participating site information. The template is a ready communication and reference tool for use throughout the clinical trial. It can be sent to the sponsor to complete initially. It can then be maintained by the CPI. This template is a reference to ensure all relevant personnel are listed and included in communications. It is the responsibility of the sponsor to inform the CPI of any staffing changes throughout the study, so the template can be updated accordingly.

CPI email distribution list

The distribution of correspondence from the HREC to trial personnel may occur by a number of means. Use of an email template requires the CPI to maintain a current email 'ethics distribution list' with all participating site staff involved in the study; that is, PIs, trial coordinators and clinical research associates (CRA) (Appendix 1.2). The email distribution can be based on a 'contact template' and updated when there are changes to staff throughout the trial.

CPI email correspondence template

An email template can be created for email correspondence or submission of documents to the HREC by the CPI (see Figure 1.1). This enables identification of ethics documents and also ensures all relevant information is provided in the template, for example, the HREC reference number.

Figure 1.1: CPI site ethics template

XXXXXXX Study: CPI site correspondence to participating sites

HREC reference number: .....

Local reference number: .....

Coordinating principal investigator: .....

Short title: XXXXXX Study

Full project title: [.....]

Dear HREC coordinator,

Please find attached:

These documents will be forwarded in hard copy today.

Regards

[CPI / trial coordinator name(s)]

CPI tracking coversheet

Tracking the progress of the ethics and research governance/SSA documents from submission to approval can be a lengthy process and a clear plan is necessary. Tracking of documents should commence when the sponsor/CRO initially provides documents for submission through to the end of the process when SSA authorisation acknowledgement occurs.

A simple tracking coversheet (Appendix 1.3) can provide a clear audit trail for progress and for the location of a document at any given time. This template is an example of how the CPI site can track documents from HREC submission to SSA authorisation. The tracking sheet for Serious Adverse Events (SAE) is also recommended for reporting events to the HREC and for informing the RGO (Appendix 1.4).

PI participating site preparation

It is important for the PI / trial coordinator to make contact with the CPI. The CPI / trial coordinator will be responsible for relaying all ethics communications to each site. Participating sites should familiarise themselves with the HREC's reporting requirements, for example, reporting of SAEs and protocol violations.

The sponsor will provide the CPI with each participating site's contact details, enabling the flow of ethics correspondence to sites. Any staffing changes at the participating site should be communicated directly via the sponsor.

Site SSA correspondence

PI email distribution list

It is advised that each participating site creates their own research governance/SSA email distribution list that includes all site personnel who need to be informed and receive correspondence pertaining to any documents submitted to the RGO; for example, the PI / trial coordinator, CRA and RGO.

PI email correspondence template

It is recommended that an email template be created for all research governance/SSA correspondence or submissions to the RGO (see Figure 1.2). This will enable identification of documents and will ensure any other relevant information is provided in the template, for example, the HREC reference number.

Figure 1.2: PI email correspondence template

XXXXXXX Study: Participating site correspondence to RGO

HREC reference number: .....

Local reference number: .....

Coordinating principal investigator: .....

Short title: XXXXXX Study

Full project title: [.....]

Dear [RGO name]

See attached documents and [insert name of reviewing HREC] approval letter dated _____ listing all items approved by the reviewing HREC.

In addition, [insert principal investigator's name] has reviewed these documents and, in their opinion, all approved changes are acceptable for conduct of the study at [insert institution name].

Please confirm [insert institution name] research governance/SSA acknowledgement by 'reply all' to this email, clarifying if any further action is required.

Regards,

[PI / trial coordinator name(s)]

PI tracking coversheet

The tracking of documents should commence when the sponsor/CRO initially provides documents for submission through to the end of the process when SSA authorisation acknowledgement occurs.

A simple participating site tracking coversheet can provide a clear timeline of the approval progress and the location of a document at any given time in the assessment process (Appendix 1.5). This template is an example of how participating sites can track documents from HREC submission to RGO approval, even when they did not submit the document to the ethics committee themselves. It is important that the CPI continues to keep participating sites informed of the approval status of all ethics documents as they progress through the system.

A participating site SAE tracking template is also recommended for reporting events to the HREC via the CPI, and for informing the RGO (Appendix 1.6).

Research governance/SSA submission

Early action: Part A – sponsor/CRO responsibilities for documents and communication

The CPI site is responsible for submitting the clinical trial application documents to the reviewing HREC (refer to the reviewing HREC's website for submission requirements). These documents are also made available to participating sites via the *National ethics application form* (NEAF) on the Online Forms website.

Early action

The research governance/SSA submission can begin when the sponsor/CRO provides electronic and hard copies of key documents that are listed in the research governance/SSA checklist on the Clinical Trial Research website at <www.health.vic.gov.au/clinicaltrials/site-specific>.

All items listed in this section may be submitted independently of the HREC submission timing. It is recommended to start as early as possible, but this will be entirely dependent on the sponsor/CRO providing the documents. There should be a check that the **correct** company name, address, financial and other contact details appear on relevant documents. Any inconsistencies will cause a delay in the research governance/SSA process.

The CPI site expects to receive the following documents from the sponsor/CRO:

- protocol
- investigator brochure
- *Medicines Australia form of indemnity* for clinical trial HREC review and conduct of the trial for each participating site
- a *Notification of intent to supply unapproved therapeutic goods under the Clinical Trial Notification (CTN) scheme* for each site, if applicable.

The CPI site should distribute these documents to participating sites as soon as possible. Sites may request additional copies as required (for example, for the RGO and site personnel).

Participating sites would expect to receive from the sponsor/CRO a complete package of documents. Using a package is preferred to avoid confusion. Timely distribution to a site is important and would include at minimum:

- *Medicines Australia form of indemnity for clinical trials: standard*
- *Clinical trial research agreement* (CTRA)
- detailed budget (may be a draft)
- research governance fee
- copy of the CTN
- express post envelopes (self-addressed)
- express post envelopes for sending any urgent correspondence or other documents.

Online forms and SSA

The preparation of the NEAF is often a shared responsibility. The Online Forms website at <www.ethicsform.org/au/> must be used to prepare the NEAF, as this facilitates the transfer of the NEAF to other parties. The sponsor/CRO may need to access the application and upload documents on the Online Forms website. This is important as Online Forms automatically allows the flow of the NEAF and the supporting documents to all associated SSA accounts.

An SSA form is generated by the CPI within the NEAF application on the Online Forms website. Thus the sponsor/CRO must provide the CPI with the email address for each PI / trial coordinator. This enables the CPI to transfer an SSA to each site using an email address via Online Forms. Once each site PI / trial coordinator receives and accepts the transferred SSA they will have immediate access to the ethics submission documents to inform their SSA application.

Quality checks

The site PI / trial coordinator should verify the site's specific details on the CTN, legal and other documents in preparation for SSA submission to the RGO. For legal documents refer to the participating institution's business details and provide the correct name, address, financial, contact and other details relevant to each document.

The sponsor/CRO should provide at least two copies of the Medicines Australia CTRA and an individual Medicines Australia form of indemnity (standard) for the PI and RGO.

All sub-investigators are required to sign the SSA.

To expedite the governance process it is advised to simultaneously arrange for completion of the FDA 1572 *Statement of Investigator form* (this must be signed before beginning participation in a clinical study conducted under the Investigational New Drugs (IND) regulations), including financial disclosures and curriculum vitae (CV), where applicable.

Early action: Part B – activities after HREC submission

The CPI / trial coordinator should alert participating sites of the HREC submission and communicate any correspondence to or from the HREC.

The CPI / trial coordinator will be required to complete the SSA and liaise with the RGO about the submission of documents. To enable this refer to the following:

- *Standard operating procedures for streamlining ethical review of clinical trials*
- *Standard operating procedures for research governance officers.*

These documents are available on the Clinical Trial Research website at <www.health.vic.gov.au/clinicaltrials/streamlining>.

Post-HREC approval: SSA authorisation

Early action: Part C – activities following HREC approval

The CPI must provide sites with:

- HREC approval letter (copy)
- copies of approved HREC documents (uploaded to the NEAF on the Online Forms website), if not already provided by the sponsor/CRO
- NEAF signature page signed by the CPI
- signed individual site CTN (original) for submission to their RGO
- executed copy of a Medicines Australia form of indemnity for HREC review.

RGOs may have different preferences on how and when the ethics approval documents are provided, as hard copy or electronic, or both. It is important that the trial coordinator is in contact with the site RGO regarding the ethics approval package.

Refer to Part C of the research governance/SSA checklist. This section outlines the remaining documents to be provided to the RGO by each PI / trial coordinator following notification of HREC approval. The HREC-approved documents will be required by each site's RGO. This is the final stage of obtaining SSA authorisation at the site.

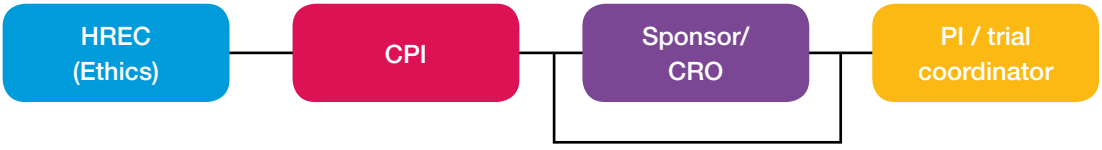
For the duration of the study, the site PI (and the CPI) will be responsible for providing their RGO with all relevant amendments or information relevant to the conduct of the study and the HREC amendment approval notification for these changes.

Notifying the RGO of an HREC amendment

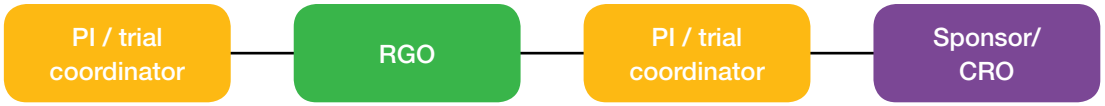
Although the CPI / trial coordinator is responsible for the submission of amendments to the HREC, the CPI may relay the relevant correspondence or information to participating site PIs using various methods:

- a CPI may prefer to send all approvals and correspondence to the sponsor/CRO to forward to each participating site PI
- the CPI may accept the responsibility of informing site PIs directly.

The CPI's preference should be clearly established by the sponsor/CRO at the beginning of the study to ensure all relevant HREC-related information and correspondence is distributed to participating sites.



When the site PI / trial coordinator receives an approved HREC amendment, or other ethics approval or acknowledgement, it is the site PI's responsibility to forward all documents to the RGO for assessment and a timely SSA authorisation decision. The RGO assessment for SSA amendment authorisation must be advised to the PI / trial coordinator, and the outcome must be communicated to the sponsor/CRO by the PI / trial coordinator (see below).



RGO requirements for authorising amendments

In instances where an amendment has a significant impact on sites, it is imperative that liaison occurs with the RGO. The RGO will be responsible for deciding whether a formal SSA amendment and other documents are required. Depending on the RGO's decision, SSA authorisation may be necessary from the chief executive officer (CEO) or delegate (as required for initial SSA authorisation).

Implementing an amendment at a site

It is important that the PI / trial coordinator understand that an amendment cannot be implemented until it is approved by the reviewing HREC and authorised at the institution, and the sponsor/CRO is informed.

It is not relevant for a participating site to inform the CPI of an SSA amendment authorisation, as the CPI reports to their local RGO and this is outside the role of the CPI. However, the CPI should be informed if RGO authorisation was not obtained.

Prompt action by the RGO at each site is important to reduce the time gap between ethics approval and SSA authorisation for implementation of an amendment.

Safety reports – document flow

A site PI / trial coordinator will be responsible for reporting any Adverse Event (AE), Serious Adverse Event (SAE), Suspected Unexpected Serious Adverse Reaction (SUSAR) and Unanticipated Serious Adverse Device Effect (USADE) that may have a **material impact** on continued ethics acceptability. Also an AE/SAE/SUSAR/USADE may indicate a need for a change to the protocol. The following actions should be taken:

- notify the sponsor as specified in the event report
- complete the relevant AE/SAE/SUSAR/USADE forms, available at <www.health.vic.gov.au/clinicaltrials>
- forward the completed AE/SAE/SUSAR/USADE forms to the CPI or delegate, and include an amendment form if the event requires a change and HREC review.

On rare occasions, and to avoid delay, the site PI may inform the CPI of the event and at the same time forward the AE/SAE/SUSAR/USADE form directly to the reviewing HREC. This is an exception to the general rule where the PI must always communicate with the reviewing HREC via the CPI.

The CPI is responsible for:

- submitting the form to the reviewing HREC in a prompt manner (copy to the site)
- forwarding a response from the reviewing HREC so that it can be communicated to the site PI.

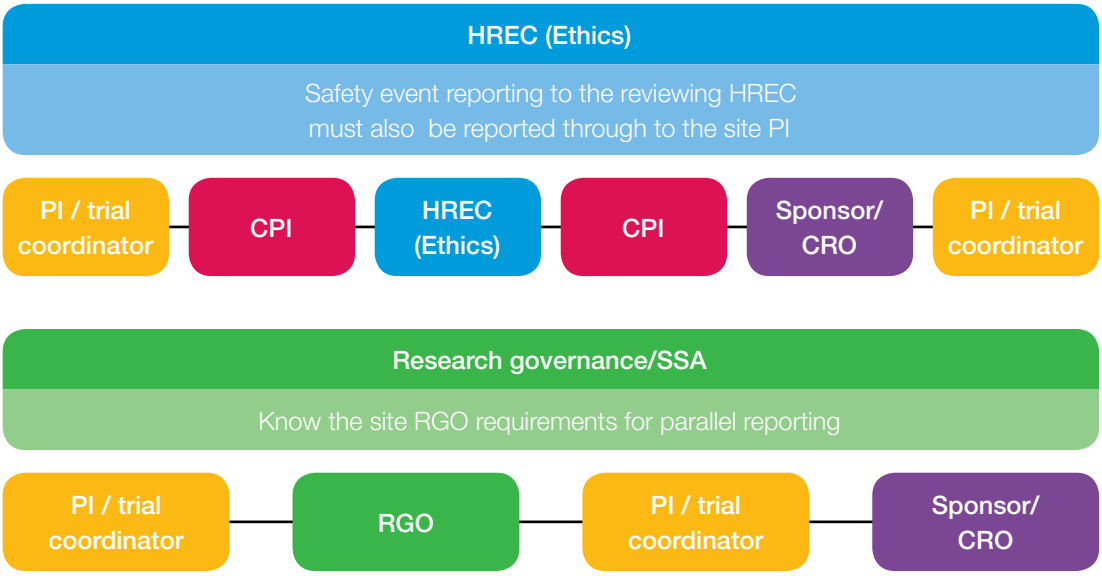
The RGO is responsible for deciding whether a formal SSA amendment and other documents are required. Depending on the RGO's decision, SSA authorisation may be necessary from the CEO or delegate (as required for initial SSA authorisation).

