Guidance Document for Sponsors and Sites to establish a Teletrial

Steps and Documents for use in Victoria

OFFICIAL

Australian Teletrial Program – Victoria (ATP-VIC)

VICTORIA State Government | Department of Health

Guidance Document for Sponsors and Sites to Establish a Teletrial

Steps and Documents for use in Victoria*

* This document has been based on the *Guidance Document for Sponsors and Sites to Establish a Teletrial. Steps and Documents Necessary within Queensland Health* (30 July 2021) found on the Queensland Health Teletrials webpage – Guidance for Sponsors and Sites and adapted accordingly.

To receive this document in another format, phone 0499 810 778, using the National Relay Service 13 36 77 if required, or email Regional Clinical trial Coordinating Centre (RCCC-VIC) <rccc@health.vic.gov.au>

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1 Introduction

1.1 Background

The Clinical Oncology Society of Australia (COSA) established the Australasian Teletrial Model in September 2016. In 2018, Queensland Health agreed to pilot this model with a pharmaceutical company and evaluate the impact of the teletrial model on sponsors, sites and participants. The pilot was successfully completed between Queensland Health and Eli Lilly Australia and was presented at ARCS Australia conferences in 2018 and 2019.

Subsequently, Queensland Health and the Commonwealth Department of Health, through the Clinical Trial Project Reference Group (CTPRG), agreed to introduce the teletrial model nationally.

The National Teletrials Compendium, comprising the *National Principles for Teletrials in Australia* and the *National Standard Operating Procedures for Clinical Trials, including Teletrials, in Australia* were peer-reviewed and published nationally.

This Teletrials initiative aims to expand the reach of clinical trials to rural, remote regions and Indigenous communities of Australia while minimising any existing or potential barriers to teletrial implementation and its impact on sponsors.

1.2 Purpose of this document

The purpose of this document is to:

- outline the additional steps required to set up and manage a teletrial
- identify the specific documents required for HREC approval and site authorisation
- guide the key steps of the trial process.

The intent is to support the timely delivery of a teletrial in the State of Victoria. This document is to be used in combination with the National Teletrials Compendium which consists of the National Principles and Standard Operating Procedures of Teletrials.

1.3 Scope

Applies to all relevant Victorian Public Health institutions and staff - including, but not limited to, visiting health professionals, contractors, consultants, managed service providers and volunteers who propose to undertake, administrate, review and/or govern human research involving patients/participants, facilities and/or staff - and other institutions collaborating with Victorian Public Health Services, who undertake a clinical trial under the Australian Teletrials Program (ATP).

All research personnel involved in the clinical study must operate within their scope of practice.

2 Glossary

Term	Description
AE	Adverse Event
AI	Associate Investigator
ATP	Australian Teletrial Program
Cluster PS	Primary Site within a cluster
COSA	Clinical Oncology Society of Australia
CPI	Coordinating Principal Investigator
CRA	Clinical Research Associate
CRF	Case/Clinical Record /Report Form
CRO	Contract Research Organisation
CTA	Clinical Trial Approval scheme
CTN	Clinical Trial Notification scheme
CTPRG	Clinical Trial Project Reference Group
CTRA	Clinical Trial Research Agreement
CV	Curriculum Vitae
DSMB	Data and Safety Monitoring Board
EDC	Electronic Data Capture
ERM	Ethical Review Manager
ICH GCP	International Council for Harmonisation of Good Clinical Practice
HHS	Hospital and Health Service
HREA	Human Research Ethics Application
HREC	Human Research Ethics Committee
IMD	Investigational Medicinal Device
IMP	Investigational Medicinal Product
IP	Investigational Product
LEAD SITE	The site at which the CPI is located (may also be a Primary Site in a cluster)
NHMRC	National Health and Medical Research Council
NMA	National Mutual Acceptance
PI	Principal Investigator
PICF	Participant Information sheet and Informed Consent Form
PS	Primary Site (within a cluster)
QCTCU	Queensland Clinical Trials Coordination Unit

Term	Description
QH	Queensland Health
RCCC	Regional Clinical trial Coordinating Centre
RGO	Research Governance Officer
SAE	Serious Adverse Event
SOC	Standard of Care
SS	Satellite Site (within a cluster)
SSA	Site-Specific Assessment
SSF	Site Study File
SSI	Significant Safety Issue
SSS	Study Start-up Specialist
SUSAR	Suspected Unexpected Serious Adverse Reaction
TGA	Therapeutic Goods Administration
TMF	Trial Master File (held at the PS)
TT	Teletrial
USADE	Unanticipated Serious Adverse Device Event
USM	Unexpected Safety Measure
VCCC	Victorian Comprehensive Cancer Centre

3 Terms

Refer to these terms when reading the Guidance Document for Sponsors and Sites to establish a Teletrial. Steps and Documents for use in Victoria.

A comprehensive list of associated terms can be found in the National Standard Operating Procedures for Clinical Trials.

Associate Investigator (AI)

Any individual member of the clinical trial team may be delegated and supervised by the PI at a trial site to perform critical trial-related procedures and/or to make important trial-related decisions.

Where the Teletrials Model is implemented:

- an AI at a Primary Site may be delegated to implement some or all of the study related activities by the PI according to their level of experience, as documented in the Delegation Log
- an AI at a Satellite Site is the local contact for study-related matters and will be under the supervision of PI at the Primary Site.

Cluster

A group of sites involved in undertaking the same study, consisting of a Primary Site who assumes overall responsibility for the conduct of the same study and one or more Satellite Sites, which conduct the study under the direction of the Primary Site using telehealth.

A cluster can be made up of sites in the same hospital health service or across different hospital health services.

Coordinating Principal Investigator (CPI)

CPI is responsible in a multisite study for the completion and submission of HREC applications and communications on behalf of all sites involved in the ethics application for which the CPI must ensure that the Master PICF includes the optional teletrials wording and additional consent question relating to ATP reporting. Refer to Appendix 1 for PICF templates.

Liaises with the reviewing HREC on behalf of all sites listed in the HREA.

Clinical Trial Research Agreement (CTRA)

A legally binding agreement that manages the relationship between Sponsor and Institution where the Sponsor may be providing the study drug or device, the financial support and/or proprietary information and the Institution may be providing data and/or results, publication or input into further intellectual property.

