UTS IMPACCT Trials Coordination Centre

Standard Operating Procedure

Glossary

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Adverse Event (AE)
Any untoward or unexpected occurrence in a clinical investigation participant where the occurrence does not necessarily have a causal relationship with the study intervention.

An adverse event can be any unfavourable, unusual or unintended sign, response, symptom, or disease where the outcome was not expected and has potentially negative consequences for the participant or the caregiver. This can include events such as:

- An abnormal laboratory finding
- An abnormal or unusual emotional or cognitive response
- Distress caused by the burden of the intervention or by participation and can occur:
    - During participation in a study, if absent at baseline
    - During participation in a study, if present at baseline, can appear to worsen
    - After completion and exiting from a study but as a direct result of participation
- Distress that occurs outside of clinical investigations in settings such as focus groups or questionnaire responses
- A response or reaction that was not anticipated

Adverse Drug Reaction (ADR)
Drugs, or medicines, are routinely trialled prior to general release to establish therapeutic dose, safety and efficacy; or to test the drug outside of the registered use. During such a trial, any noxious and unintended response to the medication related to any dose is considered to be an ADR.

The phrase ‘responses to a medicinal product’ means that a causal relationship between that medicinal product and an adverse event is at least a reasonable possibility, i.e. the relationship cannot be ruled out.

Any unintended response during a trial of a medication is regarded as an ADR or adverse event.

The reaction is considered unexpected where the nature or the severity is inconsistent with the product information or the investigators brochure.

Allocation
The assignment of an intervention to the participant enrolled in an IMPACCT Trials Coordination Centre (ITCC) or PaCCSC or CST study according to the randomisation table.

Allocation code
The code that is assigned to an intervention to which a participant is allocated. The Allocation Code is the output from the randomisation process. This code (for e.g., A=intervention 1, B=intervention 2, and C=intervention 3) does not change throughout the study or from one site to another.

Amendment
A change to a document which results in a new version and submission to a Human Research Ethics Committee (HREC) for approval or to other regulatory documents such as TGA Clinical Trial Notifications or clinical trial registries. Examples of amendments include:

- changes to the intervention or intervention period
- major changes to study design (for e.g., introduction of a further intervention arm)

- changes to inclusion or exclusion criteria
- addition of tests or procedure

Amendment Types

- **Minor change (to document)**
  The document is updated for typing, formatting, or noting of changes in non-essential site information. The change(s) do not impact on the conduct of the study, HREC approval is not required.
- **Significant change (to document)**
  The document is updated to clarify specific sections, or where the changes are defined as significant modifications (for example, protocol amendments).
- **Major change (to document)**
  The document is updated, and the changes have an impact on the content.

Annual Research Forum (PaCCSC)

An annual scientific meeting convened by PaCCSC and open to anybody with an interest in palliative care clinical trials. The aim of the forum is to share knowledge and build capacity within the palliative care research community. The forum also provides an opportunity for the presentation of current, planned or recently undertaken research studies in palliative care in Australia.

Annual Research Forum (CST)

An annual scientific meeting convened by CST and open to anybody with an interest in cancer symptom management and supportive care. The aim of the forum is to share knowledge and build capacity within the cancer symptom management and supportive care research community. The forum also provides an opportunity for the presentation of current, planned or recently undertaken research studies in cancer symptom management and supportive care in Australia.

Assessment Codes – Levels of Deficiency

As part of the monitoring process, an overall assessment is made of the site visit based on the levels of deficiencies recorded in the ITCC Corrective Actions Sheet subsequent to the review. These are:

- None
  - Complete
  - Error free, or corrected appropriately
  - Filed and accessible
  - Clear documentation of procedures
- Minor
  - Source data does not support CRF entry
  - Late approvals
  - Poor filing and documentation
  - Difficult to follow errors
- Major
  - Approvals absent
  - Protocol violation

- Critical documents not available
- Errors not accounted for

Assessment Codes – Overall

As part of the monitoring process, the overall assessment recorded in the ITCC Monitoring Report will be one of the following:

- Acceptable
  - No deficiencies
  - Few minor deficiencies
  - Major deficiencies were identified and/or corrected prior to the monitoring visit, and no further action is required
- Acceptable needs follow-up
  - Any major deficiency identified during the monitoring visit, not identified or corrected prior to the visit
  - Multiple minor deficiencies identified
- Unacceptable
  - Multiple major deficiencies identified
  - A single major blatant deficiency (total disregard for protocol)
  - Excessive number of minor deficiencies

Audit

A systematic and **independent** examination of study related activities, documents and performance to determine whether the evaluated study related activities were:

- Conducted
- The data recorded, analysed, and accurately reported according to:
  - Protocol
  - Standard Operating Procedures (SOPs)
  - Good Clinical Practice (GCP)
  - Regulatory requirement(s)

Audit is the process of evaluating the study by individuals independent of the study, at the request of the relevant Scientific Advisory Committee.

This ensures compliance by the investigating sites.