Coordinating safety reporting timelines

The trial coordinator should establish a reporting timeline with their RGO for any AE/SAE/SUSAR/USADE events. Two scenarios are possible.

- The RGO may require the event notification at the same time as it is reported to the reviewing HREC. The PI / trial coordinator should send a copy of the completed reporting form to the RGO.
- If the RGO does not require AE/SAE/SUSAR/USADE to be reported at the same time that the HREC is notified, then both the completed AE/SAE/SUSAR/USADE report and the response from the HREC can be forwarded to the RGO at the same time.

Figure 1.3: Safety event reporting flow



The RGO is notified by the PI / trial coordinator and an assessment of the HREC outcome and required action will be made. The PI / trial coordinator will be advised by the RGO regarding any SSA amendment for site authorisation, and the PI / trial coordinator in turn must notify the sponsor/CRO of SSA authorisation status.

Protocol deviation and violation reporting – document flow

To fulfil International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) requirements[1], any deviations or violations of the approved protocol must be notified to the reviewing HREC.

The PI at the site where the deviation occurred must complete the protocol deviation or violation report, available at <www.health.vic.gov.au/clinicaltrials/application-instructions>. The form is then submitted by the CPI to the reviewing HREC and copy the responsible PI (where the protocol deviation or violation occurred). Each is responsible for submitting to their institution's RGO.

1 International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use: guideline for good clinical practice E6(R1)

The impact of the protocol deviation or violation on the conduct of the study is evaluated by the PI in the submitted report and by the reviewing HREC. The sponsor/CRO may be involved where appropriate.

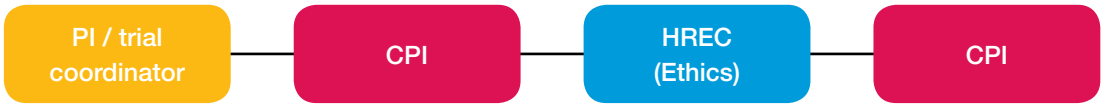
Interim and annual progress reports – reporting to the HREC

Progress reports may be frequent, depending on the risk of the approved research, and this will be determined by the reviewing HREC. The process will be the same for all progress reports, and forms are available at <www.health.vic.gov.au/clinicaltrials/application-instructions>.

Annual progress reports are due on the anniversary of the HREC approval date.

Each participating site must provide a completed *HREC progress report – site report* to the CPI / trial coordinator. In addition, the CPI should complete an *HREC progress report – CPI coversheet.*

The CPI should collate participating sites' progress reports and forward these to the reviewing HREC by the due date. If a participating site does not provide a report by the required date the reviewing HREC may suspend approval for that site until a report is received.



Interim and annual progress reports – reporting to the RGO

The CPI / trial coordinator should relay an acknowledgement or feedback from the reviewing HREC to the participating sites and sponsor/CRO. The site RGO will require copies of the following:

- progress report for their site
- copy of the CPI coversheet (other sites' reports are not applicable)
- the reviewing HREC's acknowledgement of the report.

The RGO's acknowledgement of receipt of these documents is sent to the PI and forwarded to the sponsor/CRO.

Study closure

Final study closure or site closure must be reported to the reviewing HREC and respective participating site RGOs. The CPI / trial coordinator is responsible for submitting the *HREC final report for research project completion or site closure* with attached information from sites as required. A copy must be sent to each site PI / trial coordinator to forward to their RGO.

For closure at one or more sites only, an HREC final report must be provided to the reviewing HREC listing the relevant site(s) that have closed the study. A copy must also be provided to the relevant participating site(s) so their RGO can be informed of the study closure.

Appendix 1.1: CPI site contacts template for multi-site research

CPI site contacts for multi-site research

Reviewing HREC:	**HREC reference number:**
	CPI site reference:
Reviewing HREC website: <www.health.vic.gov.au/clinicaltrials/hrec-applications> should be referred to for information regarding applications	
Postal address: Research Governance Unit [Full postal address] Email:	**Contact person:** Name Office title Street address Ph: (03) Fax: (03) Email:

Coordinating Office for Clinical Trial Research

General enquiries Information line: (03) 9096 7394 Email: multisite.ethics@health.vic.gov.au	**System information** Information line: (03) 9096 7398 Email: multisite.ethics@health.vic.gov.au
Website: <www.health.vic.gov.au/clinicaltrials> Central allocation system phone: (03) 9096 7395, Monday to Friday 10 am to 5 pm	

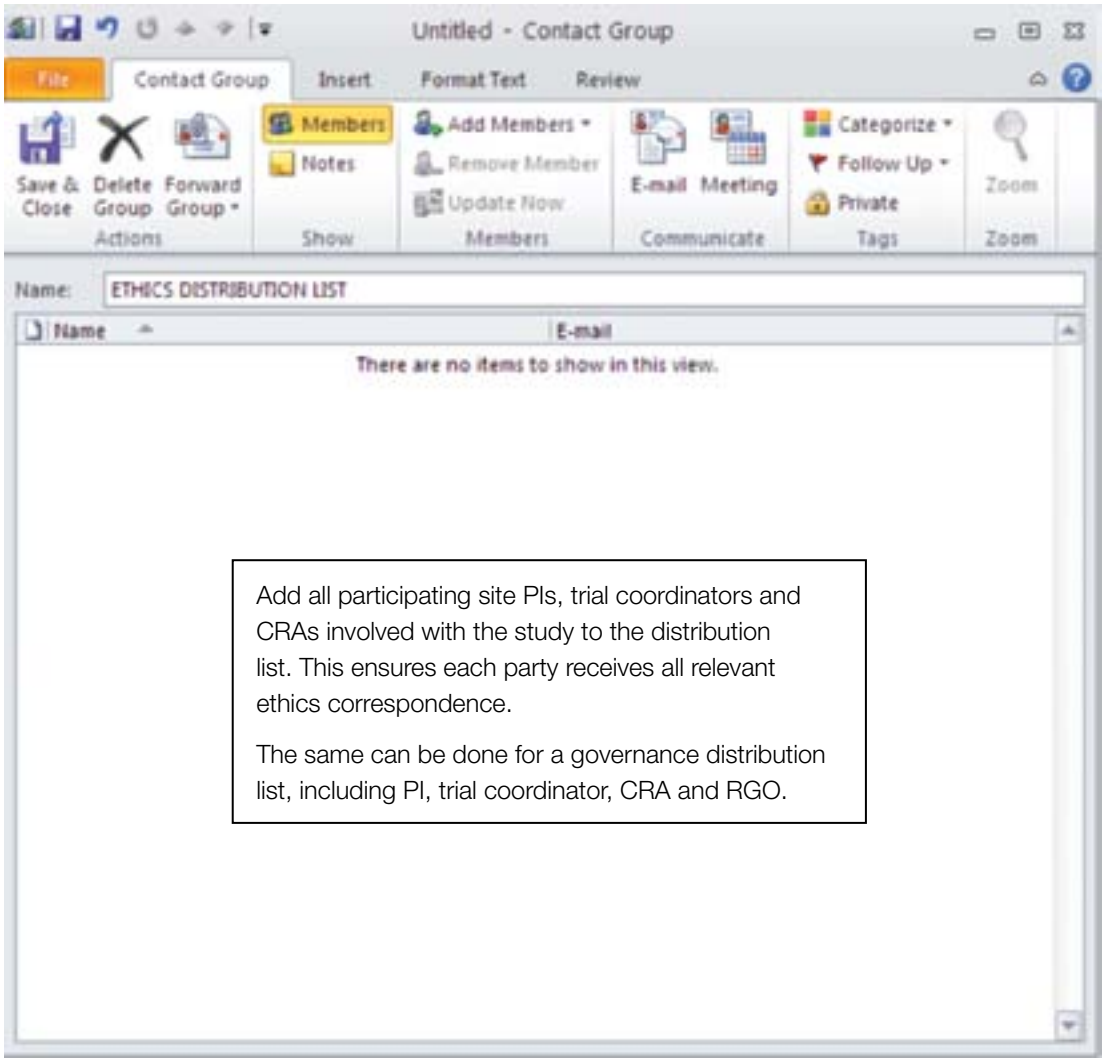
CPI site: [Site institution name]	
Site number:	
Principal investigator: [name]	**CPI / trial coordinator:** [name]
Contact details: Institution name Clinical unit name Street address Postal address Ph: (03) Mobile: Email:	**Contact details:** Institution name Clinical unit name Street address Postal address Ph: (03) Mobile: Email:

Participating site:	
Site number:	
Principal investigator: [name]	**Participating site trial coordinator:** [name]
Contact details: Institution name Clinical unit name Street address Postal address Ph: (03) Mobile: Email:	**Contact details:** Institution name Clinical unit name Street address Postal address Ph: (03) Mobile: Email:

Participating site:	
Site number:	
Principal investigator: [name]	**Participating site trial coordinator:** [name]
Contact details: Institution name Clinical unit name Street address Postal address Ph: (03) Mobile: Email:	**Contact details:** Institution name Clinical unit name Street address Postal address Ph: (03) Mobile: Email:

Participating site:	
Site number:	
Principal investigator: [name]	**Participating site trial coordinator:** [name]
Contact details: Institution name Clinical unit name Street address Postal address Ph: (03) Mobile: Email:	**Contact details:** Institution name Clinical unit name Street address Postal address Ph: (03) Mobile: Email:

Appendix 1.2: CPI – ethics distribution email list



Add all participating site PIs, trial coordinators and CRAs involved with the study to the distribution list. This ensures each party receives all relevant ethics correspondence.

The same can be done for a governance distribution list, including PI, trial coordinator, CRA and RGO.

Appendix 1.3: CPI site – tracking coversheet

CPI SITE – TRACKING COVERSHEET

CPI SITE NAME:		
STUDY NAME:		
DOCUMENT(S) FOR SUBMISSION:		
APPROVAL PROGRESS		**DATE**
[SPONSOR/CRO PROVIDES DOCUMENT(S) FOR SUBMISSION]		
HREC – SUBMISSION OF DOCUMENTS		
Fee form completed and submitted (if applicable) with document(s) ☐		
Electronically submitted ☐		
Hard copy submitted ☐		
ACKNOWLEDGEMENT/APPROVAL RECEIVED FROM HREC		
PARTICIPATING SITES NOTIFIED OF HREC ACKNOWLEDGEMENT/ APPROVAL		
SPONSOR/CRO NOTIFIED OF HREC ACKNOWLEDGEMENT/APPROVAL		
RESEARCH GOVERNANCE/SSA – SUBMISSION OF DOCUMENTS		
DOCUMENT(S) SUBMITTED TO RGO		
ACKNOWLEDGEMENT RECEIVED FROM RGO		
SPONSOR NOTIFIED OF SSA AUTHORISATION		
Original HREC approval letter (if applicable)	Email response ☐ (no further action)	
	Hard copy of letter ☐	(Date hard copy received)
File document(s) in investigator site files ☐		
COMMENTS		

Appendix 1.4: CPI site SAE tracking coversheet

CPI SITE SERIOUS ADVERSE EVENT (SAE) TRACKING COVERSHEET

SUBMITTING SITE NAME (where SAE occurred):	
STUDY NAME:	
SAE (Name of event):	
PARTICIPANT NUMBER:	
SAE APPROVAL PROGRESS	**DATE**
DATE EVENT OCCURRED	
DATE CPI WAS NOTIFIED BY PARTICIPATING SITE/SPONSOR/CRO OR BECAME AWARE OF SAE	
HREC – SUBMISSION OF DOCUMENTS	
SUBMISSION TO HREC	
ACKNOWLEDGEMENT/RECEIVED FROM HREC	
PARTICIPATING SITE NOTIFIED OF HREC ACKNOWLEDGEMENT/ APPROVAL (if applicable)	
SPONSOR/CRO NOTIFIED OF HREC ACKNOWLEDGEMENT/APPROVAL	
RESEARCH GOVERNANCE/SSA – SUBMISSION OF DOCUMENTS	
DOCUMENT SUBMITTED TO RGO	
ACKNOWLEDGEMENT RECEIVED FROM RGO	
SPONSOR/CRO NOTIFIED OF SSA AUTHORISATION/ RGO ACKNOWLEDGEMENT	
File document(s) in investigator site files ☐	
COMMENTS	

Appendix 1.5: Participating site tracking coversheet

PARTICIPATING SITE – TRACKING COVERSHEET

SITE NAME:	
STUDY NAME:	
DOCUMENT(S) FOR SSA SUBMISSION:	
HREC APPROVAL PROGRESS	**DATE**
SPONSOR PROVIDED [name of unit] WITH DOCUMENT(S)	
HREC – SUBMISSION OF DOCUMENTS VIA CPI	
CPI SITE SUBMITTED DOCUMENT(S) TO HREC	
HREC ACKNOWLEDGEMENT/APPROVAL	
CPI NOTIFIED OF HREC RESPONSE	
RESEARCH GOVERNANCE AND SSA – SUBMISSION OF DOCUMENTS	
SITE SUBMITS TO RGO	
ACKNOWLEDGEMENT RECEIVED FROM RGO	
SPONSOR NOTIFIED OF SSA AUTHORISATION	
File document(s) in investigator site files ☐	
COMMENTS	

Appendix 1.6: Participating site SAE coversheet

PARTICIPATING SITE – SERIOUS ADVERSE EVENT (SAE) TRACKING COVERSHEET

SUBMITTING SITE NAME:	
STUDY NAME:	
SAE (Name of event):	
PARTICIPANT NUMBER:	
SAE APPROVAL PROGRESS	**DATE**
DATE EVENT OCCURRED	
DATE CPI WAS NOTIFIED BY PARTICIPATING SITE OR BECAME AWARE OF SAE	
ETHICS – SUBMISSION OF DOCUMENTS	
SUBMISSION TO HREC	
HREC ACKNOWLEDGEMENT/APPROVAL FROM HREC	
PARTICIPATING SITE NOTIFIED OF HREC ACKNOWLEDGEMENT/ APPROVAL (if applicable)	
SPONSOR/CRO NOTIFIED OF HREC ACKNOWLEDGEMENT/APPROVAL	
RESEARCH GOVERNANCE AND SSA – SUBMISSION OF DOCUMENTS	
DOCUMENT SUBMITTED TO RGO	
ACKNOWLEDGEMENT RECEIVED FROM RGO	
SPONSOR/CRO NOTIFIED OF SSA AUTHORISATION/ RGO ACKNOWLEDGEMENT	
File document(s) in investigator site files ☐	
COMMENTS	

Section 2: Research governance officers

Getting started

Key actions and arrangements

The RGO role can vary among institutions. It is important to have an RGO scope of practice, including formal delegation of authority, from the institution. The RGO's scope of practice could include some or all of the following:

- managing the study files. This will be dependent on whether the RGO accepts paper or electronic files. This decision will impact on how applications are received, processed, stored and archived
- managing the study budget – authority to negotiate the research project budget and to provide final authorisation
- authorisation to sign research agreements and contracts
- managing non-standard contracts
- managing assessment of departments that may be impacted by the project and making decisions related to assessment outcomes
- managing notification of projects involving ionising radiation to the Radiation Safety Section, Department of Health, Victoria
- institutional agreements to provide RGO services to other sites
- managing the final SSA authorisation, including authorising and signing the SSA authorisation letter
- deciding to not participate in the research and not authorising an SSA
- managing research misconduct.