The agreement covers matters such as confidentiality, intellectual property, ownership of data, insurance and indemnity. The Medicines Australia CTRA is the recommended standard form.

Delegation Log

A list of appropriately qualified and trained persons to whom the Principal Investigator has delegated significant study-related duties and functions. The Log details related duties and documents which study-specific roles and responsibilities are assigned to each staff member on the study team.

Delegation Logs should be actively maintained (not constructed retrospectively) so there is evidence of appropriate delegation before any trial activities are undertaken. Each entry is signed and dated by the delegates and countersigned by the Principal Investigator.

Human Research Ethics Committee (HREC)

Human Research Ethics Committees review research proposals involving human participants to ensure that they are ethically acceptable and in accordance with relevant standards and guidelines, such as the National Statement. HRECs are usually established by organisations (public, not-for-profit or private) which conduct research involving humans.

Primary Site

Under the Teletrials Model, the Primary Site coordinates the trial across a cluster to enhance participant reach, recruitment and management. The Principal Investigator located at the Primary Site has full responsibility for conducting the clinical trial at their site and any Satellite Site within their cluster under ICH GCP.

Principal Investigator

The Principal Investigator (PI) is the Investigator responsible for the conduct, management, monitoring and reporting of a trial at their own site.

Where the Teletrial Model is implemented, the Principal Investigator at the Primary Site assumes overall responsibility and provides oversight to Satellite Site(s). Associate Investigators at Satellite Site(s) operate under the direction and responsibility of the Principal Investigator at the Primary Site.

Regional Clinical trial Coordinating Centre - Victoria (RCCC-VIC)

The Department of Health Australian Teletrial Program - Victoria (ATP-VIC) team, including the RCCC-VIC, is located within the Coordinating Office for Clinical Trial Research and is responsible for implementing the ATP in Victoria. This is a centralised service to enable and facilitate Victoria's rural/regional/remote health services to ensure the required support, policy and workforce are available to bring clinical trials and teletrials closer to home.

Research Governance Officer (RGO)

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

Site Supervision Plan and Site Delegation Log information must be attached to a Satellite site SSA submission.

Research Governance considers legal compliance, financial management, accountability and risk management associated with research at a participating site.

Satellite Site

A Satellite Site is located in a healthcare facility geographically separate from the Primary Site.

Trial activities are delegated by the Primary Site to the Satellite Site clinical team, in which the Associate Investigator will instruct and implement trial activities under supervision by the Primary Site PI.

A Satellite Site can however be located in metropolitan, regional or rural settings. Delegated activities to be performed by a Satellite Site are trial- and (Satellite) site-specific. The Primary Site must consider a Satellite Site's personnel and facilities when developing a Delegation Log and Supervision Plan suitable for a trial.

Study Start-up Specialist (SSS)

The SSSs coordinate, provide guidance and evaluate the Teletrial start-up and site-establishment process for the ATP-VIC in participating public health services in Victoria. SSSs collaborate with sites to evaluate their capacity to conduct Teletrials and address emerging service's needs. The SSSs promote and raise awareness of Teletrials functions including recruiting and supporting trial teams across multiple sites. The SSSs participate in developing clinical standard guidelines for start-up and other operational activities for clinical trials.

Supervision Plan

A management plan that outlines processes for a PI in the supervision of any individual or party delegated study-related duties and functions conducted at a Satellite Site, which includes, but is not limited to, details on joint trial meetings across a cluster (with minutes of these meetings) and clarification of activities performed by the PI and AI(s), other study staff and independent third parties i.e., external service providers.

Teletrial Sub-Contract

A legally binding agreement that manages the relationship between the Primary Site and the Satellite Site where the Satellite Site is a separate legal entity to the Primary Site.

4 Definition of a Teletrial

A teletrial uses telehealth technology to communicate between the Primary Site and Satellite Site(s) and enable the delivery of clinical trial activities as defined in the Supervision Plan.

This technology supports a Principal Investigator to supervise Associate Investigator(s) to conduct a clinical trial at a Satellite Site, which is geographically remote from the Principal Investigator's Primary Site. The Principal Investigator assumes overall responsibility for the trial.

A detailed Supervision Plan, in addition to a Delegation Log, is required for each Satellite Site regardless of its experience under ICH GCP. Trial participants may attend trial visits at either the Primary or Satellite Site, as determined by the Protocol and Supervision Plan.

The obligations of the trial are detailed under the Clinical Trial Research Agreement (CTRA) between the Sponsor and the Principal Investigator's Institution (Head Agreement) and the Teletrial Subcontract between the Primary Site and the Satellite Site Institutions (Subcontractor).

CTRA templates and a Teletrial Subcontract are available for studies under a teletrial model on the Medicines Australia webpage.

5 Core principles of Teletrials

- To increase access to clinical trials by rural, regional and remote consumers, including Indigenous communities
- to facilitate collaboration between rural, regional, remote sites and metropolitan centres, and between tertiary centres across the state.
- to deliver a greater engagement in research activity
- to improve recruitment of patients into clinical trials across the state and nationally
- to reduce the disparity in patient outcomes amongst geographically dispersed populations
- to build clinical trial capacity by providing clinical trial-related training to upskill the workforce and increase the number of “trial-ready” health services in Victoria.

6 Teletrial roles, functions and interactions

Coordinating Principal Investigator

In addition to the CPI's clinical tasks, the CPI is responsible for the completion and submission of the ethics application to the reviewing HREC and associated communications on behalf of all sites participating in the trial.

Once confirmed from a PI that their site will be a Primary Site, the CPI is responsible for notifying the reviewing HREC of all sites that will be included in the ethics approval. Participating sites are listed in the initial ethics application (the HREA) as a Regular Site, Primary Site or a Satellite Site.

If an already approved trial will be adding a teletrial component or including additional teletrial sites, the CPI is required to notify the HREC. An ethics amendment request is submitted to the HREC indicating:

- The establishment of teletrial sites **or**
- The addition of new Satellite Sites to an established teletrials cluster

The CPI ensures the Master PICF (standard template for interventional studies) includes the optional teletrial wording and additional consent question relating to ATP reporting purposes. The Stand Alone Teletrial PICF is used when adding a teletrial to an already approved multisite trial. These PICF templates are available on the Clinical Trials and Research- Ethics Application webpage.