Auditor

An individual trained in research who has also undergone specific training on study audit related activities. The auditor uses their research experience and training in the auditing process to ensure that the work being conducted is of the highest quality and meets established guidelines. The auditors are independent of PaCCSC and CST who, in conjunction with the PaCCSC/CST National Manager, audit all investigating sites, including the ITCC. The auditor's qualifications are verified and documented by the ITCC.

Auditee
The study site(s) or individual(s) whose practices, processes and outcomes are being audited. All PaCCSC and CST study sites are eligible for auditing, including the clinical teams and pharmacies where records regarding the study drugs are held. The ITCC, the organisation contracted to undertake the development of the randomisation schedules, and individual investigators may also be auditees.

Audit Report
A written evaluation by the auditor of the results of the audit.

Australian New Zealand Clinical Trials Registry
The Australian New Zealand Clinical Trials Registry (ANZCTR) is an online register of clinical trials being undertaken in Australia and New Zealand. The ANZCTR includes trials from the full spectrum of therapeutic areas of pharmaceuticals, surgical procedures, preventive measures, lifestyle, devices, treatment and rehabilitation strategies and complementary therapies. It has nationwide coverage of all clinical trials involving Australian researchers or Australian participants.

Australian Code for the Responsible Conduct of Research
The Code developed jointly by the National Health and Medical Research Council (NHMRC), the Australian Research Council (ARC) and Universities Australia to guide institutions and researchers in responsible research practices and to promote research integrity.

Blinding
The procedure in which one or more parties in the study are kept unaware of the treatment assignment (i.e. medicine 1 vs medicine 2, study medicine vs placebo) or the allocation code (i.e. A or B). Most PaCCSC and CST studies are double-blind, meaning that the participant, investigators, and other study staff are unaware of the treatment assignment. This process is also called “masking”. The allocation code and participant’s treatment assignment are known to the following:

- The Site Pharmacy at each site involved in preparation and administration of blinded medicine as the study intervention. The site pharmacy holds the record of randomisation for that site
- The external third-party pharmacy contracted by the Study Sponsor to prepare and dispense the blinded medicine as the study intervention directly to the study participants for studies using a ‘Just in time’ direct to patient model. The external third-party pharmacy holds the record of randomisation for all recruiting sites.
- The Study Statistician who is responsible for reporting unblinded analyses to the Data Safety Monitoring Committee (DSMC).
- The Central Randomisation Centre where the schedules for each site are developed.

Cancer Cooperative Trials Groups (CCTGs)
There are 14 national Cancer Cooperative Trials Groups (CCTGs) in Australia conducting world-class multi-disciplinary research for cancer control. Cancer Symptom Trials (CST) is one of these groups with a focus on cancer symptom management and supportive care.

Case Report Form (CRF)
A printed, optical, or electronic document designed to record all of the protocol required information to be reported to the ITCC for each participant. All events described within the study protocol are captured in the CRF.

Central Randomisation Service

The service where the allocation codes for the whole study, across all sites, are generated. The schedule for each site is prepared and sent to the ITCC for distribution to the individual site pharmacies or the external third-party pharmacy.

Central Registry
The location that holds the allocation codes for each participant in a study in the form of unblinding envelopes. This will vary from one study to the next and is specified within the study protocol. This location may include; the site pharmacy, a central pharmacy (a pharmacy nominated to hold the unblinding envelopes), the Coordinating Principal Investigator, or delegate, or the Central Randomisation Service.

Clinical Trial Research Agreement (CTRA)
A document between clinical trial research sponsors and institutions, formalising the roles, responsibilities and procedures in a research study. The CTRA outlines standard contractual obligations for all parties for the conduct of the study at that site. In addition, the CTRA contains detailed information about the budget, protocol and HREC submission documentation and any other site-specific clauses that are agreed to by both parties.

The CTRA templates used by ITCC were jointly developed by the Governments of New South Wales, Queensland, Victoria and South Australia; and Medicines Australia to promote fairness to all parties.

Clinical Trial Notification (CTN) Form
The Clinical Trial Notification (CTN) form is a document completed electronically and submitted by the Study Sponsor to notify the Therapeutic Goods Administration (TGA) of their intent to sponsor a clinical trial involving an 'unapproved' therapeutic good. This must take place before starting to use the goods. In the CTN form, the Sponsor must provide details regarding the trial including the therapeutic good (medicine, medical device or biological) and the institution(s) or organisation(s) at which the trial will be conducted. This submission results in the acknowledgement by the TGA to conduct the study at the named site (on the CTN form). Recruitment must not commence at the site before this acknowledgement is obtained.

Clinical Trial/Study
A research investigation in which people (participants) volunteer to test new treatments, interventions or tests as a means to prevent, detect, treat, or manage various diseases or medical conditions. Participants are assigned to receive one or more interventions (or no interventions) so that researchers can evaluate the effects of the interventions on biomedical or health related outcomes (including clinical, pharmacological and pharmacodynamic outcomes). This helps determine if a new intervention works, if it is safe, and if it is better than interventions that are already available. The terms clinical trial and clinical study are synonymous.