Sites are strongly advised to articulate these responsibilities with formal delegation within the institution.

Language related to research governance

Whereas the HREC 'approves' a project, the governance/SSA process 'authorises' the site to proceed with the research. The RGO 'acknowledges' (accepts) the advice or decision of the reviewing HREC.

Communication with a PI/trial coordinator and sponsor/CRO

The RGO may contact the site PI or CPI, reviewing HREC office or the sponsor/CRO in order to progress queries. The RGO should retain a clear and accurate record of this communication with an audit trail.

RGO access to AU RED

The health service has an end user licence agreement with the provider, Infonetica Ltd, for AU RED. The RGO can contact <helpdesk@infonetica.net> to obtain usernames and passwords for AU RED.

AU RED and the RGO

AU RED is integral to the RGO role and managing the SSA form and supporting documents, the core documents for site governance and site assessment. The SSA form is the required format for transferring documents to the RGO for consideration.

Standard Operating Procedures for Research Governance Officers

Are available at: <health.vic.gov.au/clinicaltrials/streamlining.htm>.

AU RED User Manual

The AU RED User Manual (Infonetica Ltd) can be found at:
<vic.ethicsdatabase.org/help/auDefault.aspx>

AU RED Training Manual

The Coordinating Office for Clinical Trial Research has provided an *AU RED Training Manual* that is set out according to the processing of applications and has step-by-step information. To receive a hard copy email <multisite.ethics@health.vic.gov.au>.

The institution's policy on research should be available to both the RGO and investigators in accordance with *'The Australian Code for the Responsible Conduct of Research'* joint publication of the National Health and Medical Research Council, Australian Research Council and Universities Australia.

Research governance/SSA early action checklist

RGO registers project 'stub' in AU RED

PI/trial coordinator in contact with the RGO provides legal and financial documents

The project file should be registered in AU RED by creating the SSA application 'stub' as soon as the HREC reference number is provided (via the Central Allocation System booking email). For multi-site clinical trial research in Victoria, the Coordinating Office for Clinical Trial Research sends an early alert by automated email that a trial is proposed for that site. Otherwise, the RGO may be advised by the PI or the reviewing HREC.

For single-site research the AU RED process differs. Central allocation by the Coordinating Office for Clinical Trial Research will not occur. The HREC reference number is generated by the research office using AU RED when an HREC application is submitted. The RGO should be informed by research office management so an SSA stub can be created in AU RED.

It is good practice to advise the PI/trial coordinator of the HREC reference number early in the application process so that this can be entered into the online NEAF application form.

The stub can be actioned without the SSA application or submission code; however, both of these are required for subsequent processing.

Research governance/SSA submission

Early action: Part A – sponsor provision of documents and communication plan

It is recommended that early provision of documents to the RGO occurs in parallel with HREC review process preparation. This allows scrutiny of the study to meet the legal and business requirements of the institution prior to the HREC's decision. The research governance/SSA checklist (Parts A and B) list items to be submitted before or at the same time as the HREC submission. A detailed information submission sheet for the RGO may be used (Appendix 2.1).

Legal and financial documents are the main items for early attention. These are known to be time consuming and, in some instances, hold up SSA authorisation.

Table 2.1: List of key documents to commence the RGO assessment process

Core document	RGO purpose and process
Research governance/ SSA checklist	Essential to track document submission List of document types to be or not be provided
Research governance/ SSA cover letter	A trial-specific document, with HREC and sponsor contact details and a list of documents required for an application
Detailed budget (usually part of the CTRA)	The RGO should advise if a draft is acceptable at an early stage – budget agreement can be a lengthy process and negotiation should occur early.
Study protocol	To inform the RGO of trial details and the impact on the institution's resources
Investigator brochure	To inform the RGO of trial background information
Medicines Australia form of indemnity (Standard) or *Medical Technology Association of Australia form of indemnity for clinical investigations: standard*	The Medicines Australia or MTAA *Standard Form of Indemnity* form must be used if the study is commercially sponsored. The Medicines Australia form is available at <medicinesaustralia.com.au/issues-information/clinical-trials/indemity-and-compensation-guidelines>. The MTAA form is available at <www.mtaa.org.au/policy-initiatives/clinical-investigations> These legal entity details must also be the **same** as in the **CTRA/ CIRA** and **CTN**.
Insurance certificate	Cover for the risk of conducting a trial as required by VMIA's *Clinical trials – insurance and risk management guidelines,* available at <www.vmia.vic.gov.au/Risk-Management/Clinical-trials/guidelines.aspx> Legal entity details must be correct. Check name and spelling.

Core document	RGO purpose and process
CTN or CTX (**copy** only, until HREC approval is complete)	Verify against advice by the Therapeutic Goods Administration (TGA) on notification of clinical trials, available at <www.tga.gov.au/industry/clinical-trials-forms-ctn.htm>. Legal entity details must be the **same** as those listed in the **CTRA/CIRA** and on the **indemnity** form.
Standard CTRA, *Clinical investigation research agreement* (CIRA) or other legal agreement type	Verify the CTRA against the Medicines Australia CTRA template, available at <medicinesaustralia.com.au/issues-information/clinical-trials/clinical-trials-research-agreements>. Verify the CIRA against the MTAA CIRA (device) template, available at <mtaa.org.au/policy-initiatives/clinical-investigations>. Verify Schedules 4 and 7 against the current Southern and Eastern Border States (SEBS) review panel list of agreed Schedules 4 and 7s, available from the Coordinating Office for Clinical Trial Research.
'Section 4: Use of ionising radiation' (site-specific) and part of the Victorian Specific Module (VSM)	The HREC will review ionising radiation use in the ethical and scientific considerations, but the RGO should ensure that site radiation requirements are met.
CV	Each investigator must provide a current CV that indicates their capacity to undertake their role in the project, including specific training, such as GCP, required for the research.
Additional requirements – sourced from the site	
Site specific forms	
Statement of assessment and endorsement	
Research governance/SSA site fee	

Document quality check

Recommended practice is to conduct a thorough check of the quality of documents with particular attention to the legal documents (see above). Relevant items on the research governance/SSA checklist should be considered and any unmet requirements should be addressed by the time the HREC decision is made. Detailed guidance is in Appendix 2.2 and 2.3.

The main considerations are as follows.

1. The sponsor name (enterprise business name), ABN, address and contact details must be the same on the:
   - certificate of insurance
   - indemnity form
   - standard CTRA or CIRA
   - CTN or CTX.
2. Non–standard CTRAs

   Some institutions do not accept non-standard agreements, but if accepted, the recommended practice is that local legal review is sought for any non-standard agreement. The format of non-standard agreements is diverse. A commercial sponsor will be responsible to pay for legal review and should be informed before the legal review is conducted.

   VMIA have a recommended template for non-commercial clinical trial agreements that could be used for investigator-initiated research. It is available at <www.vmia.vic.gov.au/Risk-Management/Clinical-trials/clinical-trial-research-agreements.aspx>. There may be additional Schedule 4 conditions, and it will be at the discretion of the institution whether the schedule requires legal review.
3. The RGO should make an assessment of document quality associated with the SSA application and validate the SSA in AU RED.

   SSA validation: The SSA form and site-specific supporting documents will be available to the RGO in AU RED providing the PI/trial coordinator has uploaded them in the Online Forms website.

4. Overall assessment of the proposed research and all documents submitted will include the:
   - research governance/SSA checklist
   - research governance/SSA cover letter
   - NEAF and supporting documents
   - SSA form
   - supporting and site-specific documents.

   These documents provide the RGO with a complete overview of the research project, so they can assess the suitability of the research and risk to the institution.

   All documents related to the SSA application are available in AU RED once the RGO imports the SSA form, providing the supporting documents to the NEAF (uploaded by the CPI) and the SSA site-specific documents (uploaded by the site PI/trial coordinator) are present in Online Forms.

   For instructions on the use of AU RED refer to the *Standard Operating Procedures (SOPs) for Research Governance Officers,* the *AU RED User Manual* (Infonetica Ltd) and the *AU RED Training Manual* (Coordinating Office for Clinical Trial Research).

Post-HREC approval: SSA authorisation

Research governance/SSA checklist – Section C

The site PI/trial coordinator is responsible for ensuring all HREC-approved documents are available to the RGO. The RGO should refer to the research governance/SSA checklist to ensure that all submission documents have been received.

The decision whether paper or electronic files are submitted to the RGO will affect processing, storage and archiving of application documents. It is recommended practice that original signed documents are provided to the RGO (exceptions may occur, for example, a copy of the CTN).

The typical post-HREC approval document package may include the following.

Hard copy

- HREC approval letter
- Any original signed documents, for example, a CTN (original signed by the HREC delegate) or finalised CTRA now submitted for institutional signature

Electronic (via Online Forms)

- HREC approval letter and all HREC-approved documents
- Final SSA form and relevant site-specific supporting documents, for Master or Site Master PICF
- VSM

The RGO should check that the HREC approval letter, final approved versions of ethics documents and site-specific documents are available in AU RED on the Application–Checklist tab and in files on the Documents tab.

For this document flow to occur in AU RED, investigators / trial coordinators must upload supporting documents to both the NEAF and SSA forms on Online Forms.

Note: Some of these documents may have already been submitted as part of the early action items on the research governance/SSA checklist, so there may be more than one version. The most recent version will be listed first.

Document quality and actions for endorsement

Table 2.2: Document quality and actions for endorsement of documents

Core document	RGO process
Research governance/ SSA checklist	Check for all listed documents and the correct version date
Cover letter for HREC application	Trial specific: contact details for the reviewing HREC, sponsor and other contacts
Medicines Australia form of indemnity (standard) or the MTAA form of indemnity (standard) for the site	Finalise signature of CEO or delegate*
CTN	Finalise institutional signatures*: • Section 2 is signed by the site PI • Section 3 is signed by the reviewing HREC representative • Section 4 is signed by the site CEO or delegate
Standard CTRA or CIRA, or other collaborative research agreement	Finalise signature of the CEO or delegate*
'Section 4: Use of ionising radiation' (for PI site) or Victorian Specific Module	If ionising radiation is involved, the HREC will review the ethical and scientific considerations, but the RGO should ensure that site requirements are met.
PICF (Master or Site Master)	Check that: • you have a track-changed and clean version of the PICF showing the changes in the Master with local site version details • the footer refers to both the Master and the local governance versions • both the HREC reference number and the local reference number are included • the Site Master PICF includes any HREC-approved special site clauses. A site may only amend the Master PICF site contact details (researcher and complaints) and the site letterhead. Site contact details are required as follows: • site PI name and position • site contact details (including emergency contact) • contact details with a 24-hour service • contact details for complaints. Check if any special clauses, such as a specific pregnancy clause, have been added.

* The document(s) that the CEO or delegate signs must be returned to the RGO.

RGO recommendation for SSA authorisation

Once the RGO is satisfied that the submission is complete, the recommendation can be made to the CEO or delegate, who has the authority to authorise the research at the site. On the basis of the RGO's recommendation the CEO or delegate will decide whether the project is authorised, authorised with conditions or not authorised.

The authority delegated to the RGO may vary among institutions. In one model, the RGO assesses the submission and makes a recommendation to the CEO or delegate for final authorisation. Following this, the research agreements can be actioned for institutional signature, the SSA authorisation letter released and the process completed.

The appropriate outcome must be recorded in AU RED and the clock stopped for the SSA process.

SSA notification to the PI/trial coordinator

The PI should be notified of the SSA authorisation decision within one working day of the decision date. The RGO may notify the PI/trial coordinator via email, then send a hard copy of the SSA authorisation letter and relevant documents (see Appendix 2.4 and 2.5).

The SSA authorisation letter should include:

- the name of the reviewing HREC and the date of HREC approval
- any site conditions for HREC approval
- the names of site-specific documents, referring to the Master PICF or Site Master PICF and the local SSA authorisation date.

A hard copy of the SSA authorisation letter sent to the PI/trial coordinator should be accompanied by:

- the original site CTN (with signatures), which should be returned to the sponsor, who will sign Section 1 and forward it to the TGA
- a signed CTRA in duplicate (one copy for the sponsor and one for the institution)
- a signed standard indemnity form in duplicate (one copy for the sponsor and one for the institution)
- any other site-specific documentation required.

RGO mandatory notification and record requirements

Following SSA authorisation and notification to the PI/trial coordinator, the RGO has mandatory notifications to complete.

1. VSM 'Section 4: Use of ionising radiation'

   Notify the Radiation Safety Section, Department of Health, Victoria of the approved and authorised research at <www.health.vic.gov.au/radiation/forms>.

2. Insurance certificate of currency

   VMIA policy for commercially sponsored clinical trials requires the RGO to submit, via email to <clinicaltrials@vmia.vic.gov.au>, copies of:

   - the RGO authorisation letter (providing details of the name and duration of the clinical trial)
   - a certificate of currency for the commercial sponsor's insurance policy, even if it has been previously submitted during a pre-approval process.

   A complete record of documents must be kept in the research governance office. The RGO must retain original copies of the fully executed CTRA and indemnity forms and a copy of the site CTN.

RGO management of amendments

During the research project the SSA remains a living document.