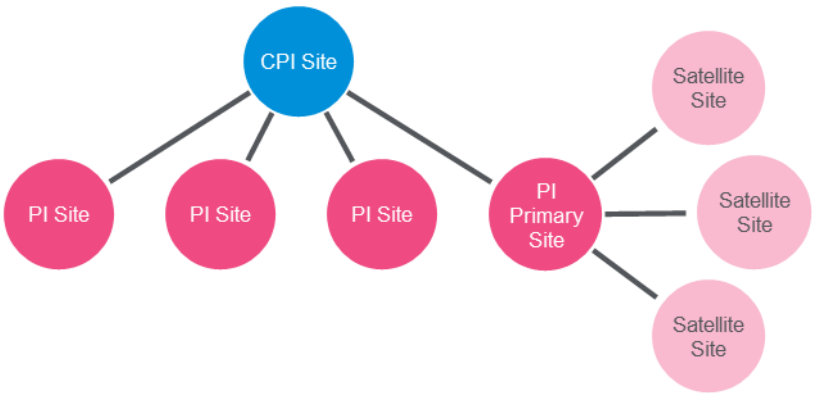
Any other teletrial related information e.g., post approval requirements are required to be reported to the HREC.

Primary Site

Site selection is determined by the sponsor and for consideration as a Primary Site. If a Primary Site PI identifies potential trial participants at a remote site, where a clinician agrees to be involved (which may include discussions with the site's Research Governance Officer), the remote site can then become a Satellite Site to the Primary Site if confirmed by the sponsor.

Each teletrial cluster comprises one Primary site which can be associate with one or more Satellite Sites.

Multisite trial including a teletrial component



Principal Investigator

The PI is responsible for the conduct of the clinical trial at the Primary Site. The PI assumes overall responsibility and also provides oversight to each Satellite Site within the cluster.

For each Satellite Site, the PI must have a specific Supervision Plan that details the tasks, reporting and meeting schedules, and other activities relating to conducting the trial at that Satellite Site.

Satellite Site

A Satellite Site is located in a healthcare facility geographically separate from the Primary Site. Trial activities are delegated by the Primary Site to the Satellite Site clinical team, in which the Associate Investigator will instruct and implement trial activities under supervision by the Primary Site PI.

A Satellite Site can however be located in metropolitan, regional or rural settings. Delegated activities to be performed by a Satellite Site are trial- and (Satellite) site-specific. The Primary Site must consider a Satellite Site's personnel and facilities when developing a Delegation Log and Supervision Plan suitable for a trial.

The Sponsor must also ensure that the Satellite Site is appropriately resourced and positioned to conduct the trial.

Associate Investigator

Any individual member of the clinical trial team may be delegated and supervised by the PI at a trial site to perform critical trial-related procedures and/or to make important trial-related decisions.

Where the teletrials model is implemented:

- an AI at a Primary Site may be delegated to implement some or all of the study related activities by the PI according to their level of experience, as documented in the Delegation Log
- an AI at a Satellite Site is the local contact for study-related matters and will be under the supervision of PI at the Primary Site.

Regional Clinical trial Coordinating Centre Victoria (RCCC-VIC)

The Department of Health ATP-VIC team, including the RCCC-VIC, is located within the Coordinating Office for Clinical Trial Research and is responsible for implementing the ATP in Victoria. This is a centralised service to enable and facilitate Victoria's rural/regional/remote health services to ensure the required support, policy and workforce are available to bring clinical trials and teletrials closer to home.

The RCCC-VIC:

- contributes to the Victorian elements of the ATP
- facilitates the national ATP reporting requirements, twice per year
- manages ATP payments and milestones according to the Department of Health Subcontract with Queensland Health and other policies for the Program
- participates in Victorian governance of the Program and national ATP governance meetings including the National RCCC Group.

Human Research Ethics Committee (HREC) review and amendments

The NHMRC certified HREC that undertakes the review of the ethics application is responsible for approving any changes to an existing approved project e.g. establishment of teletrial sites, addition of new Satellite Sites. It is recommended that a Master Supervision Plan and Master Delegation Log is submitted to the HREC for review.

An ethics amendment request is submitted to the reviewing HREC requesting approval of adding a teletrial component to a trial or the addition of new Satellite Sites to an established teletrials cluster.

Changes to the consent process due to the requirement of conducting the clinical trial under the teletrials model is also considered by the HREC such as the use of telehealth and the consent process followed by the AI at a Satellite Site

Research Governance Officer (RGO) at Primary Site

The RGO at a Primary Site undertakes an assessment of the research governance application (SSA form) of the clinical trial at the Primary Site. The RGO assesses the submission and can *Authorise* for the trial to be conducted at the site.

The RGO manages the CTRA (Head Agreement) between the Sponsor and the Primary Site Institution and can provide a Teletrial Subcontract for each Satellite Site and its associated Primary Site for execution as a subcontractor.

Research Governance Officer (RGO/delegate) at Satellite Site

The RGO or delegate at a Satellite Site undertakes an assessment of the research governance application (SSA form or suitable risk assessment form) of the clinical trial conducted at the site. This may be in collaboration with the RGO at the Primary Site, particularly in situations where the Satellite Site does not have the relevant expertise or authority to assess a research governance application under the Teletrials model. The assessment should include a Site Supervision Plan and Site Delegation Log (Satellite Site).

A Teletrial Subcontract must be executed and returned to the Primary Site before a teletrial study can commence.

Supervision Plan

The PI is responsible for the Supervision Plan at each Satellite Site. It should document the study responsibilities delegated to the Satellite Site and frequency of supervision undertaken by the PI.

The PI should ensure all investigational staff at both the Primary Site and Satellite Site(s), or external service providers are qualified to perform their delegated duties.

7 Objectives and benefits for sponsors

The Sponsor will decide if a trial will include a teletrial component and inform the Primary Site PI accordingly.

The anticipated overall advantages for sponsors, to conduct a trial under the Australian Teletrials model, include:

- an increased potential to reach recruitment targets in a shorter period
- minimal additional site management impact and costs (as agreed by the Sponsor) while the Commonwealth-funded Teletrial Support Program is in place
- minimal impact as Satellite Site management and communication is undertaken by the Primary Site in accordance with the Supervision Plan.