Clinical Trial/Study Report
A full and comprehensive written description of a trial/study of any therapeutic, prophylactic, or diagnostic agent conducted in participants, in which clinical and statistical description, presentations, and analyses are fully integrated into a single report.

Concurrent Medication
Any compound taken by a participant for medicinal purposes during the course of their participation in a clinical trial. Concurrent medications include (but are not limited to):

- Prescription medications
- Herbal / homeopathic medications
- Over-the-counter medications

Confidentiality
Prevention of disclosure, to other than authorised individuals, of a sponsor's proprietary information or a participant's identity.

Conflict of interest
A conflict of interest can arise when a person is faced with a decision that may be influenced by two or more competing interests. These may include:

- A financial conflict of interest, involving money, shares, stock or other matters
- A non-financial conflict of interest, related to personal matters
- A real conflict of interest actually exists
- A perceived conflict of interest may be thought to exist and may require confirmation by others

Coordinating Centre (PaCCSC and CST)
The Coordinating Centre for PaCCSC and CST is the IMPACCT Trials Coordination Centre (ITCC) at IMPACCT (Improving Palliative, Aged and Chronic Care through Clinical Research and Translation) at the University of Technology Sydney. The PaCCSC/CST National Manager and National Project Officer at this centre work closely with the Coordinating Principal Investigator, all Principal Investigators, the local site staff, the Study Statistician, and the Central Randomisation Service to manage the operational study procedures.

Coordinating Principal Investigator (CPI)
The coordinating principal investigator who leads the study protocol development. The CPI of a multi-centre study also takes responsibility for the coordination of the principal investigators at different participating/recruiting sites involved in a trial.

Data Collection Worksheet
Data collection worksheets are designed to capture required data and to enable smooth data entry in electronic case report forms (eCRFs) through similar question and response structures to minimise data entry errors. These worksheets may be considered source documentation, where the worksheet is the first recording of study data.

Data Custodian
Person or entity responsible for holding a dataset. Data custodians collect and hold research data on behalf of the Coordinating Principal Investigator.

Data Management Plan
A document that describes what data will be collected during a project and how it will be managed. A Data Management Plan addresses:

- Data ownership and responsibilities
- Legal rights
- Data securing and sustainability
- Access and reuse of data

Data Owner
Data resulting from any activity of the Palliative Care Clinical Studies Collaborative (PaCCSC) or Cancer Symptom Trials (CST) is owned by University of Technology Sydney. Accountabilities for working with the data are assigned as follows:

- PaCCSC Chief Investigator – holds overall authority regarding the collection, storage, access, security and primary and secondary use of all data created or held by PaCCSC from any activities.
- CST Chair – holds overall authority regarding the collection, storage, access, security and primary and secondary use of all data created or held by PaCCSC from any activities.
- PaCCSC/CST National Manager/ ITCC National Project Officer – act as delegates of the PaCCSC Chief Investigator to ensure that the collection, storage, access, security and primary and secondary use of all data created or held by PaCCSC from any activities is managed according to the relevant Standard Operating Procedures and risk management strategies engaged by PaCCSC.

Day 1
The day the intervention commences. Days are numbered according to the study schema (detailed in the study protocol).

Delivery
Where the Investigational Product is given to the participant after dispensing by the pharmacy. For example, where the Investigational Product is delivered by a study team member to the participant for either self-administration or for administration via an infusion or other route.

Destruction
A means by which records are destroyed, which renders them unable to be read, accessed or used at any time in the future.

Dispensing

Where the Investigational Product is provided to the study participant by the pharmacist who prepared the drug. In most cases this will be a secondary process, as the Investigational Product may be dispensed to the study team member for delivery to the participant.

Dispensing (Direct to Patient)

The process of providing the Investigational Product directly to the study participant by a third-party pharmacy that is external to the recruiting site and has been contracted by the Sponsor to prepare the study medication. Provision of the Investigational Product is on a ‘Just in Time’ basis upon receipt of a prescription.

eCRF

Electronic case report forms (eCRFs) are designed to capture required data in the REDCap Electronic Data Capture (EDC) database and to enable smooth data entry in data collection worksheets through similar question and response structures to minimise data entry errors.

e-Consent

E-Consent, or electronic consent, is where the process of obtaining participant consent for a clinical trial uses electronic means, and may include passive and interactive systems and webpages, the inclusion of multiple media such as text, graphics, audio, and video etc to convey information related to a clinical trial and to document the informed consent.

e-Monitoring

E-monitoring, or electronic monitoring, is carried out remotely on the eCRFs generated in the REDCap EDC database. It follows that the procedures related to source data verification are conducted by the local PI and by the local study team.

The central monitor checks that eCRF data entry is up to date and monitors the completion of participant data collection worksheets. The central monitor discusses with the site PI and local study team the issues identified during data verification activities, by following the REDCap data resolution workflow.