The original SSA is the initial expectation of how the project would impact the institution. Amendments approved by the HREC may affect the conditions for research described in the SSA. The RGO may authorise SSA amendments but, depending on the impact to the institution, may need to seek further advice. If the impact on the site is substantial, it is good practice for all parties to re-sign the SSA. Deciding when to re-sign is at the discretion of the institution.

Amendments

An amendment refers to a written change to an HREC-approved protocol for ongoing research. Irrespective of HREC approval, an amendment may have a minor or a substantial impact on research governance/SSA at the site. For example, the workload at the site should be monitored so that any sudden increase in the number of trials meets the requirement for an appropriate number of staff. Inappropriate workloads may occur in trials staffed with less experienced PIs/trial coordinators.

Following HREC approval of an amendment, the CPI notifies the PI. The PI must notify the RGO and provide them with the HREC amendment approval letter or correspondence, all relevant documents and any site-specific documents. All amended documents should be accompanied by a track-changed copy to compare the originally approved version with the amended version.

The RGO should acknowledge the CPI's notification by email, copying the PI and other relevant parties.

Types of amendments and timeliness

Low-impact amendments

Usually these will be administrative updates and may be authorised immediately by the RGO.

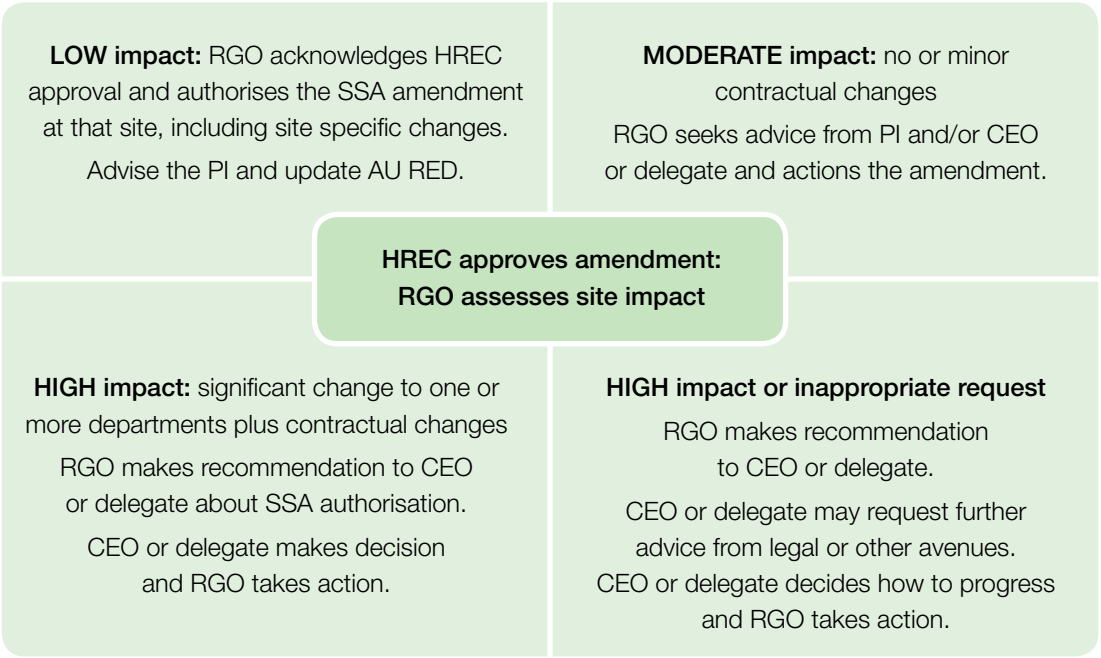
Moderate-impact amendments

These may include administrative or minor safety updates, budget updates, change of CPI or site PI, a change in the number of participants, change to the study end date or extension of the HREC approval date.

High-impact amendments

Changes that may impact on various departments of the institution should be assessed carefully as they may require sign-off from the departments involved. These could include changes to the study drug or device, the number of study procedures, or restarting the study after a safety issue.

Figure 2.1: Summary of amendment type and actions



Unless there is an urgent safety issue, an HREC approved amendment cannot be implemented at a site until the RGO has assessed and authorised the amendment. While the RGO manages the authorisation process, the delegated authority for authorisation may vary depending on the impact of the amendment on the institution.

An update to the SSA form is encouraged if the amendment:

- has an impact on the institution
- requires SSA authorisation and sign-off.

The timeline for processing an amendment is important, as a clinical trial may be temporarily suspended and medical treatment of participants could be disrupted.

Delay in SSA authorisation of an amendment may result in an impact on:

- participant recruitment
- participant treatment
- trial costs
- trial data management.

The RGO must notify the PI/trial coordinator of authorisation of an SSA amendment within one working day of the decision.

For instructions on the use of AU RED refer to the *Standard Operating Procedures (SOPs) for Research Governance Officers,* the *AU RED User Manual* (Infonetica Ltd) and the *AU RED Training Manual* (Coordinating Office for Clinical Trial Research).

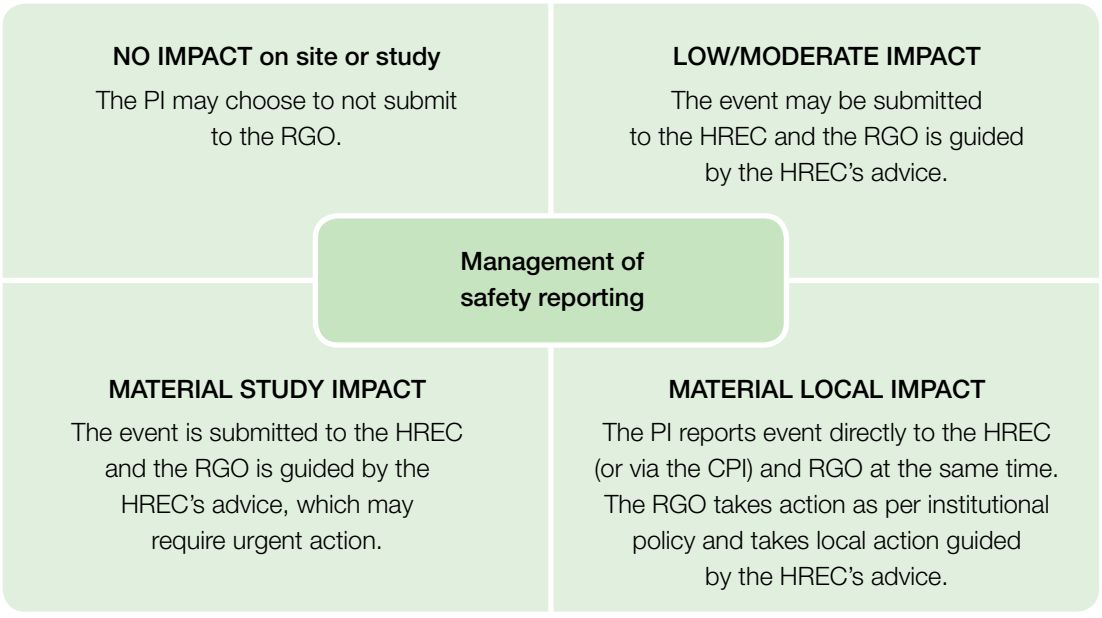
Safety reporting

The HREC that has approved the clinical trial is responsible for reviewing SAE/SUSAR/USADE reports from all study sites. Guidelines for Monitoring SAE/SUSAR and reporting them to the reviewing HREC are set out in the *NHMRC Australian Health Ethics Committee (AHEC) Position Statement: Monitoring and reporting of safety for clinical trials involving therapeutic products* (May 2009). Protocol deviations and violations must also be reported to the reviewing HREC.

Sites usually notify the CPI of an adverse event. The CPI may then decide to provide this documentation to the reviewing HREC. Following review of a SAE, SUSAR or USADE report, the reviewing HREC will communicate the outcome to the CPI, who then notifies the PI/trial coordinator, who in turn informs the RGO.

There may be changes requested by the reviewing HREC in addition to those indicated on the AE/SAE report, and these should be detailed in correspondence from the HREC to the CPI. The CPI must send copies of this correspondence to all participating sites.

Figure 2.2: Summary of safety reporting



RGO's institutional reporting and decision making

Material local impact for SAE/SUSAR/USADE

If a local SAE/SUSAR/USADE arises at the RGO's site and has a material impact on the study, the PI must report this event to the CPI and the RGO at the same time.

VMIA must be advised according to their *Insurance and Risk Management Guidelines for Clinical Trials.* If a high-risk SAE/SUSAR/USADE occurs at a site, the institution can suspend or close the study at that site. The site (institution) bears the legal liability for the participants.

The RGO should check whether an entry needs to be made in RiskMan.

If there is no material local impact from the SAE/SUSAR/USADE line listing reports, the CPI generally advises the reviewing HREC only. After reviewing a SAE/SUSAR/USADE line listing report, the HREC communicates the outcome to the CPI, and this should be copied to all participating site PIs / trial coordinators to forward to their RGO.

A standard RGO email to the PI to acknowledge these reports is acceptable.

The reviewing HREC is responsible for reviewing protocol deviations or violation reports. The RGO needs to be aware of any local impact, such as a recurrence of the same violation or deviation.

Safety reporting requiring SSA authorisation must be recorded in AU RED. For instructions on the use of AU RED refer to the *Standard Operating Procedures (SOPs) for Research Governance Officers,* the *AU RED User Manual* (Infonetica Ltd) and the *AU RED Training Manual* (Coordinating Office for Clinical Trial Research).

Changes in the study status must be recorded in AU RED by changing the 'Study State' on the Application – Post Approval tab (refer to the *AU RED Training Manual)*

Progress reports: interim and annual

Progress reports are required at least annually by the reviewing HREC for ongoing ethics approval. The due date for submission to the reviewing HREC is the anniversary date of the HREC approval. Note that the SSA authorisation anniversary date and the trial start date at the site will be different to the anniversary date of the HREC approval. The HREC date takes precedence for reporting purposes.

In terms of reporting to the RGO, a separate SSA annual or progress report is not recommended. A copy of the annual or progress report(s) submitted to the HREC is sufficient.

The site-specific reporting template *HREC progress report: site report* is available from the Clinical Trial Research website at <www.health.vic.gov.au/clinicaltrials/application-instructions>.

The PI must provide a copy of the site progress report to:

- the CPI, to collate with other site reports for the reviewing HREC
- the RGO.

The site PI must send the HREC's acknowledgement of a progress report to the RGO. This will be sufficient for the RGO to continue SSA authorisation at the site.

If the reviewing HREC has not received the progress report in a timely manner, the study may be suspended at a site until a report is provided.

Study closure

Final reporting

A particular site may close or the entire research project may be completed. In each case the site must submit a site final report to the reviewing HREC.

The site PI/trial coordinator should use the template *HREC final report* available at <www.health.vic.gov.au/clinicaltrials/application-instructions.htm>.

The reviewing HREC requires a final report when the research project is completed or when a site is closed. The report is reviewed by the reviewing HREC, and a copy is received by the RGO (via the PI) for notification of site closure.

Progress reports should be recorded in AU RED by the RGO. Refer to the *Standard Operating Procedures for Research Governance Officers.* These describe annual, progress and final reporting to the RGO. For instructions on the use of AU RED refer to the *AU RED User Manual* and the *AU RED Training Manual.*

Note that the reviewing HREC coordinator must change 'Study State' on the **Application – Post Approval** tab in AU RED to reflect the status of the trial (refer to the *AU RED Training Manual).*

The clinical trial close-out process ensures that the file is complete. The RGO must confirm that all required documents and reports are received and acknowledged and that the final report has been processed appropriately.

Clinical trial records are retained for a minimum of 15 years. However, the RGO should check with their institution regarding site policies on file retention, archiving and destruction.

After the clinical trial 'study close-out' has occurred, closure of the file on the research by the RGO is required.

Appendix 2.1: Information sheet for research governance officers

Instructions

This information sheet provided by the research governance officer (RGO) must be completed by the site's principal investigator / trial coordinator and returned to the RGO with a new application.

This is a living document and may be updated throughout the process.

Project title
SSA reference number
<Institution name> local reference number
HREC reference number
Reasons for wanting to undertake this research project at <institution name>

	Yes	N/A
General requirements		
Have you registered your project with the <institution name> research governance office?	☐	
Have you included the local reference number, a version number and date in the footer of all documents?	☐	
Have you read the *Standard operating procedures for streamlining ethical review of clinical trials,* available at <www.health.vic.gov.au/clinicaltrials/streamlining>?	☐	
Have you submitted an electronic copy of your application as per the standard operating procedures (SOPs) above?	☐	
Are all relevant documents attached separately and in order?	☐	
Have you provided one hard copy with original signatures?	☐	
Has your submission been proofread?	☐	☐
Have you read the following <institution name> policies relating to research? <Title of relevant policy 1> <Title of relevant policy 2>	 ☐ ☐	 ☐ ☐

	Yes	N/A
HREC application		
Reviewing HREC Approval Letter(s)		
Have you provided a copy of the reviewing HREC approval letter(s) relating to this application in Australia?	☐	
Have you uploaded these to your SSA form using the Online Forms website?	☐	
Documents approved by reviewing HREC		
Have you provided a copy of all documents approved by the reviewing HREC including any amendments?	☐	
Have you uploaded these to your SSA form using the Online Forms website?	☐	
Research governance/SSA application		
Site-specific assessment (SSA) form (mandatory)		
Have you completed the SSA form using the Online Forms website?	☐	
Have you checked that the HREC reference number is correct?	☐	
Did all investigators, department heads and supporting department heads sign the application after the submission code was generated? Have you sent a hard copy of the SSA form with original signatures? Have you submitted the SSA form and uploaded a scanned copy of signature pages on the Online Forms website?	☐	
Have you completed all sections relevant to you project?	☐	
Have you uploaded all supporting documentation to your SSA application on the Online Forms website?	☐	
Have you generated a submission code?	☐	
Victorian Specific Module		
If your project involves ionising radiation, have you completed Section 4 of the Victorian Specific Module (VSM) available from the Clinical Trial Research website?	☐	
Have you included the VSM checklist and only the relevant sections in your application?	☐	
Have you uploaded this to your SSA form using the Online Forms website?	☐	