These advantages are enabled by the following principles:

- Sponsor communicates with Primary Site only, and the Primary Site communicates with the Satellite Site. However, there are no restrictions on Sponsors communicating directly with Satellite Sites if desired
- contract negotiations are with the Primary Site only
- monitoring is conducted at the Primary Site only, unless a Sponsor agrees otherwise and is documented in the monitoring plan and/or Supervision Plan.

8 Procedures for Teletrials

8.1 Sponsor responsibilities

The following Sponsor responsibilities assume that a Primary Site has been identified, evaluated, and selected by the Sponsor in the usual manner.

8.1.1 Operational requirements

Site assessment

Overall assessment of the Primary Site includes:

- the suitability of the clinical trial protocol to be conducted under the Teletrials model, with specific considerations of trial management, Investigational Product logistics such as delivery to Primary Site only, or to Satellite Site/s as well, pathology and other trial related tests or investigations Assessment checklists - the *Evaluation of a trial as a Teletrial checklist* and the *Evaluation of a site as a Satellite Site checklist* can found on the Clinical Trials and Research - Teletrials webpage.

Assessment of Satellite Sites includes:

- evaluate the Satellite Site and/or
- accept the evaluation and recommendation of the Primary Site, which must include full details on the proposed method to transfer IMP to Satellite Sites (if relevant), arrangements for pathology samples, and evidence of the Satellite Site's agreement to participate e.g., an email trail between PI and proposed AI at the Satellite Site.

In evaluating a Satellite Site, the Sponsor may consult with the Contract Research Organisation (CRO) (if applicable) for further discussion. If the Sponsor chooses to undertake an evaluation of a proposed Satellite Site, the inspection may be undertaken - as agreed between the Sponsor and AI at the Satellite Site - either as soon as the potential Satellite Site is proposed, or when a potential participant at that Satellite Site has been identified.

If the Satellite Site has been considered in the initial site selection by the Primary Site, a formal site selection letter from the Sponsor should name each agreed site and its role in a cluster e.g., Site X is the Primary Site and Site Y is the Satellite Site.

Once a Satellite Site has been selected, the Sponsor should formally acknowledge the selection in a formal letter to the Primary Site, stating the following:

- agreement to conduct the clinical trial as a teletrial
- name of the Satellite Site and any other Satellite Site(s) (within a cluster) previously established for the trial by the Primary Site.

The letter may be either sent by the Sponsor to each Satellite Site or forwarded by the Primary Site to the Associate Investigator at the Satellite Site. This should then be provided to the Satellite Site RGO.

HREC approval

If the trial is to be conducted under a Teletrials model in the first instance, the Sponsor/CPI should ensure all sites – Regular, Primary or Satellite are included as participating sites in the ethics

application (the HREA). The Master PICF (standard template for interventional studies) should include the optional teletrial wording and additional consent question relating to ATP reporting purposes. A Master Supervision Plan and Master Delegation Log should be submitted to the HREC.

If it is agreed that an approved trial will be **adding a teletrial** component or including the addition of teletrial sites, the HREC must approve these changes.

The sponsor/CPI will need to submit an ethics amendment request to the reviewing HREC seeking approval. The Sponsor should include a copy of a formal agreement letter in the ethics amendment request application. The Stand Alone Teletrials PICF should be used between the Sponsor and Primary Site and included in the ethics amendment submission and amended Master Supervision Plan and Site Delegation Log (if required).

Other documents should include an amended Supervision Plan and Delegation Log to a Master version (if required) and the Stand Alone Teletrials PICF between the Sponsor and Primary Site is used in this instance.

See Appendix 2 of this document for guidance on HREC Teletrials Submission and Notification requirements.

Research Governance

The Sponsor must review and approve site specific versions of Master documents, in the same way that the Sponsor reviews site specific versions of clinical trial Master documents.

For commercially sponsored research, there will be a research governance fee for the Primary Site and Satellite Sites. For non-commercial clinical trials, there may be a fee, in accordance with local policies.

Supervision Plans

The Sponsor is responsible for reviewing and approving each individual supervision plan developed by the Primary Site to collaborate with the corresponding Satellite Site in the cluster.

Delegation, Signature, and Training Logs

It is the Sponsor’s responsibility to confirm that all staff conducting trial-related activities within the cluster are listed as required on respective logs.

Site Initiation

The Sponsor is responsible for:

- conducting the Site Initiation Visit at the Primary Site. If Satellite Site(s) are known at the time of Site Initiation, they should participate in the Site Initiation Visit electronically, (or in person if possible)
- providing additional training required by the protocol or other trial processes to the Primary Site and known Satellite Site research team members at the same time
- provide the Primary Site with necessary training resources to use when on-boarding new Satellite Sites.

Electronic Data Capture (EDC) Platform

The Sponsor is required to provide all research team members with data entry access in the cluster, in accordance with the responsibilities specified in the Delegation Log.

Communication

The Sponsor confirms the communication strategy with the Primary Site, i.e., the Sponsor communicates with the Primary Site and the Primary Site is responsible for communications within the cluster unless otherwise agreed.

Trial Master File

The Sponsor ensures the Trial Master File has been provided to the Primary Site and it is current and collated adequately – either electronically or in hard copy depending on the sponsor's and Primary Site's agreed preference. If the Sponsor has agreed to provide the Site Study File to a Satellite Site, this must occur before any participant is enrolled at that Site.

Monitoring of Clinical Trial

The Sponsor must ensure that clinical trials are conducted in accordance with the protocol. Adequate monitoring and source data verification plans for the cluster should be approved by the Sponsor prior to study commencement.

Archiving of Trial Documents

The Sponsor confirms the process for archiving of study documentation at the Primary Site and Satellite Site(s) at the completion of the clinical trial.

8.1.2 Regulatory requirements

Clinical Trial Notification (CTN)

It is the responsibility of the Sponsor to complete and submit the CTN via the TGA online portal. The CTN should be updated as Satellite Sites are on-boarded to the study. If the study is to be under the CTA scheme, refer to the TGA Clinical trials webpage for further guidance.

The TGA acknowledgement should be provided to sites for inclusion in their governance application,

The IMP or Pathology Kits that contain unregistered therapeutic goods may be managed differently depending on the trial. Accordingly, specific actions taken for site listings may vary in the CTN form. However, the TGA advises that any site and facility that is undertaking clinical trial related activities should be named on the CTN form.