Essential documents
Documents that:

- Permit evaluation of the conduct of a trial and the quality of the data produced
- Are usually audited and inspected by the regulatory authorities to demonstrate compliance with GCP and all other regulatory requirements
- Assist with trial management
- Are those usually audited and monitored
- Confirm the validity of the trial conduct and the integrity of the data collected

Exclusion Criteria
A list of conditions that exclude a potential study participant from participating in the study. These conditions may include (but are not limited to):

- Age groups
- Disease groups or types
- Clinical events
- Family circumstances
- Previous medical history
- Concurrent medications
- Clinical investigation results (for e.g., blood tests)

File Notes
Short documents that are used to explain discrepancies in data, deviations from protocol, and where sites have specific procedures that vary from the study protocol. Examples include (but are not limited to):

- Discrepancy between source documents and CRF entries
- Source data cannot be located
- A deviation between randomisation request and allocation is found

File notes serve to provide verification that data was collected and recorded according to established procedure.

Good Clinical Practice (GCP)
A standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical studies that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of participants are protected. The GCP guideline was developed by International Conference on Harmonisation (ICH) in 1996.

Grading
Where possible, the grade or severity of the event is established. The Common Terminology Criteria for Adverse Events are recommended, and the relevant sections are included in study protocols and CRFs. See https://ctep.cancer.gov/protocolDevelopment/electronic_applications/ctc.htm#ctc_50

Human Research Ethics Committees (HREC)
An independent body (a review board or committee, institutional, regional, national or supranational), duly constituted of medical professionals and non-medical members, whose responsibility it is to ensure the protection of the rights, safety and well-being of participants involved in a trial and to provide public assurance of that protection by, among other things, reviewing and approving/providing acceptance opinion on the study protocol, the suitability of the investigator team, facilities, and the methods and material to be used in obtaining and documenting informed consent of the participants.

Impartial Witness
A person, who is independent of the study, who cannot be unfairly influenced by people involved with the study, who attends the informed consent process if the potential participant or their legally acceptable representative cannot read, and who reads the informed consent form and any other written information supplied to the potential participant. The witness signs the consent form to indicate that the consent process was followed, not to witness the signature alone. Some PICFs contain a witness signature block, if no witness was required as part of the consent process, this block can be left blank.

Inclusion Criteria
A list of requirements that potential study participants must meet in order to be eligible to participate in the study.

Informed Consent
A process by which a participant voluntarily confirms his or her willingness to participate in a particular study, after having been informed of all aspects of the study that are relevant to their decision to participate. Informed consent is documented by means of a written, signed and dated consent form, unless otherwise dealt with in an institutional ethics approved protocol.

Where a potential participant lacks the capacity to give consent (as with PaCCSC and CST studies using a proxy consent process), the person or appropriate statutory body exercising lawful authority for the potential participant should be provided with relevant information and decide whether he or she will participate.

Intellectual Property
Intellectual property (IP) means any proprietary right which arises under, or is capable of being obtained under, legislation relating to copyright, patents, designs, circuit layouts or plant varieties, or which otherwise exists at law, including trade secrets, know-how and other confidential information and unregistered trademarks and tradenames.

Interim Analysis
An analysis of the data before a trial has been completed, to obtain any evidence that the treatment might be harmful.

Interim Clinical Trial/Study Report
A report of intermediate results and their evaluation based on analyses performed during the course of a trial.

Intervention
The investigational product, equipment or procedure being tested by the study protocol. The interventions vary according to each study protocol. Interventions in ITCC/PaCCSC/CST studies may include investigational products prepared so that the active and inactive (or active and comparator) are identical in look, smell and taste.

Investigational Product (IP)
A pharmaceutical form of an active ingredient or placebo being tested or used as a reference in a clinical study, including:

- A product with a marketing authorisation when used or assembled (formulated or packaged) in a way different from the approved form.
- A product with a marketing authorisation when used for an unapproved indication.
- A product with a marketing authorisation when used to gain further information about an already approved use.

Journal Notes
Journal notes provide rich additional data to explain data held within the Case Report Form (CRF). For example, when quality of life (QOL) is being measured and the participant has had a recent bereavement, a journal note can record the bereavement to explain why the QOL may record unexpected data. Journal notes do not replace study data recorded within the CRF.

Key Performance Indicators (KPIs)
Key performance indicators are data elements that are monitored routinely and identify how effectively study sites and the study are meeting the mutually defined endpoints and timelines. Examples of KPIs include:

- Recruitment numbers
  - Referral to screening
  - Screening to eligibility
  - Eligibility to consent
  - Consent to completion
  - Screening to completion
  - Loss to follow-up
- Actual versus projected recruitment estimates
- Withdrawal rates and reasons for withdrawal
  - Safety monitoring
  - Missing data

Specific KPIs vary from study to study. Each study has particular issues related to recruitment, retention or follow-up which require specific focus. KPIs in the ITCC/PaCCSC/CST studies are similar between studies, mainly due to the target population of the studies (people receiving palliative care and or cancer symptom management and supportive care).