	Yes	N/A
Participant information and consent form (PICF)		
Have you used the latest approved version of the Master PICF approved by the reviewing HREC?	☐	
Does page 1 clearly identify the institution either by letterhead or logo?	☐	
Does the footer contain a version number and date?	☐	
Are all pages (including attachments) numbered in the footer (page X of Y)?	☐	
Is the <institution name> contact person for complaints listed as <title and contact details>?	☐	
Have you performed a find and replace (Ctrl+F in Microsoft Word) on 'insert institution'?	☐	
Have you checked that formatting throughout document is consistent?	☐	
Have you uploaded this to your SSA form using the Online Forms website?	☐	
Local investigator curriculum vitae		
Have you used the local investigator curriculum vitae (CV) template or a similar format for each researcher that has not previously submitted an application? (Full CV not required.)	☐	☐
Clinical Trial Research Agreement (CTRA or CIRA)		
Which research agreement have you used?		
Clinical trial research agreement: Medicines Australia – Standard form	☐	☐
Clinical trial research agreement: Medicines Australia CTRA: Contract Research Organisation acting as a local sponsor	☐	☐
Clinical trial research agreement: Collaborative or Cooperative Research Group (CRG) studies – standard form	☐	☐
Clinical trial research agreement: Phase 4 clinical trial (medicines)	☐	☐
Victorian Managed Insurance Authority (VMIA) *Clinical trial research agreement: for an investigator initiated study*	☐	☐
Have you provided the correct details for <institution name> on Page 1?	☐	☐
Have you provided the required number of copies signed by the sponsor and principal investigator?	☐	☐
Have you placed signature tags where the <institution name> authorising officer is to sign?	☐	☐

	Yes	N/A
Notification of intent to supply unapproved therapeutic goods under the Clinical Trial Notification (CTN) scheme		
Have you provided the *Notification of intent to supply unapproved therapeutic goods under the Clinical Trial Notification (CTN) scheme* or Clinical Trial Exemption Scheme application (CTX), signed by the PI and the reviewing HREC?	☐	☐
Have you included a copy of page 5 for each participating <institution name> site?	☐	☐
Have you placed signature tags where the <institution name>authorising officer is to sign?	☐	☐
Medicines Australia Form of Indemnity for clinical trials		
Have you used the *Medicines Australia Form of Indemnity for clinical trials (Standard)* for medicines?	☐	☐
Have you used the Medical Technology Association of Australia Form of Indemnity for clinical investigation (Standard) for devices?	☐	☐
Have you included the required number of copies signed by the sponsor?	☐	☐
Have you placed signature tags where the <institution name> authorising officer is to sign?	☐	☐
Certificate of currency		
Is the certificate of currency compliant with the VMIA requirements?	☐	☐
SSA fee form		
Have you completed the SSA fee form?	☐	

List of attachments

Record all site documents to be submitted as part of your application – add the *National Ethics Application Form* (NEAF) and any documents not already listed.

Each of the site documents is to be uploaded to the SSA form via the Online Forms website (NEAF documents are automatically uploaded by the CPI via the Online Forms ethics application).

Document type	Version number	Version date
SSA form Submission code:		
PICF		
HREC approval letter		
Victorian Specific Module – Section 4		
SSA fee form		

Principal investigator	
Email address	
Telephone	
Signature	**Date**

Appendix 2.2: Site-specific checklist for research governance officers

Project Title	
HREC reference number	
Local reference number	
SSA reference number	

HREC approval		☐
Reviewing HREC	HREC approval date	
Appropriate for the institution to undertake (that is, the SSA is completed and signed)		☐
Staff		☐
Facilities		☐
Budget		☐
Heads of departments		☐
Heads of supporting departments		☐
Radiation notification approved or noted		☐
Clinical trial registration		☐
Register	Registration number	
Indemnity		
Standard		☐
ABN correct		☐
Institution details correct		☐
Signed by sponsor		☐
Insurance		
Compliant with Victorian Managed Insurance Authority (VMIA) requirements		☐

Clinical trial research agreements	
Standard Medicines Australia CTRA, MTAA CIRA or VMIA CTRA	☐
Signed by institution and sponsor	☐
Schedule 4 or 7 approved by Southern and Eastern Border States (SEBS) review panel	☐
If specific Schedule 4 or 7 approval required, note date	
Notification of intent to supply unapproved therapeutic goods under the Clinical Trial Notification (CTN) scheme	
Sponsor name (same as on the CTRA)	☐
Signed by principal investigator, HREC and institution	☐
VMIA notification sent	☐
Site-specific assessment authorisation letter sent	☐
Notes	

Name of manager or research governance officer	Date

Appendix 2.3: Site-specific assessment checklist

The research governance officer (RGO) should use this checklist to ensure consistent site-specific assessment (SSA) document management.

1	**Human Research Ethics Committee (HREC) approval and master documents**		
	A	HREC approval letter	Although the research governance process may commence prior to HREC approval, HREC approval is essential for SSA authorisation. Check that the HREC approval letter includes: • the date of approval • correct project details (title, number and so on) • a list of approved sites. Check that you have all the documents listed on the letter Ensure the HREC representative has signed the *Notification of intent to supply unapproved therapeutic goods under the Clinical Trial Notification (CTN) scheme* (CTN).
	B	Approved documents	Electronic format only (for example, in AU RED)
	C	Site-specific documents	Electronic only for all documents Additional hard copies of the agreement and contract only Original signatures on applications should be scanned and returned to researchers.
	D	Curriculum vitae (CV)	The CV provides a good check on whether the researchers have the skills to undertake the research. Ensure that you have a current document – an abbreviated version is acceptable. If you feel that the CVs are inadequate, discuss your concerns with the research team. Check that a person is nominated as a backup if the principal investigator (PI) goes on holiday.
2	**Site-specific documents**		
	A	Cover letter	The cover letter is required to request SSA authorisation and lists the attached documents and their identifiers (for example, version and date) for consideration.
	B	Site-specific requirements	For example: researchers who undertake research involving people with mental illness, or using mental health resources, must provide information and documentation to the RGO as per site policy.
	C	Research governance/SSA checklist	Ensure the front page is complete for all items.

D	Budget	All projects must demonstrate that institutional costings have been adequately accounted for and agreed to, and can be tracked. Check that the following budget information is included: • *Clinical trial research agreement* (CTRA), Schedule 2 – 'Payments' • SSA Form Section 10 – 'Study budget' • *National Ethics Application Form (NEAF),* Section 3 – 'Resources' Check that research governance fees are included for an initial and amended submission. The RGO may choose to reconcile the budget between the NEAF and SSA documentation.
E	Site specific assessment (SSA) form	Ensure the form is complete and sections are consistent. For example, Section 3 – 'Research personnel' and Section 9 – 'Departments and services' should be consistent with the 'Declarations' section and the rest of the submission. Signatures • the site Principal Investigator and all other site co-investigators • head of the department undertaking the research • head of all departments affected by the project • chief executive officer or delegate • RGO as recommending authorisation
F	Victorian Specific Module (VSM)	The VSM is mandatory for all Victorian projects involving: • drugs and therapeutic devices (VSM Section 1) • recruitment of adult research participants who may be incompetent to consent according to the *Guardianship and Administration Act 1986 (VIC)* (VSM Section 2) • collection, use and disclosure of personal and health information as per privacy legislation (VSM Section 3) • use of ionising radiation as per the *Code of Practice for the Exposure of Humans to Ionizing Radiation for Research Purposes* (2005) and Victoria's *Radiation Act 2005* (VSM Section 4) • the removal of tissue or blood from a living or deceased adult or child, or performance of a post mortem as per the *Human Tissue Act 1982* (VSM Section 5). **For trials, complete the cover pages and Section 1 at a minimum.**

	G	Ionising radiation i) Medical Physicist Letter of Risk Assessment ii) Department of Health notification	For ionising radiation procedures deemed to be standard clinical care, check that sections 4.1, 4.2 and 4.3 are completed and signed by the PI and the Radiation Safety Officer (RSO). Notify the Radiation Safety Section, Department of Health. **For ionising radiation procedures deemed to be in addition to standard clinical care, the following documentation is to be completed and submitted:** • Check VSM Section 4 for completeness, and ensure it has been signed by the PI, medical physicist and RSO • Medical Physicist Report including a radiation risk assessment Ensure that the project is submitted for approval to the Radiation Safety Section, Department of Health prior to project commencement.
	H	Site-specific study documents	Once the reviewing HREC has approved the master templates, site specific details may be added. Check for a track-changed and clean copy of the document. When reviewing site-specific PICF, check that: • the site-specific PICF matches the Master PICF • the footer refers to both the Master and the local governance version • appropriate letterhead is used. Check that the following details are included: • the HREC reference number and local reference number • the name and position of the site's principal investigator • site contact details (including emergency contact) • 24-hour contact details • site complaints contact details.
3	**Legal and regulatory requirements**		
	A	Indemnity form	Indemnity covers the potential liability of each party involved and the insurance requirements. Ensure that the Medicines Australia or MTAA form of indemnity is provided and populated with the correct information. Each site must have a separate indemnity form for conduct of the trial at the institution. It is preferable that the form(s) have been signed by the sponsor; however unsigned forms may be accepted.

B	Insurance certificate of currency	As outlined by Victorian Managed Insurance Authority (VMIA) guidelines at <www.vmia.vic.gov.au/Risk-Management/Clinical-trials/guidelines.aspx>, a commercial sponsor must provide evidence that it has appropriate and adequate insurance for the study in the form of a certificate of currency. *Pre-HREC approval* During the HREC approval process for new commercially sponsored clinical trials, VMIA clients should: • review the commercial sponsor's insurance certificate of currency provided by the sponsor against the VMIA Minimum Insurance Requirements <www.vmia.vic.gov.au/Risk-Management/Clinical-trials/guidelines.aspx>; • email the certificate of currency to VMIA at <clinicaltrials@vmia.vic.gov.au> if non-compliance or assistance is required. *Post-HREC approval* Upon SSA authorisation, email VMIA at <clinicaltrials@vmia.vic.gov.au> with copies of the: • SSA approval letter (providing details of the name and the duration of the clinical trial) • the commercial sponsor's certificate of currency for the relevant trial, even if it has been previously submitted during the pre-approval process.
C	CTN	Refer to <www.tga.gov.au/industry/clinical-trials-forms-ctn.htm>. Section 1 is completed by the trial sponsor, who takes responsibility for the overall conduct of the research project. Section 2 is completed by the site PI Section 3 is completed by the HREC responsible for review, approval and monitoring Section 4 is completed by the authority approving the conduct of the trial. More than one location can be listed on the CTN, if all other details are the same.

D	Research agreements (CTRA or CIRA)	Research that involves multiple parties requires an agreement, unless written authorisation to waive this requirement is obtained from the responsible executive. Standard Medicines Australia CTRA forms are available at <medicinesaustralia.com.au/issues-information/clinical-trials/clinical-trials-research-agreements>. Use the current version of the CTRA on the Medicines Australia website. There are four types of CTRA plus the *Clinical investigation research agreement* (CIRA) for device studies. It is not acceptable to make changes to clauses in the body of a research agreement. Changes must be referenced in the special conditions in Schedule 7 of the standard CTRA and *Clinical trial research agreement: Contract Research Organisation* or Schedule 4 of the *Clinical trial research agreement: Collaborative Research Group (CRG) studies* and the *Clinical trial research agreement: Phase 4 clinical trial (medicines).* Check the Schedule 7 or Schedule 4 against standard and agreed schedule clauses for inclusion in a CTRA or CIRA for commercially sponsored clinical trials released by the Southern and Eastern Border States (SEBS) review panel and available from the Coordinating Office for Clinical Trial Research. If the Schedule 7 or Schedule 4 is not the agreed version, email the Coordinating Office for Clinical Trial Research at <multisite.ethics@health.vic.gov.au>. SSA applications using a non-standard clinical trial agreement will most likely require local legal review. For non-clinical trial research agreements discuss details with the site's research office.

4	**SSA authorisation**		
	A	SSA authorisation letter	The SSA authorisation letter is drafted from the AU RED template as part of completing SSA authorisation. Open the SSA authorisation letter in AU RED and cut and paste details as required. The letter must include: • the name of the site PI • the site name to which the authorisation applies • a list of the HREC approved relevant documents with versions and dates • a list of site-specific documents with versions and dates. There is no need to list the CTRA or the application forms. The letter is signed by the institution's RGO or delegate.
	B	Signatures	Ensure all required signatures are present.
5	**RGO fees**		
	A	SSA assessment	SSA fees are accrued for assessment of commercially sponsored clinical trials, comprising both the initial submission and amendments to the protocol (GST included).
	B	Invoices	Ensure the name of the person or organisation receiving the invoice is found on the research governance/SSA cover letter
6	**Protocol amendments**		
	A	General	Amendments may not be acted upon without approval from the reviewing HREC and the RGO (unless expedited for an urgent safety issue). The PI/trial coordinator should upload post-approval documents to the Online Forms website so the RGO can access these new submission documents electronically. After HREC approval the PI/trial coordinator must notify the RGO and provide the HREC letter of approval and all associated documents, as well as any site-specific requirements relevant to the Master PICF, with changes indicated. The RGO or delegate must respond to the PI and relevant parties.
	B	Major amendments	Changes that may impact on the institution should be assessed carefully as they may require sign-off from the departments involved. Major amendments could involve: • the type of study medications • the number of tests required • the number of participants • the study end dates • extensions to the study. The SSA form should be updated if there is an impact on the institution and SSA authorisation is required.
	C	Minor amendments	Changes sent as administrative updates may be authorised immediately.

7	Safety reporting and adverse event reporting	
A	General	The HREC that has approved the research project is responsible for review of SAE/SUSAR/USADE reports arising from affected sites, as required. The details in regard to SAE/SUSAR reporting are set out in the *NHMRC Australian Health Ethics Committee (AHEC) Position Statement: Monitoring and reporting of safety for clinical trials involving therapeutic products* (2009). The HREC providing approval is also responsible for reviewing USADE reports for events involving devices. In general, sites advise the coordinating principal investigator (CPI) of an adverse event. The CPI then advises the HREC. Following review of a SAE/SUSAR/USADE report, the reviewing HREC communicates the outcome to the CPI, who advises the site PI, who then advises the RGO. If the reviewing HREC has requested any changes in addition to those indicated on the SAE/SUSAR/USADE report, this must be detailed in the letter to the CPI. Note that changes in the study status must be recorded in AU RED by changing the 'Study State' on the SSA Application – Post Approval tab (refer to *AU RED Training Manual).*
B	Local SAE or SUSAR or USADE	If a SAE/SUSAR/USADE occurs at a site and it may have a material impact on the site or on ethics approval, or requires change to the protocol, the PI reports to the CPI and the RGO at the same time. VMIA must be advised by the RGO as detailed in their *Insurance and Risk Management Guidelines for Clinical Trials.* If a high-risk SAE/SUSAR/USADE occurs at a site, the institution at which the event has occurred has the right to suspend or close the study at that site. The institution has legal liability for the participants. Check whether a RiskMan entry needs to be made.
C	SAE/SUSAR/ USADE reporting	In general, the CPI advises the HREC of an event line listing. Following review of a SAE/SUSAR/USADE report, the reviewing HREC communicates the outcome to the CPI, who advises the site PI, who then advises the RGO. A standard RGO email response to the PI is an acceptable acknowledgment.
D	Protocol deviation/ violation	Although the HREC reviews a protocol deviation or violation for ethical impact, the RGO needs to be aware of a local impact, such as a recurrence of the same deviation or violation. Check for less experienced coordinators, or if a site has a sudden increase in the number of trials without more staff.