Below is a table which summarises the specific actions taken in different scenarios regarding the management of IMP and Pathology Kits that contain unregistered therapeutic goods.

Scenario	Action
Pathology Kits are stored at the trial sites	List any site that stores a supply of Pathology Kits
IMP is stored at the trial sites	List any site that stores IMPs
The new Satellite Site joins a trial that has already commenced and requires IMP storage on-site	Update CTN form and add the new Satellite Site in the list
Pathology Kits or IMP is stored at the Primary Site, and is shipped to the Satellite Site on a visit-by-visit basis	• The Satellites Site does not have to be named on CTN • The PI is the Primary Site PI

Scenario	Action
	• The Approving Authority is the Primary Site legal entity name
Pathology Kits or IMP is stored at the Satellite Site	• The Satellite Site is identified as a Site on the CTN • The PI at the Primary Site should be identified as Satellite Site PI • The Approving Authority is the Satellite Site's legal entity name

Investigational Medicinal Product / Medical Device or other Investigational Technology

The Sponsor is responsible for:

- distributing IMP (or Medical Device/Investigational Technology) in accordance with the process negotiated when initially agreeing to the Teletrials,
- approving individual Satellite Sites in accordance with the CTN form
- ensuring that the Primary Site has Standard Operating Procedures or Work Unit Guidelines detailing handling, tracking, managing and dispensing IMP/Medical Device or Investigational Technology.

Budget

The Sponsor undertakes budget negotiations with the Primary Site in a routine manner. Additional budget items may be negotiated by the Primary Site such as:

- reimbursement for costs if the Primary Site is responsible for sending and retrieving Investigational Products and/or pathology supplies/samples to and from Satellite Sites
- Satellite Site pharmacy or other provider fees if IMP is to be delivered, stored, and dispensed at a Satellite Site
- costs associated with the use of telehealth services
- costs associated with clinical trial-related specialty assessments and/or treatments that may not be available at the Satellite Site
- costs associated with the processing of source documents for monitoring purposes.

Clinical Trial Research Agreements

It is recommended that research projects use a standard template for their research agreements. Medicines Australia (MA) have templates for the Clinical Trial Research Agreement (CTRA).

The CTRA is used as the Head Agreement between the Sponsor and the Institution (Primary Site) and the role of the Sponsor is to complete the agreement with the Primary Site.

The following teletrial-specific changes relate to the CTRA but should be incorporated into the relevant sections, and these changes are made by the Sponsor:

Schedule 1 – particulars of the Primary Site and Satellite Site(s)

Schedule 2 - include additional teletrial-related costs in the budget as agreed. Payments and invoicing, and terms and conditions for the Satellite Site(s)

When additional Satellite Sites join a cluster, the Sponsor should amend Schedules 1 and 2 of the CTRA, as above.

The Teletrials Subcontract is designed to complement the MA CTRA (Head Agreement) when a study is conducted under the Teletrials model. The Subcontract is between the Institution (Primary Site) and the Subcontractor (Satellite Site) and should detail the management of clinical trial activities and formalise its relationship with each Satellite Site.

Indemnity and Insurance

The Form of Indemnity – Standard from Medicines Australia is used for institutions and staff conducting the clinical trial and HREC review.

For commercially sponsored clinical trials, the Sponsor is required to provide indemnity to both the Primary Site and Satellite Site(s).

For non-commercial clinical trials, if indemnity is provided by the Sponsor or Collaborative Group, the Satellite Sites should be named and covered.

In Victoria, state-wide insurance is provided through the Victorian Managed Insurance Authority (VMIA) for public hospitals and clinicians.

Where indemnity is not provided by the Sponsor, each participating site (Primary or Satellite) must hold valid insurance to conduct the trial. This would apply to private organisations or entities. Private hospitals and non-employed clinicians must have their own professional and medical indemnity. Each Satellite Site should maintain professional indemnity and public liability insurance and provide a Certificate of Insurance.

8.2 Primary site responsibilities

Unless requested by the Sponsor in the first instance, to conduct their clinical trial under the Teletrials model, research teams should consider the suitability of every trial to be conducted under the Teletrials model, as early as possible, when offered a new trial, or as soon as time permits, for trials that are already underway.

The following Primary Site responsibilities, relating to establishing a cluster under the Teletrials Model, assume that the Primary Site has been identified, evaluated and selected by the Sponsor as per usual practice.

8.2.1 Operational requirements

Evaluation of the Primary Site

The Primary Site evaluates each clinical trial being undertaken within the clinical trial unit, by confirming:

- its suitability to be conducted under the Teletrials model; and
- the likelihood of identifying participants in regional, rural or remote sites as well as participants from Indigenous communities. Interrogation of clinical databases or registries may be required to establish this.

If the Sponsor has not approached the Primary Site in the first instance, to request that the trial is conducted under the Teletrials model, it is the Primary Site's responsibility to notify the Sponsor of the trial's suitability, and to obtain agreement from the Sponsor to run the trial as a Teletrial.

Evaluation of the Satellite Site

It is the responsibility of the Primary Site to:

- liaise with the key clinician in the proposed Satellite Site to ascertain the willingness and site's capacity to undertake a teletrial
- identify potential participants within their proposed cluster catchment, ascertain their willingness to participate in the clinical trial
- undertake an evaluation of each proposed Satellite Site
- provide details of the proposed Satellite Site to the Sponsor, such as clinical trial experience of the staff, any anticipated education and training program, and anticipated additional costs of shipping IMP or pathology.

Requirements for HREC submission

If the study is a single-site study, the PI will be responsible for the entire study and Satellite Site(s). In the case of multisite trials, the Primary Site is responsible for notifying the CPI of the Sponsor's agreement to conduct the trial under the Teletrials Model.

The notification to the CPI should include the following:

- evidence in a letter with the Sponsor's agreement to conduct the trial under the Teletrials Model
- clarification on whether the Master PICF (standard template for interventional studies) which includes the optional teletrial wording, and/or whether a Stand Alone Teletrials PICF is to be used to inform an amendment to the ethics approval
- Master Supervision Plan and Master Delegation Log relating to the Primary Site and Satellite site/s
- the specific way informed consent will be collected at the Satellite Site

If the trial is to be conducted under a Teletrials model in the first instance, the CPI (or Sponsor) should ensure all sites – Regular, Primary or Satellite are included as participating sites in the ethics applications (the HREA). The Master PICF (standard template for interventional studies) should include the optional teletrial wording and additional consent question relating to ATP reporting purposes. A Master Supervision Plan and Master Delegation Log are required for ethics review.