Legally Acceptable Representative
An individual or juridical or other body authorised under applicable law to consent, on behalf of a potential participant, to their participation in the study. This is also referred to 'Third party consent' or 'Proxy consent'.

Management Advisory Committee (CST)
The Cancer Symptom Trials (CST) Management Advisory Committee (MAC) is responsible for the strategic governance of CST. The MAC operates in accordance with its terms of reference.

Monitoring
The act of overseeing the progress of a clinical study, and of ensuring that it is conducted, recorded, and reported in accordance with the protocol, SOPs, GCP, and any applicable regulatory and legislative requirements.

Monitoring is a process internal to the clinical study, where the study management, investigators or other groups within the study can monitor their own progress and ensure that the study complies with internal and external requirements.

This process differs from 'audit' which is a process conducted by personnel external to the study. Monitoring enables problems and deficiencies to be detected and corrected at an early point, to be dealt with prior to auditing and to assist sites' ability to meet study requirements. Monitoring enables the study team to be confident about undergoing an external audit process.

Monitor
An individual trained in research who has also undergone specific training on audit related activities. Within ITCC/PaCCSC/CST, the monitors include the site coordinators who, in

conjunction with the PaCCSC/CST National Project Officer or delegate, monitor other PaCCSC and CST investigating sites.

The study monitor is thoroughly familiar with the study protocol, investigational product, consent processes and related study requirements.

The study monitor has completed training at the ITCC and is responsible for:

- Answering study related questions.
- Providing additional support to the site in order to successfully complete their recruitment and regulatory obligations.
- On site data verification.
- Resolution of outstanding data queries.
- Documenting and reporting visits.
- Completing a monitoring log for filing at the study site

Monitoring Log
A record of all monitoring visits for a specific study at a specific site. The monitoring log is held at each site for each study. It is signed by the monitor at the end of each monitoring visit.

Monitoring Report
A written evaluation by the monitor of the outcomes from the monitoring visit.

Multi-centre Trial
A clinical trial conducted according to a single protocol but at more than one site, and therefore, carried out by more than one principal investigator.

Non-serious or Expected Adverse Event

Expected adverse events are recorded and reported within the ITCC/PaCCSC/CST participating sites in accordance with the ICH GCP guidelines. These events are reported to the local HREC as part of the annual reporting requirements, and also aggregated by the Coordinating Centre.

In ITCC/PaCCSC/CST studies, non-serious or expected adverse events include expected death in the palliative care setting, where there is no indication that the intervention contributed to a hastened death, especially if the study requires participation or follow-up to death, or where death is expected as part of the disease trajectory, and where death is attributed to the underlying disease or sequelae.

Each HREC associated with ITCC/PaCCSC/CST sites have provided direction on the reporting of expected deaths of participants. These reporting timeframes are negotiated locally, and the outcomes are summarised in the table “Reporting Expected Deaths”.

Participant
An individual who participates in a study, either as a recipient of the investigational product(s) or as a control or who provides study data in some other capacity.

Participant Identification Number (PID number)
A unique identifier assigned by the principal investigator to each participant in the study to protect their identity and used in lieu of the participant’s name. The PID number is usually a combination of the study code, site code and participant number. For example, 01/02/001.

Patient Master Index
A list of all people who proceed to the screening stage (following pre-screening and obtaining consent) of recruitment, regardless of whether the participant goes on to be randomised. A Patient Master Index is maintained for each study at each site and is used for reporting on Key Performance Indicators for the site. The Patient Master Index is an Essential Document which provides a link between the study PID and the participant personal details for the purposes of identifying each participant with the medical record.

Permanent Record
A record which has archival value and may be required to be permanently retained after the administrative value or 15 years has elapsed (whichever is sooner). Research record that are kept as a permanent record relate to:

- Legitimate and sustained allegations of misconduct that resulted in a formal inquiry and appeals
- The preparation and submission of applications to conduct research
- The establishment of committees/boards/task force, and the records of the meetings
- Meeting the requirements of the National Health and Medical Research Council (NHMRC) such as annual reports
- Evaluation of significant programmes
- Obtaining resources to undertake significant projects, which may include project plans, grant proposals, funding applications
- Development of agency wide policies relating to research and ethical research conduct
- Master copies of final reports, published and unpublished produced by the researcher which document the findings and outcomes

Pilot Study (also known as a Feasibility Study)
A small scale, preliminary study conducted to test the feasibility of a large-scale study. Elements tested in a pilot study include (but are not limited to):

- Practical application of the protocol
- Ability to recruit
- Effect size (statistical variability)
- Prediction of appropriate sample size for a larger study

Phase III (3) Study
Clinical trials are conducted in a series of steps (phases). Each phase is designed to answer a separate research question. Phase III (3) clinical trials is when the intervention (Investigational Product) is given to a large group of people to confirm its effectiveness, monitor side effects, compare it to commonly used treatments, and collect information that will enable the intervention to be used safely.