8	**Progress reports**		
	A	General	Annual progress reports must be provided in a timely manner. The site PI is responsible for providing a copy of the *HREC progress report: site report* to the RGO for monitoring purposes at their site. The report is available from <www.health.vic.gov.au/clinicaltrials>. The PI must also provide a copy of this report to the CPI to collate with other site reports and submit to the reviewing HREC. The reviewing HREC coordinator sends an acknowledgement letter to the CPI, who then forwards it to the PI. The PI/trial coordinator sends a copy to the RGO.
	B	Progress	Sites use the *HREC progress report: site report* from <www.health.vic.gov.au/clinicaltrials>. The individual *HREC progress report: site report* submitted by the PI is also copied to the RGO by the PI/trial coordinator. Site progress reports may be directly acknowledged by the RGO. **If the HREC has not received a progress report they may suspend the study at that site.**
9	**Final reports**		
	A	General	An HREC final report is required for research project completion or site closure, using the *HREC final report for research project completion or site closure.* This is reviewed by the reviewing HREC and then sent by the PI/trial coordinator, together with the HREC letter, to the RGO for acknowledgment. Note that changes in the study status must be recorded in AU RED by changing the 'Study State' on the Application – Post Approval tab (refer to A*U RED Training Manual).*
10	**Close-out**		
	A	Record storage	After the clinical study 'close-out', the RGO closes the SSA file for the project. Proper close-out ensures that the file is complete. Ensure that all SSA documents are complete and that the final report has been made. Clinical trial records are retained for a minimum of 15 years. Check with the institution with regard to site policy on file destruction.

11	**Quality assurance and audit**		
	A	General	The purpose of a research auditing program is to review how research is conducted and to detect, correct and prevent potential and existing shortcomings. In addition to regular progress reports from the researcher, audits may include: • a full audit or site visit by the research governance office • a desktop self-audit • themed audits. Researchers should be encouraged to complete a *Site audit report for research* at a scheduled time advised by the RGO (for example, three months after SSA authorisation). The template is available at <www.health.vic.gov.au/clinicaltrials/application-instructions>.
12	**Misconduct reports**		
	A	Complaints	A misconduct policy should be in place at each institution. All complaints should be written using the *Complaints report to HREC: site report* template available at <www.health.vic.gov.au/clinicaltrials/application-instructions>.

Appendix 2.4: Sample template 1: Site specific assessment authorisation letter

<Date>

<PI name>
<PI title>
<PI address>

Dear <PI name>,

<Project title>

HREC reference number: <HREC reference number>
SSA reference number: <SSA reference number>
Protocol number: <Protocol number>
Protocol version: <Protocol version>

Thank you for submitting an *SSA form* for authorisation of the above project at <institution name>. I can confirm that the valid submission was received on <date valid submission received>.

Ethics approval for this project was granted on <date of HREC approval> by <name of reviewing HREC> under streamlined ethical review. A list of all the approved documents is contained in <name of reviewing HREC> letter of approval dated <date of HREC approval letter>.

I am pleased to inform you that authorisation has been granted for this project to be conducted at <institution name>.

The documents reviewed and authorised that are relevant to this authorisation are listed below.

Document	Version date
SSA application	<submitted date>
Participant information and consent form (PICF) for <institution name> (based on Master PICF Version <Date of Master PICF>)	<version date>
Advertisement or any other site-specific documents	<version date>

The following conditions apply to the research project at this site. These conditions are additional to those imposed by the Human Research Ethics Committee (HREC) that granted ethics approval.

1. The principal investigator will immediately report anything to the Research Governance Officer that might warrant review of authorisation of the project in the specified format, including:
   a. any serious or unexpected adverse event at this site
   b. unforeseen events that might affect continued ethics acceptability or governance of the project.
2. The research governance officer will be notified if the project is discontinued at this site before the expected date of completion, and why.
3. The principal investigator will provide progress reports to the Research Governance Officer, in the specified format, and provide a final report at the completion of the project. Note that annual reports are due on the anniversary of HREC approval date.

If any matters arise concerning the conduct of the research at your site, please ensure you contact the Research Governance Officer:

<RGO name>
<RGO title>
Telephone <telephone number>
Email <email address>

Guidelines are available on the <institution name> website at <website address>.

For further information regarding the responsibilities of the principal investigator, please refer to the *Standard operating procedures for streamlining ethical review of clinical trials.*

Yours sincerely,

<Name>
<Title>

Appendix 2.5: Sample template 2: Site specific assessment authorisation letter

<Institution name> SSA authorisation to conduct a research project

Project title
SSA reference number
<Institution name> local reference number
Principal investigator
HREC reference number
HREC approval date
HREC approval end date (if applicable)

I am pleased to advise that the above project has received ethics approval by <reviewing HREC> on <HREC approval date> and satisfies <institution name> research governance /SSA requirements, and may now be conducted at <institution name>. Conduct of the project is subject to compliance with the conditions set out below and any additional conditions specified by <reviewing HREC> as the reviewing HREC.

Documents specific to this authorisation

Document type/title	**Version date of master document** (if applicable)	**Version date of research governance: SSA version** (if applicable)

Conditions of authorisation

In order to comply with the *National Statement on Ethical Conduct in Human Research* (NHMRC, 2007), *Australian Code for the Responsible Conduct of Research, Guidelines for Good Clinical Research Practice (CPMP/ICH/15/95)* and local research policies and guidelines, you are required to notify the <institution name> Research Governance Office of:

- the actual start date of the project at <institution name>
- any amendments to the project after these have been approved by the reviewing HREC
- any adverse events involving patients of <institution name>, in accordance with the <institution name> policy and guidelines for safety reporting
- any unexpected developments in the project with ethical implications
- your inability to continue as principal investigator and any other change in research personnel involved in the project at <institution name>
- any proposed extension to the duration of the project, past the HREC approval date stated above
- any decision taken to end the project prior to the expected date of completion or to withdraw <institution name> as a site participating in the project.

You are also required to submit to the Research Governance Office:

- An annual progress report for the duration of the project on the anniversary of the HREC approval;
- a comprehensive final report upon completion of the project.

Additional conditions

Submit a copy of the letter from the person responsible for radiation safety at <institution name>. This condition applies only if the project involves exposure to ionising radiation and the <Institution Name> Radiation Safety Officer has reviewed and advised on the project. This letter will form part of the notification of the project to the Radiation Safety Section, Department of Health, Victoria.

Note: The project cannot commence at <institution name> until you have confirmed that the project has been notified or approved by the Radiation Safety Section, Department of Health, Victoria.

The <institution name> Research Governance Office may conduct an audit of the project at any time.

Please refer to the <institution name> Research Governance Office website <website address> for access to forms, policies and guidelines and other information and news concerning research at <institution name>.

Yours sincerely,

<Name>
<Title>

Telephone: <telephone number>
Email: <email address>

Section 3: Industry sponsor and contract research organisation

Getting started

Sponsor/CRO responsibilities – site selection

Early action from the sponsor is crucial in successfully gaining ethics, research governance and regulatory approval in an efficient and timely manner. The sponsor should obtain all available supporting project documentation from the global project team as early as possible. Ideally, these documents should be provided to the site at the time of site selection and feasibility.

Supporting documents will include but will not be limited to:

- protocol
- investigator brochure
- Master PICF
- relevant background information.

During site selection the following should be considered.

- The requirements of the RGO at each individual site should be discussed.
- An evaluation should be conducted to determine which site will be a CPI (lead) site or an accepting site.
- Draft budgets should be made known to all sites. This would include details of allowances for the CPI coordinating the trial. Negotiations about budget and any other issues should be addressed.
- Sites should be made aware of the importance of their institutional websites being up to date with current documents and requirements.
- A clear communication plan should be established to determine the flow of correspondence between the CPI and participating sites, and whether the sponsor/CRO will have partial responsibility for document flow.
- Ensure the sites understand the relevant RGO approval process.
- Ensure staff training requirements are met and that staff have appropriate experience with clinical trial research.
- Ensure the availability of RGO staff, and back-up staff and arrangements.
- Timeliness for the process and the sponsor/CRO's expectations for submission to the research governance office should be clear to all parties.

A commitment should be sought from the site staff and RGO to conduct research governance in parallel with the ethics review process.

Key documents for reference are the Research Governance Checklist and Research Governance/ SSA Cover Letter at <www.health.vic.gov.au/clinicaltrials/site-specific>.

Once sites are selected the sponsor should clarify the communication pathway for trial documents both for ethics and research governance/SSA, including the CPI providing a response to the HREC and sending a copy of that response to the sponsor/CRO.

Documents and site contracts

Following confirmation of site involvement, the trial monitor should obtain appropriate details from each site so that all documents submitted to the RGO are consistent. Examples of documents requiring correct entity details:

- the institution's business name and ABN. The ABN lookup at <www.abr.business.gov.au> is the public view of the Australian Business Register
- a contact for legal notices
- finance contact details
- CTN
- CTRA or CIRA
- insurance certificate of currency
- indemnity forms (standard and HREC review only).

Where a sponsor has a CRO performing the budgetary negotiations the sponsor should ensure appropriate support and oversight is provided for the CRO. The sponsor's research departments should work to ensure consistency and fairness across contracts.

The site budget is generally reviewed by multiple parties, including the institution's departmental representatives. This is often the cause for delay in research governance/SSA submission and authorisation. Therefore the site budget and draft CTRA should be provided by the sponsor/CRO at the earliest possible opportunity.

The clinical trial site budget procedure costs should be aligned with local procedural costs with consideration of the principles of fair market value. The proposed study budget should not simply be costs converted from a global schedule. The local budget and fees must be fair and reasonable according to acceptable local expectations.

Australian institutions accept the Medicines Australia agreed standard CTRA templates. Since the 16 November 2012 release, there are four CTRAs for clinical trials and these are updated from time to time. They are as follows:

- *Clinical trial research agreement: Medicines Australia – Standard form*
- *Clinical trial research agreement: Medicines Australia CTRA: Contract Research Organisation acting as the local sponsor*
- *Clinical trial research agreement: Collaborative or Cooperative Research Group (CRG) studies – standard form*
- *Clinical trial research agreement: Phase 4 clinical trial (medicines).*

Guidance on the preparation of CTRAs is available at <medicinesaustralia.com.au/issues-information/clinical-trials/indemity-and-compensation-guidelines>.

The Medical Technology Association of Australia (MTAA) is the national association representing companies in the medical technology industry. An important distinction between investigation agreements developed for the pharmaceutical and the medical technology industries is the use of the international standard ISO 14155:2003 Parts 1 and 2 for the study of medical technology. The MTAA agreement references this standard and is available at <www.mtaa.org.au/policy-initiatives/clinical-investigations>.

It is important that the sponsor/CRO uses the standard CTRAs (medicines) and CIRA (devices) to eliminate the need for legal review at each site and to minimise legal costs to industry companies.

A schedule for 'Special conditions' in each of the agreements allows limited customisation for company, study-specific or institutional purposes and standard schedules can be agreed through the Southern Eastern Border States (SEBS) review panel. For details of this process see the Medicines Australia website at <medicinesaustralia.com.au/issues-information/clinical-trials/clinical-trials-research-agreements>. This is a collaborative initiative among jurisdictions and each provides a list of agreed schedules to their respective RGOs as a reference for review of CTRAs. The sponsor/CRO receives a notification from each individual SEBS jurisdictional member with a copy of the standard schedule.

To save time and cost in the site assessment process, it is important for the sponsor/CRO to familiarise industry staff with the guidance on seeking special conditions for CTRA/CIRA standard schedules.

A research agreement has been developed by VMIA for use in Victoria for non-commercial, investigator-initiated research. The Investigator Initiated Agreement is available at <www.vmia.vic.gov.au/Risk-Management/Clinical-trials/clinical-trial-research-agreements.aspx>.

Clinical trial notification (CTN)

The sponsor/CRO should prepare the master CTN. This can begin early in the start-up process and should not be rate limiting. In most circumstances a master CTN can be prepared in advance of the HREC submission. The site-specific versions of the CTN can then be prepared from the master version.

The CPI sends the CTN to the reviewing HREC for approval and signature. All CTNs are sent from the reviewing HREC to the CPI who then distributes the CTN to each individual site PI for their signature.

The CTN is then forwarded by the PI/trial coordinator to the RGO for signature by the institution's authority.

Finally, the CTN is returned by the site PI/trial coordinator to the Australian sponsor/CRO, who provides the final signature on the CTN and submits it to the TGA. It takes five to ten working days to receive the TGA's acknowledgement of receipt of the CTN. This is usually the last document needed for a study to commence at a site and before investigational products can be shipped to the site, so while waiting for the TGA acknowledgement, it is the ideal time to finalise other site documents for investigational product release.

Indemnity and insurance

Medicines Australia represents the discovery-driven pharmaceutical industry in Australia and has negotiated industry-accepted standard forms of indemnity. These are considered mandatory formats in Australia and there are two forms of indemnity from Medicines Australia in use:

- the standard form of indemnity is for institutions and staff conducting the clinical trial and HREC review
- the HREC review only form of indemnity is for an HREC that is providing ethical and scientific review for a clinical trial only. In accordance with Medicines Australia: "For use where the Indemnified Party is providing ethical review for a multicentre clinical Study where the ethical review will be adopted by hospitals, institutions or sites that are independent from the Indemnified Party, **OR** as a Reviewing HREC for a single centre study at a hospital or institution that is independent from the Indemnified Party."

For devices, the forms of indemnity and compensation guidelines are as follows and available at <www.mtaa.org.au/policy-initiatives/clinical-investigations>:

- *Medical Technology Association of Australia form of indemnity for clinical investigations: Standard*
- *Medical Technology Association of Australia form of indemnity for clinical investigations: HREC review only*
- *Guidelines for compensation for industry resulting from participation in a company sponsored clinical investigation.*

Ensure that names, legal details, and the correct version number and date are the same on all relevant documents. Documentation must be accurate and correct before it is submitted to the RGO. Otherwise delays can result.