If it is agreed that an approved trial will be adding a teletrial component or including the addition of teletrial sites, the HREC must approve these changes. The CPI (or Sponsor) will need to submit an ethics amendment request to the reviewing HREC seeking approval. A copy of:

- a formal agreement letter between the Sponsor and CPI
- the Stand Alone Teletrials PICF (between the Sponsor and the Primary Site)
- the Master Supervision Plan and Master Delegation Log for the study.

Supervision Plan

A management plan needs to be developed specifically for each Satellite Site. This is in the form of a Supervision Plan. It should outline the processes for the PI in the supervision of any individual or party delegated study-related duties and functions conducted at each Satellite Site, specifying the responsibilities of both Primary and Satellite Site(s) for all trial-related activities.

Once the Supervision Plan for each Satellite Site has been finalised it is sent to the Sponsor for approval and included as an ethics supporting document for HREC review.

The Supervision Plan will also be required for the RGO governance review.

Research Governance

The Primary Site undertakes research governance processes for their site, notifying their RGO that the trial will be conducted under the Teletrials model, or that there is an intention to approach the Sponsor for permission to do so.

Satellite Site Initiation

It's important to establish that staff at the Satellite Site have undertaken education and training in clinical trials processes including GCP.

Site initiation must cover the following:

- protocol training
- CRF completion and access to the Electronic Data Capture (EDC) platform
- IMP logistics including shipment arrangements along with Work Unit guidelines detailing the process, dispensing, compliance checking and all relevant logs
- pathology handling including the shipment of pathology kits, processing, storage and shipping requirements
- Site Study File (SSF) preparation and management
- Delegation, Signature and Training Logs - content and timelines
- Supervision Plan and Communication Strategy, ensuring all parties are aware of the processes agreed
- the specific manner in which informed consent will be collected at the Satellite Site

See Appendix 3 - guidelines for RGO review of Victorian Teletrials.

8.2.2 Regulatory requirements

Budget

Commence budget development including each Satellite Site requirements.

Clinical Trial Research Agreements

The Primary Site liaises with the Sponsor to ensure the contract contains the following changes:

- Schedule 1 - All known Satellite Sites linked to the Primary Site within the cluster must be named. This means that contract amendments will be required each time a new Satellite Site joins the cluster
- Schedule 2 - Any agreed updates to the study budget for the Primary Site with consideration of inclusion of Satellite Sites. If exact costs of are unknown for Sponsor agreed additional items relating to the establishment and management of Satellite Sites, they should be noted as a pass-through cost in the Schedule.

The Teletrial Subcontract (between the Primary Site and a Satellite Site) details are confirmed before sending the Subcontract to the Primary Site RGO and Satellite Site RGO/delegate for signing.

8.3 Satellite site responsibilities

Generally, the Satellite Site is first approached by the Primary Site. However, the Satellite Site may contact the Primary Site to be considered as a Satellite Site when they have identified potential participants.

Once a potential participant has indicated the willingness to participate in a clinical trial, the Primary Site must evaluate the suitability of the Satellite Site to operate under the Protocol and confirm agreement from the clinician/s at the Satellite Site regarding their capacity to fulfill the requirements to undertake a Teletrial. Once this occurs, the Primary Site seeks confirmation from the Sponsor to allow the site to join a cluster as a Satellite Site.

Suitability of Satellite Site

The potential Satellite Site works with the Primary Site to review the protocol and consider the resources and logistics required for undertaking a clinical trial at their location. No additional work relating to establishing a Satellite Site is undertaken until the Sponsor has agreed on the site's participation as a Satellite Site under the Teletrials Model.

Supervision Plan and Delegation Log

The Primary Site will collaborate with its Satellite Site to develop a specific Supervision Plan and Delegation Log. It is recommended that the Primary Site closely supervises the informed consent visit and subsequent patient activity/treatment visits for the first patient at the Satellite Site.

Education and Training

The Satellite Site undertakes education and training as required. Training requirements will depend on the clinical trial experience of the individual Satellite Site research staff.

Consultation with the Study Start-up Specialist (SSS) may be required to guide training opportunities, some of which may be facilitated by Department of Health.

Research Governance

The Satellite Site will prepare the Satellite Site's Research Governance application for their site authorisation unless agreed otherwise with the Primary Site. Guidance documents and ERM training should be accessed if required.

The governance application should include:

- creation of the Satellite Site SSA form using ERM. If the Satellite Site does not have an administration licence for ERM then the SSA should be saved as a pdf and submitted to the Satellite Site RGO in hard copy. It should not be submitted in ERM to an RGO unless some arrangements have been agreed with the Primary Site.
- confirmation of Satellite Site specific processes for participant identification, recruitment, and consent
- confirmation of resources and logistics required to undertake the clinical trial at the Satellite Site
- confirmation of required details for the Teletrials Subcontract
- agreement on the study budget and provision of the relevant information e.g., Teletrials Subcontract required for funds transfers.

Preparation of Satellite Site before Enrolling the First Participant

The following steps must be addressed at each Satellite Site before the first participant can be enrolled:

- authorisation of the project through the Satellite Site RGO
- evidence of education and training of research staff
- site initiation must be completed, and required pathology kits, IMP and other study materials must be available either at the Satellite Site or the Primary Site, as agreed by the Sponsor
- Site Study File at the Satellite Site must be set up and all relevant documentation filed
- all relevant study logs (Delegation, Signature, Training) are completed and filed as required
- Satellite Site staff are trained to use data capture platforms and are provided with access.
- the Satellite Site has copies of all trial worksheets compiled by the Primary Site, if applicable
- the Sponsor has agreed to the process for monitoring and source data verification established for the trial
- both parties have copies of executed contracts and the Supervision Plan.

Ongoing identification of potential participants

The Satellite Site has an ongoing responsibility to search for potential participants for the Teletrial during the recruitment period, or as instructed by the Primary Site.