Pharmacy Communications Plan

A document that outlines the ‘Direct to Patient’ dispensing arrangement between the Sponsor and the contracted external partners and includes details related to the investigational product, licensing, supply, randomisation, returns and destruction process and records management. The

plan details the scope of work and how critical information will be handled and delivered between the parties throughout the study and at what frequency, particularly in relation to adverse events and maintaining participant privacy and confidentiality A pharmacy communication plan is to be prepared for each ITCC/PaCCSC/CST study utilising 'Just In Time' direct to patient dispensing through a contracted pharmaceutical development and manufacturing organization, and their sub-contracted external third-party pharmacy.

Pre-screening
The evaluation of a set of characteristics assessed and recorded prior to screening that determine eligibility to participate in the study. Examples of pre-screening include chart review and discussion with clinical team. The pre-screening information assists the study team member to determine if the potential participant should proceed to screening.

Prescribing
The written prescription (where applicable) detailing the Investigational Product for a specific participant.

Privacy Act
The Privacy Act 1988 (Privacy Act) regulates how personal information is handled. The Privacy Act defines personal information as:

> *"[…] information or an opinion, whether true or not, and whether recorded in a material form or not, about an identified individual, or an individual who is reasonably identifiable."*

Common examples are an individual's name, signature, address, telephone number, date of birth, medical records, bank account details and commentary or opinion about a person.

The Privacy Act includes thirteen Australian Privacy Principles (APPs), which apply to some private sector organisations, as well as most Australian and Norfolk Island Government agencies. These are collectively referred to as 'APP entities. The Privacy Act also regulates the privacy component of the consumer credit reporting system, tax file numbers, and health and medical research.

Privacy Act - Health and Medical Research
In certain circumstances, the Privacy Act permits the handling of health information and personal information for health and medical research purposes, where it is impracticable for researchers to obtain individuals' consent. This recognises:

- The need to protect health information from unexpected uses beyond individual healthcare
- The important role of health and medical research in advancing public health

To promote these ends, the Privacy Commissioner has approved two sets of legally binding guidelines, issued by the National Health and Medical Research Council (NHMRC). Researchers must follow these guidelines when handling health information for research purposes without individuals' consent. The guidelines also assist Human Research Ethics Committees (HRECs) in deciding whether to approve research applications. The guidelines are produced under sections 95 and 95A of the Privacy Act. The guidelines are:

- Guidelines under Section 95 of the Privacy Act 1988, which set out procedures that HRECs and researchers must follow when personal information is disclosed from a Commonwealth agency for medical research purposes.

- Guidelines under Section 95A of the Privacy Act 1988, which provide a framework for HRECs to assess proposals to handle health information held by organisations for health research (without individuals' consent). They ensure that the public interest in the research activities substantially outweighs the public interest in the protection of privacy.

Principal Investigator (PI)
The person responsible for the conduct of a clinical study at a participating/recruiting trial site. If a study is conducted by a team of individuals at a study site, the Principal Investigator is the responsible leader of the team. The Principal Investigator is qualified by education, training, and experience to assume responsibility for the proper conduct of the study, is thoroughly familiar with the use of the investigational product and is aware of (and complies with) the applicable regulatory requirements. The qualifications of the Principal Investigator are appropriate to their role in the study.

Protocol
A document that describes the objective(s), design, methodology, statistical considerations, and organisation of a study. The protocol also includes the background and rationale for the study (these can be provided in other protocol referenced documents). Consistent with the ICH GCP Guidelines, the term protocol refers to protocol and protocol amendments.

Protocol Amendment
A written description of a change(s) to, or a formal clarification of a protocol. An amendment results in a new version. Changes to an approved protocol are required to be approved by the Human Research Ethics Committee before the changes can be implemented. Examples of changes include (but are not limited to):

- Changes to the intervention or intervention period
- Significant changes to study design (for e.g., introduction of a further intervention arm)
- Changes to inclusion or exclusion criteria
- Addition of tests or procedure

Randomisation
The process of allocating participants to one treatment group or the other using an element of chance to determine the assignment. Randomisation is intended to reduce the chance of systematic bias that can be encountered when principal investigators, study staff, or study participants make decisions regarding which intervention is received by which participant. In most cases, blocks and standard random number tables are used to generate the allocation codes. An independent research group not associated with ITCC/PaCCSC/CST have been contracted to undertake the randomisation for ITCC/PaCCSC/CST studies.

Receipt
Where the prescribed Investigational Product has been handed over to another person. In most cases this will be to the study team member for transport and delivery to the participant.

Record holder
The person (nominated by the Principal Investigator) responsible for supervising the archiving, storage and destruction record of the study materials at the participating/recruiting site of a trial.

Recruitment
The process where people are identified, screened, and contacted for the study, or identified, screened and determined not to be eligible.

Reporting Expected Deaths
Each study protocol states the conditions and events that are excluded from the definition of an Adverse Event (AE) or Serious Adverse Event (SAE) and those which constitute a non-serious or Expected Adverse Event.