Clinical trials must have a certificate of currency for public and products liability insurance from the commercial sponsor.

The certificate of currency must:

- specifically name the Australian corporate entity acting as commercial sponsor, or if using the global entity name, then the global entity must provide a letter to say the local entity is wholly owned and a named insured under the relevant insurance policy
- cover the conduct of the relevant clinical trial in Australia
- be current throughout the entire period in which the clinical trial is conducted
- not have a defined statute of limitations
- have acceptable deductibles and level of indemnity – see information in the VMIA certificate of currency checklist at <www.vmia.vic.gov.au/Risk-Management/Clinical-trials/guidelines.aspx>
- have a limit of liability per claim and in the annual aggregate of AUD$20 million for New South Wales and AUD$10 million for other jurisdictions in Australia
- ensure the excess deductible is no greater than AUD$25,000 for each and every claim or series of claims arising out of one originating cause.

In Victoria, statewide insurance is provided through VMIA, and details of requirements for clinical trials can be found on their website at <www.vmia.vic.gov.au>.

Specific information relating to clinical trials is contained in VMIA's *Clinical Trials Insurance and Risk Management Guidelines* (September 2012) at <www.vmia.vic.gov.au/Risk-Management/Clinical-trials/guidelines.aspx>.

Note: VMIA may exercise its discretion regarding insurance arrangements, and this consideration may include such matters as:

- the level of clinical risk associated with the trial
- the financial strength of the insurer
- the financial strength of the commercial clinical trial sponsor.

In the event that it is not possible to obtain a certificate of currency that specifically names an insured that is an Australian corporate entity acting as commercial sponsor, it will be sufficient to sight a certificate naming the Australian entity's overseas parent company and its subsidiaries worldwide. This applies if a parent company provides written confirmation of the Australian corporate entity acting as commercial sponsor and is a wholly owned, operated or controlled subsidiary company of the parent, and that such a subsidiary is also a named insured under the relevant insurance policy for the purpose of the conduct of the trial in Australia.

In some Australian jurisdictions global sponsors might be asked to produce insurance to cover any risks which may arise with trial monitors entering a public hospital.

Use of ionising radiation

Victorian requirements must be followed for studies that use ionising radiation. An explanation is available on the Clinical Trial Research website at <www.health.vic.gov.au/clinicaltrials/application-instructions>.

The VSM and guidelines are available on the Clinical Trial Research website with essential information regarding use of ionising radiation.

Equipment for device studies

- All unapproved devices need to be listed on the CTN whether they are owned by the sponsor or the device is under investigation.
- Where devices are approved for use in Australia or internationally, an Instruction for Use (IFU) document could be submitted as a replacement for the investigator brochure.
- Studies in which equipment is loaned or stored within a hospital for use for the duration of the study per protocol may require completion of a loan of equipment application form. The equipment may also require to be assessed by Biomedical Engineering for quality assurance prior to installation at the hospital.
- Where pharmaceutical studies adhere to ICH GCP, device trials may be conducted in accordance with ISO-14155.
- During the site initiation visit, training and information is provided regarding protocols, devices and GCP. The site visit should also establish that investigators have sufficient experience with the device or implant and are confident with their use.

- Ensure sufficient time for shipment of unapproved devices, as customs can take some time for processing the documentation and releasing the material.
- All unapproved devices must be labelled appropriately, with wording like “Investigational Use Only”.
- The site must have appropriate storage conditions for investigational devices.
- Funding for the device (if applicable) needs to be agreed by all parties during the study set-up.

Communication plan

A clear communication and documentation plan is critical for efficient management of research governance/SSA requirements and for the ongoing conduct of the trial. It should include information on timelines and personnel responsible for the documentation.

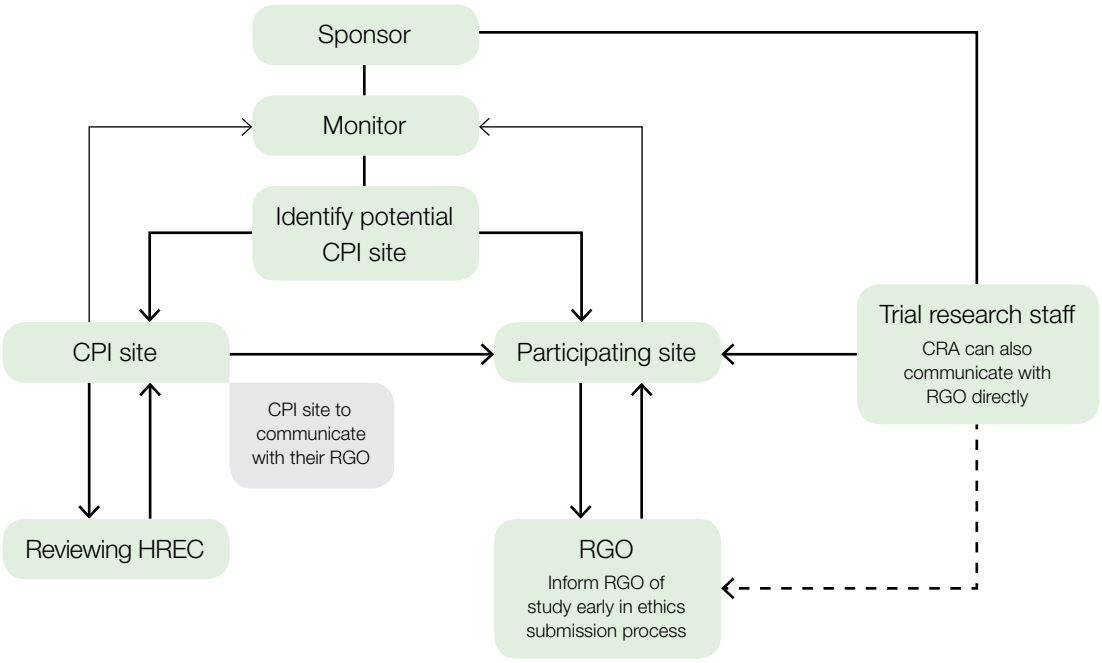
The sponsor/CRO should establish a local liaison, ideally the monitor, to communicate with the CPI/trial coordinator and the participating sites. It is imperative that every project has one nominated site and sponsor/CRO contact person who will ensure all trial content is maintained, communicated and tracked. It would be most appropriate to assign a trial monitor and a trial coordinator from the coordinating site as the main contact persons.

A clear communication strategy, document flow and communication plan should be put in place once the CPI, trial monitor and participating site PI/trial coordinator are alerted of participation in the study. This plan should assign responsibilities for:

- the HREC submission, study contacts and distribution lists
- SAE reporting
- protocol deviation reporting
- safety reports
- annual reports and final clinical study reports.

Final sign-off can sometimes be delayed and it is imperative that backup arrangements are in place so that SSA submissions are actioned. These arrangements should be documented in the communication plan, discussed at the initial site meeting and noted in site governance/SSA checklists.

Figure 3.1: Communication plan – pre-HREC approval



- The monitor working with the CPI (lead site) is responsible for discussing the communication plan with that site.
- The CPI's site should communicate the plan to participating sites.

Research governance/SSA submission

Communication

It is imperative that the sponsor/CRO is copied into all communications to ensure participating sites and the CPI are notified. Clear communication is particularly important if prompt follow-up is required from participating sites (for example, a request for further information or HREC approval notification to the CPI).

The sponsor/CRO should use a spreadsheet for tracking the location of documents (Appendix 3.1).

It is the responsibility of the trial monitor to:

- provide the contact details of all monitors involved in the multi-centre submission process
- provide the CPI with contact information for participating sites (PI details and their nominated site contact person)
- provide all participating sites with CPI site contact information (CPI details and their nominated site contact person)
- notify the CPI of changes in participating site contacts
- notify the CPI and participating sites of any changes to sponsor/CRO staff
- keep distribution lists up to date to ensure that staff are included in information flow
- maintain a master contact list for sites
- confirm that the ethics submission meets all state-specific and legislative requirements
- prepare a preliminary document package for parallel submission of research governance/SSA documents to the RGO of participating sites. Initial documents include but are not limited to indemnity, insurance certificate of currency, protocol, investigator brochure and draft budget.

Although most information is provided to the RGO via the site personnel, the monitor should obtain contact details for relevant RGO personnel at each participating institution.

Each site is responsible for informing the sponsor/CRO of any site changes. A master contact list will be maintained by the sponsor/CRO and provided to the monitor on a regular basis or as required.

State-specific requirements

The CPI should ensure that:

- all state-specific documents are included in the HREC submission (for example, VSM, NSW privacy module)
- a review of all state requirements is conducted and discussed with each participating site.

Parallel submission to the HREC and RGO

The sponsor/CRO should ensure that both HREC and research governance/SSA site-specific documents are prepared and ready for submission. Documents should be submitted to the RGO in parallel with the expected timing of the HREC review process.

The recommended practice is to submit according to the research governance/SSA early action checklist (Part A). As many of the listed documents as possible should be submitted either before or at the same time as the submission to the reviewing HREC. Although some documents will be provided to the RGO at a later date (such as a final site-specific PICF, HREC-approved documents and so on) these should not hold up the initial SSA submission and assessment process.

The sponsor/CRO should:

- provide documents in electronic format to support site administration and allow trial coordinators to make electronic submissions to the reviewing HREC and RGO
- review institutional websites prior to the SSA submission to ensure that any site-specific requirements are addressed
- prepare a set of pre-HREC approval documents to be submitted to the RGO as early as possible.

Although there will be follow-up documents to be provided to the RGO upon HREC approval this should not hold up the initial SSA submission and assessment process. These follow-up documents can be provided to the RGO as a final step prior to HREC approval or immediately after notification of approval.

The trial monitor should confirm the documents and versions listed are correct before submission to the RGO. The trial monitor should be informed if there is any deviation from the checklist.

The Clinical Trial Research website provides research governance/SSA requirements, including the research governance/SSA checklist, at <www.health.vic.gov.au/clinicaltrials/site-specific>.

While the PI/trial coordinator will complete the SSA form on Online Forms, it is recommended that the sponsor/CRO provides generic text in electronic format. This will assist completion of the SSA form and avoid additional work where multiple sites are involved. During the submission process, the site may request additional information from the sponsor. It is recommended that responses are provided within five working days.

Trial master files

Trial master files should be part of the initial communication plan and discussions. The CPI and participating sites should discuss the following with the trial monitor:

- targeted timelines for each of the listed documents
- who is responsible for the provision and review of the documents (see the CPI responsibilities guide at <www.health.vic.gov.au/clinicaltrials/application-instructions.htm>)
- nomination of back-up individuals within each organisation in the event of absent staff.

The sponsor/CRO and their site personnel may use a document location sheet for CPI and participating sites. A template is available at Appendix 3.2.

It may be useful to use a spreadsheet to track what communications and documents have been received to and from the CPI and participating sites (Appendix 3.2).

RGO acknowledgement of a SSA submission

The RGO should acknowledge receipt of the checklist Part A–Early Action items within three working days (see the *Standard operating procedures for research governance officers* at <www.health.vic.gov.au/clinicaltrials/streamlining>. This will allow the PI/trial coordinator to promptly address any documentation that is missing or incomplete.

Recommended practice is for the PI/trial coordinator to submit the SSA form and supporting documents, then have a discussion with the RGO. If a response is required from the sponsor/CRO or site investigator team, a turnaround of five working days should be expected.

If no feedback is provided by the site within four weeks, the sponsor/CRO could consider making direct contact with the RGO.

Post-HREC approval: SSA authorisation

SSA authorisation notification

A standard SSA authorisation letter should be provided by the RGO, listing all authorised documents with the correct version numbers.

The sponsor/CRO may ask the RGO to provide a draft copy of the SSA authorisation letter to verify that all documentation is listed and complete (that is, all documents that were part of the assessment are accounted for). This process may save time at the final signature step and is a recommended quality check.

The SSA authorisation letter must be sent to the PI/trial coordinator and in turn sent to the sponsor/CRO.

The timeline for SSA authorisation will be dependent on relevant site documents being submitted to the RGO and assessed prior to receipt of HREC approval. The RGO should notify the PI of SSA authorisation within one day of the decision (see *Standard operating procedures for research governance officers* at <www.health.vic.gov.au/clinicaltrials/streamlining>).

Post-SSA authorisation reporting

A communication plan should identify items that must be reported throughout the course of the research, with agreed time lines for communication and document provision among the parties.

The communication plan will assist sites and trial monitors to effectively manage the ongoing activities of the research and ensure that appropriate document flow occurs (Table 3.1). This may involve telephone, emails, remote and onsite monitoring activities, newsletters, follow-up letters and project-specific web portals.

The sponsor/CRO may provide some post-SSA authorisation documentation to the CPI and participating sites through an online website or portal. The information provided in this booklet aims to address the workflow rather than the distribution system for these documents.

A comprehensive suite of standard reporting forms are available at <www.health.vic.gov.au/clinicaltrials/application-instructions>.

Table 3.1: Project-level document flow for amendments

1. Protocol deviations
    - The CPI should check with the reviewing HREC on the frequency of notifications for protocol deviations.
    - The CPI should communicate this information by email to participating sites and the monitor.
    - The monitor should be copied into all correspondence between the CPI and participating site(s).
    - Any correspondence received from the reviewing HREC regarding protocol deviations should be forwarded by the CPI to the monitor within two working days.
2. Protocol amendments and updated PICFs
    - The monitor will provide the amendments to the CPI and participating site(s) for information and record keeping.

- The CPI should work with the monitor to update a multi-centre Master PICF. Policy-specific wording (for example, wording about contraceptives) may be included in either the Master PICF or in a Site Master PICF if required.
- The CPI will be responsible for submitting amendments to the reviewing HREC and must provide copies of the submission documents and HREC approval notification to all participating sites and the monitor.
- Following HREC approval of a multi-centre Master PICF, the CPI/trial coordinator is responsible for providing the updated PICF and associated approval letters to the monitor.
- The monitor should confirm that the amended PICF is correct. The CPI/trial coordinator is responsible for providing these documents to all PI/trial coordinators at participating sites (as listed on the distribution list provided by the sponsor/CRO) as soon as possible.
- Participating sites must send a copy of the site-specific PICF and SSA authorisation letter to the sponsor/CRO.