Safety Reporting in Clinical Trials

The Satellite Site investigator/s must be aware of reporting responsibilities for the clinical trials, as specified in the Supervision Plan and the HREC-approved Study Protocol, following the NHMRC *Safety monitoring and reporting in clinical trials involving therapeutic goods* (November 2016) guidelines.

The Satellite Site investigator/s must undertake safety reporting (the same as required for the Principal Investigator). While reporting to the Sponsor, it must also copy in the Principal Investigator on the report.

Institutional notifications should include the RGO at the relevant Satellite Site and also the RGO at the Primary Site. See Appendix 4 - Teletrial Monitoring and Safety Reporting Plan.

Other Reporting in Clinical Trials: The Satellite Site must be aware of other reporting requirements for the trial, as specified in the Supervision Plan.

8.4 Study Start-up Specialist (SSS)

The Study Start-up Specialists may be involved to assist with the following:

- identify research staff at the proposed Satellite Site
- staff at the Satellite Site have commenced education and training in clinical trials processes including GCP
- once the Sponsor has agreed on the participation of the Satellite Site, the SSS may be contacted by the Satellite Site to commence trial preparations in line with the protocol following the Workflow Checklist.
- discuss the Confidentiality Agreement and protocol including the logistics involved in transporting Investigational Products to each Satellite Site (sent directly by the Sponsor or forwarded from Primary Site), pathology, imaging and other trial-related assessments and investigations

- support budget negotiations with the Satellite Site
- may liaise with the Primary Site and the relevant Satellite Site to confirm all details in the Teletrials Subcontract are correct before sending the Subcontract to the Primary Satellite Site RGO or equivalent for signing
- collaborate with the Sponsor, Primary Site and Satellite Site to organise site initiation of the Satellite Site

Appendix 1 - Participant Information Sheet and Consent Form (PICF)

- The Primary Site will use the standard templates for interventional studies. Templates can be found on Clinical Trials and Research - Ethics Application webpage
- The Stand Alone Teletrials PICF is used for an approved trial when a teletrial component or addition of teletrial sites will be added and can be found on the Clinical Trials and Research - Teletrials webpage.

Appendix 2 - Guidelines for Victorian HRECs reviewing Teletrial ethics applications

Initial ethics application to a Victorian HREC

There is no change to the ethics submission (HREA) process for HREC review when an application for a clinical trial is intended to be conducted under the Teletrials Model.

It is recommended that the reviewing HREC receive the Primary Site Supervision Plan and Delegation Log of duties and responsibilities in the ethics submission. These will be 'Master' documents. The Primary Site Supervision Plan and Delegation Log are submitted to the Reviewing HREC to ensure patient safety and to check the PI and other CV's reflect appropriate experience and expertise to undertake the assigned research activities.

All participating sites are identified in the HREA (ERM Filter Questions) as a Regular Site, Primary Site or Satellite Site.

The agreement from the Sponsor to allow the inclusion of Satellite Sites under the Teletrials Model should also be included with the HREC application.

The HREC approval letter should list each Satellite Site as a participating site supervised by a (named) Primary Site.

Participant Information Sheets and Consent Forms and consent process

The Master PICF (standard template for interventional studies) with the optional teletrials wording and additional question relating to ATP reporting purposes is used and included in the ethics application for HREC review.

However, if an approved trial is to be converted to a teletrial, the Stand Alone Teletrial PICF is used and will need HREC approval prior to its use. This form is used when some but not all participating sites will conduct the trial as a teletrial at their site. Use of this PICF means that the Master PICF does not require amending to incorporate the teletrial specific wording. If an approved trial with every participating site agrees to convert to a teletrial then the Master PICF should be amended to include the specific teletrial wording.

The agreed process for consent at Satellite Site(s) should be included in the Supervision Plan as indicated in the Delegation Log.

Investigator Curricula Vitae

The HREC may request a copy of the Associate Investigators' Curriculum Vitae at each Satellite Site, even though Associate Investigators at Satellite Sites are under the supervision of the Principal Investigator at the Primary Site. The HREC must be satisfied that Associate Investigators at Satellite Sites are appropriately qualified for the role.

Ethics amendments

The following changes to an approved trial require HREC approval:

- Changing an approved clinical trial to a teletrial and every participating site agrees to convert to a teletrial

  - An ‘Ethics Amendment Request’ form is submitted by the CPI to the HREC indicating the relevant amendment category – *Become teletrial*. Associated ethics supporting documents, including the Sponsor agreement letter are included in the submission
  - The Master PICF (standard template) is amended to include the teletrial specific wording
- Changing an approved trial to a teletrial (some but not all participating sites will conduct the trial as a teletrial at their site) and new teletrial sites will be added
  - An ‘Ethics Amendment Request’ form is submitted by the CPI to the HREC indicating the relevant amendment category – *Become teletrial* and *Add site.* Details of new sites (Primary Site or Satellite Site) are provided and associated ethics supporting documents, agreement letter
  - The Stand Alone Teletrial PICF is included in the submission
  - The Master Primary Site Supervision Plan and Master Delegation Log is included in the submission.

The HREC’s Form of Indemnity must also be updated to include the Satellite Sites.

Participants at new sites may not be enrolled until:

- an Ethics Amendment Approval letter/certificate from HREC has been received
- research governance requirements at the participating site have been fulfilled – Authorisation of SSA form, Supervision Plan and regulatory requirements e.g., CTRA, Teletrial Subcontract
- site initiation has been completed.

Patient Enrolment – Urgent Cases

In situations where a patient has been identified as a potential participant in a particular clinical trial at a site that is not already a Satellite Site, and recruitment and administration of trial IMP are urgent or time-sensitive, the participant must be transferred to the suitable Primary or participating Satellite Site where the trial has already been activated or implemented. The Site Initiation Visit has been conducted and Site Activation Letter has been received and provisions regarding urgent medical procedures under the *Medical Treatment Planning and Decisions Act 2016* has been considered.

Post approval reporting

For single site studies, the PI is responsible for post approval reporting to the reviewing HREC.

For multisite studies, the Primary Site takes responsibility for all reporting to the CPI on behalf of each Satellite Site under the Supervision Plan.