Relatedness of Adverse Event to an Intervention
The principal investigator includes the best estimate of the relationship between an intervention and an adverse event (AE) in the report. A guide to grading the degree of certainty about such a relationship is available at
https://ctep.cancer.gov/protocolDevelopment/electronic_applications/ctc.htm#ctc_50

A summary of this grading:

Unrelated	Where the AE is clearly not related.
Unlikely	Where the AE does not have a clear relationship to the intervention.
Possible	Where the AE follows a known pattern of response.
Probable	Where the AE reduces or ceases with withdrawal of the intervention or has a close temporal relationship to the intervention's introduction and is clinically plausible.
Definite	Where the AE ceased with withdrawal of the intervention or is an incontrovertible temporal relationship to the introduction of the intervention.

Research Data
The information, records, files, or other elements that form the basis of the main inferences, observations, findings, conclusions, outcomes or elements of a research project or publication, irrespective of the form in which it exists (for e.g., in print, electronic, physical, multi-media or other forms).

Data are pieces of information, for example:

- What people say in interviews, focus groups, questionnaires, personal histories, and biographies
- Study protocols, or part thereof; study instruments; any type of data collection form such as study diaries
- Analysis of existing information (clinical, social, observational or other)
- Information derived from human tissue such as blood, bone, muscle and urine

Data may be collected, stored or disclosed in three mutually exclusive forms:

- Individually identifiable data
- Re-identifiable data
- Non-identifiable data

Research data management system (RDMS)
Research Data Management Systems have been developed to support research work conducted through IMPACCT by providing access to a tool that:

- Enables the online design of data collection forms and questionnaires
- Allows for web-based and email-based form completion
- Enables data entry from multiple sites with a single coordinating site
- Provides for basic reporting of results with features such as percentages, graphs, and tables
- Allows export of data to other programs such as Excel, Access, or SPSS

The password protected system is used by ITCC for entry of all participant data collected during the course of each study.

Return
Where all used **and unused** Investigational Product and the associated records are returned to the pharmacy of origin after each participant has ceased their participation in the study.

Scientific Advisory Committee (CST)
The Scientific Advisory Committee is responsible for implementing the strategic objectives as determined by the Cancer Symptom Trials (CST) Management Advisory Committee (MAC) including the scientific review of clinical study proposals developed by the members, or through collaborative arrangements.

Screening
Screening is the collection of information that is additional to the clinical care from (or about) a potential participant. The information informs the potential participant's eligibility for the study. Screening data may include assessments for cognition, functional ability, taking blood samples, requesting medication history, etc. Screening information is collected following obtained consent.

Screen Failure
Where the person has provided consent after being fully informed of the study, and has been found ineligible, either because the inclusion criteria have not been met or an exclusion criterion was met.

Serious Adverse Event (SAE)
Any untoward medical occurrence that:

- Results in death (requiring rapid reporting on the day of discovery)
    - Results in attempted suicide (requiring rapid reporting on the day of discovery)
    - Is life-threatening (requiring rapid reporting on the day of discovery)
    - Requires a change in planned clinical management
    - Requires inpatient hospitalisation or prolongation of existing hospitalisation
    - Results in persistent or significant disability/incapacity
    - Requires ongoing medical or professional attention
    - Is judged to represent significant hazard
    - Results in anomaly or birth defect

In certain circumstances, serious adverse events do not require reporting:

- Planned surgery or medical intervention that was known at the start of the study (screening) for a pre-existing condition. By contrast, if this elective admission is extended due to some unexpected occurrence, this admission becomes a serious adverse event and should be reported.
- Overdose with no associated adverse reaction.

Site Pharmacy
The pharmacy that is contracted to undertake the randomisation at the study site, maintains the allocation logs, and supplies the study medicines. The Site Pharmacy collates and records the allocation codes for participants randomised at each study site and may provide out-of-hours access to the allocation codes (if acting as the Central Registry). The Site Pharmacy maintains a register of people in the study, and the allocation code for that site for the duration of the study.

Site-Specific Assessment (SSA)
The Site-Specific Assessment is where each site is required to address specific questions regarding the local approval, resources and implementation factors that may impact on the conduct of the study at that site. Each Australian state has different requirements; the SSA may be an 'add-on' to the ethics application system, a separate 'module' to be submitted with the ethics application system or a series of other locally developed documents. The SSA is assessed by the local research governance office prior to approval for local recruitment.