3. Investigational new drugs safety reports and AE line listings

   - The sponsor/CRO will provide these to the CPI and participating sites for review, information and record keeping. These documents may be provided in a number of ways, including hard copy, email or online.
   - The CPI is responsible for submitting these documents to the reviewing HREC within the timeframe required by the HREC.
   - The CPI will be responsible for providing documentation relating to any submissions and acknowledgements from the HREC to participating sites and the monitor.
   - Participating sites are responsible for informing their RGO according to reporting timelines and providing supporting correspondence to the trial monitor in a timely manner.

4. Safety and pregnancy reporting

   - Sites are expected to:
     - Report SAEs occurring at a site to the sponsor as required, usually within 24 hours
     - Send a copy of the SAE/pregnancy report to the relevant RGO. Send a copy to the reviewing HREC (depending on HREC requirements), and copy the monitor.
   - The sponsor/CRO and monitor should be informed by the CPI/trial coordinator on:
     - HREC reporting requirements for SAE and pregnancy events
     - the reviewing HREC's response or acknowledgement to the CPI.

5. Annual study reports

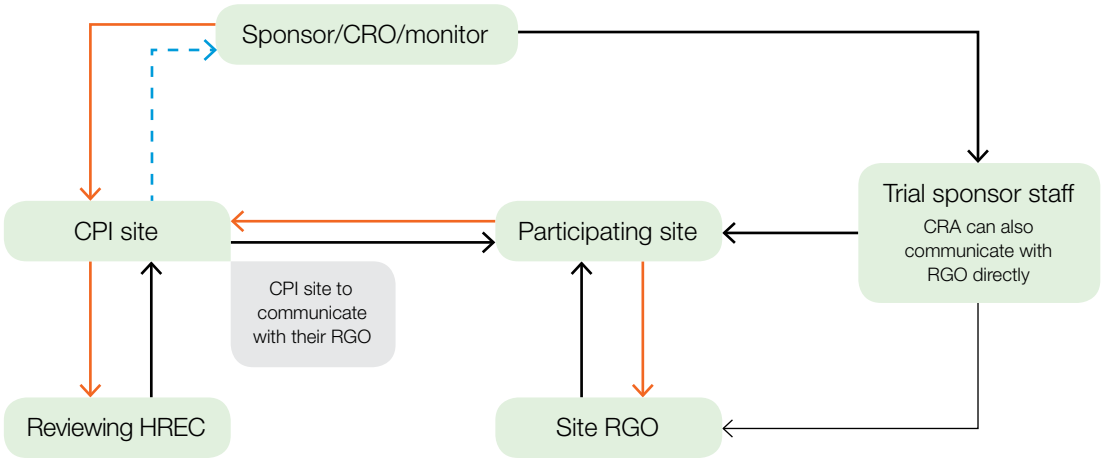
   - The CPI's site should send a reminder to participating sites at least one month prior to the annual report due date.
   - The CPI will collate the annual reports and submit them to the reviewing HREC with a coversheet summary.
   - Participating sites submit their annual report (or the collated annual report) to their RGO.

Amendments

The document flow will be different depending on whether the change occurs at the project level and requires HREC review (for example, protocol amendment) or at the site level (for example, administrative changes or a site SAE).

Figure 3.2 identifies the document flow for amendments that arise from either the sponsor/CRO or a site.

Figure 3.2: Communication plan – amendment: post-HREC approval and SSA authorisation



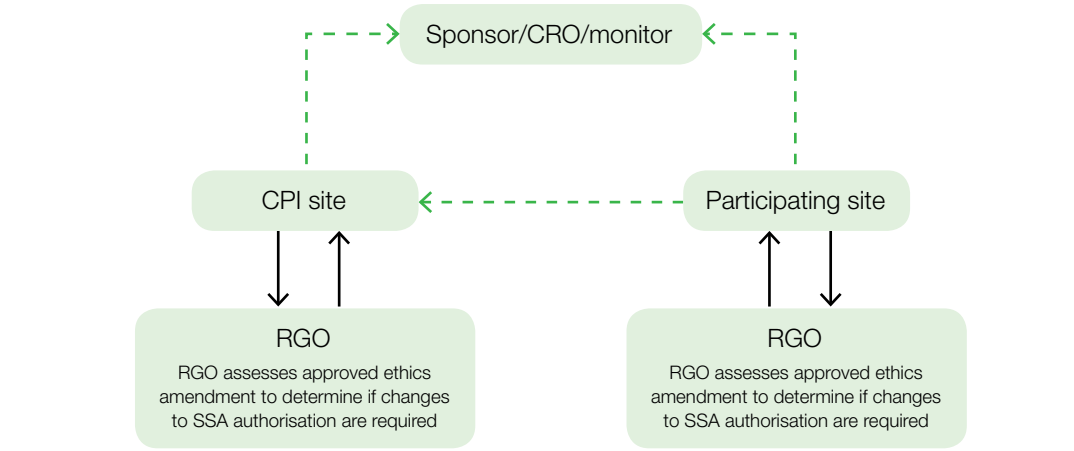
Examples of site-specific documents may include but not be limited to:

- site SAEs or safety reports
- site annual or progress reports
- single-site closure (for example, early termination due to non-recruitment)
- site protocol violations
- protocol amendments
- site PICF amendments
- site complaint reports for the reviewing HREC.

When a change requires an amendment such as a safety report or a progress report, the documentation must be provided to the RGO, who will assess whether any change to SSA authorisation is necessary.

Figure 3.3 identifies the document flow to the RGO for site-specific assessment of an amendment.

Figure 3.3: Communication plan – RGO assessment of amendment for SSA authorisation



Study closure

When there are no longer study participants at a participating site, the sponsor/CRO should communicate this to the CPI/trial coordinator. The CPI should notify the HREC of site closures throughout the study. Each participating site should notify their relevant RGO.

The CPI/trial coordinator should forward any acknowledgements of site closure by the reviewing HREC to the relevant site(s) and the monitor for filing.

In the event that the CPI site no longer has participants in the study but the participating sites do, the role of the CPI should be discussed, and CPI responsibilities may be transferred to another site. This discussion should involve input from the CPI, sponsor/CRO and participating site(s).

Appendix 3.1: Document location sheet for coordinating principal investigator (CPI) and participating sites

Document	Filed in site file of CPI site	Filed in site file of participating site
Initial submission		
National Ethics Application Form (NEAF)	Copy signed by CPI	Copy signed by CPI
Victorian Specific Module (VSM) (if applicable)	Completed by Victorian sites only – copy filed with ethics submission documents in CPI file	Only required for Victorian sites – signed by principal investigator (PI)
SSA form	Only require CPI site-specific form	Copy of site-specific form signed by PI and filed
Notification of intent to supply unapproved therapeutic goods under the Clinical Trial Notification (CTN) scheme	Only require CPI site-specific form	Site-specific form filed
Medicines Australia form of indemnity for clinical trials: HREC review only	Yes (for CPI and PI)	Yes – site-specific form filed
Medicines Australia form of indemnity for clinical trials: standard	CPI form	Site-specific form filed
Master participation information and consent form (PICF)	Yes	Yes
Site master PICF (ensure any site-specific requirements have been included, for example, wording on contraceptives)	Only require CPI site-specific form	Only require PI site-specific form
Radiation safety report (if applicable)	Only require CPI site-specific form	Yes
Human Research Ethics Committee (HREC) approval letter	Yes	Yes
HREC membership list	Yes	Yes
Cover letter – Research Governance/ SSA application	Yes	Yes
Research governance officer (RGO) submission and authorisation letter	Yes (if applicable)	Yes – site-specific forms filed
Additional approved documents	Yes	Yes

Document	Filed in site file of CPI site	Filed in site file of participating site
Ongoing submissions – Post SSA authorisation		
HREC submission and approval letter – protocol amendment and Master PICF update	Yes	Yes
Research governance/SSA cover letter	Yes	Yes
SSA form – protocol amendment and Master PICF update (if required)	Only require CPI's site-specific form	Site-specific form filed
SSA submission and authorisation letter – protocol amendment and Master PICF update	Yes (if applicable)	Yes
Amended Master PICF	Yes	Yes
Amended Site Master PICF	Yes	Yes
HREC submission and acknowledgment letter – collated annual progress report	Yes	Yes
SSA submission and approval letter – collated annual progress report	Only require CPI site-specific form	Only require PI site-specific form
SSA submission and approval letter – site-specific annual progress report	Only require CPI site-specific form	Only require PI site-specific form
Site-specific annual progress report	Yes, for all sites	Site-specific form filed
Collated annual progress reports	Yes	Yes
HREC submission and acknowledgment letter – Serious Adverse Event (SAE) line listings, investigator letter and protocol deviations	Yes	Yes
SSA submission and acknowledgment letter – personal and social responsibility inventory (PSRI), development safety update report (DSUR), investigator letter, investigator brochure, protocol deviations	Only require CPI site-specific form (if applicable)	Only require PI site-specific form
SAE line listings, investigator letter, investigator brochure, protocol deviations	Yes	Yes
HREC submission and approval letter – local SAEs	Yes	Yes
RGO submission and approval letter – local SAEs	Yes (if applicable)	Yes
Local SAEs	Yes	Yes – site-specific SAEs only

Appendix 3.2: Sponsor/CRO spreadsheet for tracking communications between CPI and participating site(s)

Study name:							
	Site 1	**Site 2**	**Site 3**	**Site 4**	**Site 5**	**Site 6**	**Site 7**
Site number							
Site name							
Site contact person							
Site contact email							
Site contact telephone							
Introduction email sent (insert date)							
Response received regarding site-specific clauses for inclusion in participation information and consent form (insert date)							
Protocol signature page received (insert date)							
National Ethics Application Form (NEAF) signed by principal investigator (PI) (E = electronic, H = hardcopy)							
PI curriculum vitae (CV) received (insert date)							

	Site 1	Site 2	Site 3	Site 4	Site 5	Site 6	Site 7
Signed clinical trial notification (CTN) received from sites (insert date)							
Human Research Ethics Committee (HREC) approval letters emailed out (insert date)							
Signed CTNs distributed (insert date)							
Research Governance Officer (RGO) authorisation letter received (insert date)							
RGO authorisation letters emailed to CPI's site by monitor							

Summary

Research Governance/Site Specific Assessment – Process and Practice

	Getting started	Research governance/ SSA submission
Coordinating principal investigator (CPI)/trial coordinator	**CPI/trial coordinator and sponsor/CRO to identify key personnel:** • PI/trial coordinator at each site • local RGOs • trial monitor **CPI site develops:** • contacts template • distribution (email) lists • CPI tracking coversheet	**CPI/trial coordinator actions:** • distribute key project documents to participating sites • prepare NEAF on Online Forms, generate SSA and transfer each SSA form to a site
Principal investigator (PI)/trial coordinator	**Participating site PI/trial coordinator develops:** • tracking cover sheet	**PI/trial coordinator actions:** • quality check all SSA-related documents • submit to RGO
Research governance officer (RGO)	**Receipt of CAS notification:** • HREC reference number, title, CPI name, reviewing HREC **Communicate with:** • PI/trial coordinator • sponsor/CRO **Request:** • 'early action' part A checklist items **Create AU RED stub**	**RGO actions:** • document quality check • acknowledgement of SSA submission to PI/trial coordinator • process SSA in AU RED • assess all documentation including HREC-related and SSA
Sponsor/ contract research organisation (CRO)	**Sponsor/CRO and CPI/ trial coordinator to identify key personnel:** • PI/trial coordinator at each site • local RGOs • trial monitor **Provide key project documents to sites:** • protocol • investigator brochure • master PICF • other information **Trial monitor obtains site details for:** • legal documents, insurance, CTN etc. **Communication plan:** • local liaison persons • study liaison persons • delegated responsibilities	**Sponsor/CRO actions:** • document and quality checks • update document location sheet

Post HREC approval: SSA authorisation (to end of study)	Study closure
CPI/trial coordinator actions: • receive HREC approval letter and approved documents, indemnity (copies), CTN (original) • make available to sites the HREC approval letter, approved documents, indemnity (copies), CTN (original) • determine document flow for amendments and reporting, regarding participating sites (via sponsor/CRO or CPI responsibility) • safety reports – for material impact notify HREC and sponsor/CRO throughout the study	**CPI/trial coordinator actions:** • provide HREC with the final study closure report or site closure report; copy to participating sites and sponsor/CRO • provide any HREC acknowledgement/communication to participating sites and sponsor/CRO
Site PI (including CPI)/trial coordinator actions: • complete and send AE/SAE/SUSAR/USADE pro-forma to CPI according to NHMRC *Position Statement* • liaise with RGO regarding SSA requirements for amendments – site RGO advice/authorisation is required before implementation	**Site PI/trial coordinator actions:** • receive the final study closure report or site closure report (same as sent to HREC) • provide final study closure report or site closure report to the site RGO • provide any HREC acknowledgement/communication to the site RGO
RGO actions: • once notified of HREC approval complete SSA authorisation • process in AU RED and provide SSA authorisation to PI/trial coordinator • notify VMIA and Radiation Safety Section (Health Department), if applicable • for amendments, protocol deviation/violation, progress and safety (material impact) reports, liaise with PI/trial coordinator • assess implications on the site for SSA amendment authorisation • document quality check, action and notify SSA amendment authorisation to site PI/trial coordinator	**RGO actions:** • receive a copy of the final study closure report or site closure report from PI/trial coordinator (same as sent to HREC) and HREC acknowledgement/communication • send an acknowledgement for the report to the site PI/trial coordinator • process in AU RED • ensure the file is complete and closed
Sponsor/CRO actions: • receive standard SSA authorisation letter signed by RGO/authority • develop post-SSA authorisation communication plan and document location guide for amendments and reports throughout the trial • liaise with site staff	**Sponsor/CRO actions:** • receive a copy of the final study closure report or site closure report from the CPI/trial coordinator (same as sent to HREC) and HREC acknowledgement/communication • receive a copy of the RGO acknowledgement of the report from the site PI/trial coordinator

Contributors to the process and practice project

Stream working groups

Investigators / trial coordinators	Research governance officers	Sponsors / contract research organisations
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The Coordinating Office for Clinical Trial Research, Department of Health, Victoria has managed this initiative and assisted in production.

Consultation

A May 2013 Workshop entitled 'Clinical Trials – Process Improvements', was attended by a broad range of participants from the clinical trials sector. Some stream group members above presented their work, and a panel session was held with questions and answers. This provided further information for this document. The Workshop attendees are thanked for their contribution.