For each clinical trial that is conducted under the Teletrials Model, the CPI/Sponsor is responsible for completing a ‘Project Progress Report’ (annual report) and submitting to the HREC. It includes collated information from each participating site (Regular site, Primary Site or Satellite Site).

The Project Progress Report should also include any specific impact of the Teletrials Model on the conduct of the study in the ‘Summary of progress’ section.

Safety reporting

The Primary Site takes a responsibility for all safety reporting to the CPI on behalf of the cluster.

Safety reporting includes the following:

- Annual Safety Report
- Safety Report
- Serious Breach Report

- Suspected Breach Report

Safety reporting to the HREC should follow NHMRC Guidance *Safety monitoring and reporting in clinical trials involving therapeutic goods* (November 2016) and any specific requirements requested by the HREC in the approval letter.

Appendix 3 - Guidelines for Victorian RGOs reviewing Teletrial governance applications

Initial governance application to RGO

A Research Governance checklist is available on the clinicaltrialsandresearch website which includes all requirements for a governance application.

If the site RGO uses ERM to process governance applications, they will have automatic access to all documents uploaded to the ethics application (if Victoria or QLD HREC review). This means that only site governance documents need to be uploaded to the SSA.

The PI uses ERM to submit the governance application (SSA form) to the site RGO, including:

- Cover letter from the Primary Site PI with -
  - A statement: “The study is to be conducted under the Teletrial Model with [Primary Site name] and [insert sites] as the Satellite Site/s.
  - List of documents uploaded to the SSA form for RGO review
  - Information if ionising radiation is standard of care (SOC) or study specific, or if study-specific reporting is required in addition to SOC (where applicable).

    The following website link describes Victorian requirements

    Look for ‘Use of ionising radiation’ section at:
    https://www.clinicaltrialsandresearch.vic.gov.au/ethics-application
- The SSA form will include the following uploaded documents –
  - Copy of HREC Approval letter/certificate
  - Copy of HREC Amendment Approval letter (if relevant) plus latest ethics approved amendment documents
  - Research team documents e.g., CVs, GCP training
  - Supporting Department(s) Declarations
  - Site PICF (site version of Master PICF) or Site PICF (site version of Stand Alone PICF) plus site version of Master PICF - Appendix 1 - Participant Information Sheet and Consent Form (PICF)
  - CTRA, Teletrial Subcontract (if a Satellite Site)
  - Indemnity Form +/- Insurance Certificate
  - Evidence of CTN/CTA if required by RGO
  - Other site-specific documents as required, for example the Site Supervision Plan and Site Delegation Log, based on the Master documents reviewed by the HREC.

For submission to a RGO that does not use ERM, a SSA form can be completed in ERM and saved as a pdf (**View as PDF**) and submitted to the RGO as hard copy/email, but not submitted in ERM unless an arrangement is agreed with the Primary Site.

RGO authorisation

For RGO review:

- SSA form and supporting governance documents

- CTRA – check details are correct. A Research Agreement Checklist is available in the Research Governance and Site Specific Assessment-Process and Practice guidance document Appendix 6
- Teletrial Subcontract agreement between the Primary Site and each Satellite Site – check details are correct
- Indemnity – check details are correct. An Indemnity Checklist is available in the Research Governance and Site Specific Assessment-Process and Practice guidance document Appendix 7

Authorisation:

- An Authorisation letter/certificate should list all documents reviewed by the RGO for accuracy/completeness and in line with the site's resources
- Communication with the Satellite Site RGO/delegate to highlight any local site's governance considerations. This is to ensure that the Satellite Site RGO/delegate has evaluated the site capability and capacity to conduct the trial.

Appendix 4 - Teletrial Monitoring and Safety Reporting Plan

Safety monitoring and reporting should align with the NHMRC *Safety monitoring and reporting in clinical trials involving therapeutic goods* (November 2016) guidelines.

- For clinical trials of IMPs or Investigational Devices, all significant safety issues, including SUSARs, USMs, or USADES arising from sites within the cluster, must be reported to the Sponsor within 24 hours of becoming aware of the event.
- Where a SUSAR, USM or USADE occurs at a Satellite Site, the Satellite Site investigator is responsible for reporting to both the Principal Investigator of the cluster and the Sponsor within the required timeframes.
- All SUSARs, USM or USADEs must be reported to the Primary Site RGO, and Satellite Site RGO or equivalent if occurring at a Satellite Site.
- All documentation must be signed by the Primary Site PI and relevant Satellite Site AI.
- All documentation must be submitted to the RGO(s) electronically via ERM where possible, otherwise alternative submission methods should be used.
- On receipt of an updated Investigator Brochure, protocol amendment, or other routinely supplied safety updates, the PI is responsible for distributing the information to AI at each Satellite Site within the cluster.
- For urgent safety updates, the PI is responsible for contacting all AIs within the cluster to update and advise.

Appendix 5 - Websites used in this document

Reference	Website
Clinical Oncology Society of Australia (COSA)	https://www.cosa.org.au/about/
International Conference on Harmonisation Good Clinical Practice (ICH GCP)	https://www.ich.org/
Medical Technology Association of Australia CIRA (MTAA CIRA)	https://www.mtaa.org.au/clinical-investigation-research-agreements
Medicines Australia CTRAs Teletrial Subcontract	https://www.medicinesaustralia.com.au/policy/clinical-trials/clinical-trial-research-agreements/
Medicines Australia Forms of Indemnity	https://www.medicinesaustralia.com.au/policy/clinical-trials/indemnity-compensation-guidelines/
National Teletrials Compendium and Standard Operating Procedures and Principles (TT SOPs)	https://www.health.gov.au/resources/collections/the-national-teletrials-compendium
NHMRC Guidance on Safety Reporting in Clinical Trials involving Therapeutic Goods	https://www.nhmrc.gov.au/about-us/publications/safety-monitoring-and-reporting-clinical-trials-involving-therapeutic-goods
NHMRC: The National Statement on Ethical Conduct in Human Research	https://www.nhmrc.gov.au/about-us/publications/national-statement-ethical-conduct-human-research-2007-updated-2018
Victorian Clinical Trials and Research website PICF templates	https://www.clinicaltrialsandresearch.vic.gov.au/ https://www.clinicaltrialsandresearch.vic.gov.au/ethics-application
Therapeutic Goods Administration	https://www.tga.gov.au/clinical-trials#clinical-trials-guidance