Source Documents
Original documents, data, and records such as hospital records, clinical file charts, laboratory notes, diaries, checklists, dispensing records etc. These documents allow for reconstruction and evaluation of the study. Data held within source documents are the **first record** of clinical observations. Examples include:

- Pathology reports to confirm blood results used at eligibility screening and throughout the study
- Clinical records charting patient clinical assessment, used to monitor patient eligibility or progress
- Dangerous Drug Accountability signature sheets to show correct checking and dispensing procedures
- Case Report Forms (CRF) where participant vital signs are recorded during a consultation (this is particularly relevant if this forms the only record of the vital signs and is not a transcription of vital signs recorded elsewhere)
- Quality of life (QOL) forms completed as part of the study measures, and where this recording is the original or only recording of the QOL at that time
- Other notations or records that form the data for the study

Source documents may also include the data recorded within CRFs (or contained on audiotapes) if these data form clinical data from which analysis is conducted, are not contained within other source documents and are specified within the study protocol. For example, if clinical observations are recorded within the CRF and used as study data, this is then source data.

Standard Operating Procedure (SOP)
Detailed, written instructions to achieve uniformity of the performance of a specific function.

State Records
Individual Australian states and territories have hospital, file archive and destruction procedures and facilities. 'State Records' refers to such a facility.

Stopping Rule
The criteria, defined in the trial protocol, for stopping a trial prior to completion due to evidence that continuing the trial may put the participants at risk or that there is already sufficient evidence of the efficacy of treatment.

Storage
Where the Investigational Product is stored on a temporary basis due to a delay (either planned or unplanned) in the transport from the receipt to delivery.

Stratum and Strata
A “stratum” designates the study group within which an individual participant is categorised (the pleural term for stratum is “strata”). This may be determined by demographic grouping (age group, gender, diagnosis), disease stage or other parameter where the investigators decide that stratification is required. Not all studies require stratification at the point of randomisation.

Study Site
The local site for participant enrolment and study conduct. Each site has a Principal Investigator, local site study staff, and an associated site pharmacy.

Study Statistician
The lead statistician for the study. The Study Statistician is responsible for all study analyses, and final study reporting. The Study Statistician is also responsible for reporting unblinded data to the Data Safety Management Committee or Medical Monitor). The Study Statistician may vary between studies.

Sub/Acting-Investigator
Any individual member of the clinical study team designated and supervised by the Principal Investigator at a study site to perform critical study-related procedures and/or to make specific study-related decisions.

Temporary Record
A record that does not have archival value and can be destroyed when the retention period has elapsed. In most cases this is 15 years.

Third-Party Pharmacy

A central pharmacy that is external to the recruiting sites and has been contracted by the Sponsor to undertake the randomisation for all participating study sites. The Third-Party Pharmacy maintains the allocation logs and supplies the study medicines. The Third-Party Pharmacy collates and records the allocation codes for participants randomised at each study site and may provide out-of-hours access to the allocation codes (if acting as the Central Registry). The Third-Party Pharmacy maintains a register of people in the study, and the allocation code for each recruiting site for the duration of the study.

Toxicity

The degree to which a substance can harm humans or animals. Toxicity can be acute, sub-chronic, or chronic:

- Acute toxicity involves harmful effects in an organism through a single or short-term exposure
- Sub-chronic toxicity is the ability of a toxic substance to cause effects for more than one year but less than the lifetime of the exposed organism
- Chronic toxicity is the ability of a substance or mixture of substances to cause harmful effects over an extended period, usually upon repeated or continuous exposure, sometimes lasting for the entire life of the exposed organism

Transporting
Where specific Investigational Product is moved from one location to another. For example, from the pharmacy to the participant in their own home.

Unblinding
The process by which the allocation code is broken, revealing the intervention allocated to the participant. The usual reason for unblinding in a study context is that a participant has encountered an urgent medical problem necessitating the need for the clinician to know his/her intervention allocation. People are not unblinded at the end of their participation in the study.

Version
The tracking system whereby different versions of the same document are used and identified. ITCC uses a specific and standardised version control. Versions are referred to with Vx.x.x with these being defined as:

- Vx.x.x – a minor modification or amendment

Example: V3.2.1 becomes V3.2.2 when a minor amendment is made

- Vx.x.x – a significant modification or amendment

Example: V3.2.1 becomes V3.3.1 when a significant amendment is made

- Vx.x.x – a major modification or amendment

  Example: V3.2.1 becomes V4.1.1 when a major amendment is made

Wellbeing (of study participants)
The physical and mental integrity of the participants participating in a clinical research study. The study protocol should specify that participants have had the benefit and burden of participation in the study clearly identified and dealt with in a way that complies with the National Statement on Ethical Conduct in Human Research (2007) (Updated May 2018).

History			
Version	Date	Author	Reason
1.1	5/03/2008	B Fazekas	Initial development
1.2	12/09/2010	B Fazekas	Periodic review
2.0	3/02/2011	B Fazekas	Update resulting from MAB feedback on SOPs
2.1	9/06/2015	C Hope	Periodic review (update following periodic review of all PaCCSC SOPs)
2.2	28/02/2018	B Fazekas, S Kochovska	Periodic review Publication of the ICH GCP E6 (R2)
2.3	16/06/2020	L James B Fazekas	Periodic review
2.4	09/05/2022	J Hao C Strauss	Periodic review

Approval		
Version	Approval Name	Approval Signature
2.4	Meera Agar