Standard Operating Procedure

4.8 Informed Consent

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Introduction / Background

The International Conference on Harmonisation of Good Clinical Practice (ICH GCP) guidelines and the National Health and Medical Research Council (NHMRC) National Statement on Ethical Conduct in Human Research describe in detail the process of obtaining consent from potential participants, including the use and detail of the participant information sheets and consent forms. These principles and requirements apply to all studies conducted by the IMPACCT Trials Coordination Centre (ITCC) and are underpinned by the suite of ITCC Standard Operating Procedures (SOPs).

Objective

This SOP operationalises the national and international requirements by describing:

- the manner by which informed consent is obtained; and
- the manner by which the process is documented in all studies undertaken or auspiced by the ITCC, where the suite of ITCC SOPs form the guiding procedural framework.

While this level of detail is not covered by other applicable clinical trial documents, the special considerations for the study population of the ITCC studies necessitate this level of detail.

This SOP does not replace other requirements from the ICH GCP, NHMRC and Human Resource Ethics Committee (HREC) documents.

This SOP also encompasses new procedures related to electronic consent.

Scope

This SOP applies to all staff involved in clinical studies conducted by the ITCC/PaCCSC/CST, irrespective of individual organisational employment, role or position.

Ownership and Responsibility

Responsibilities of the Principal Investigator and/or other designee(s) as documented in the Staff Signatures and Delegation Log (refer SOP 4.2.4 Delegation of Duties).

- To ensure that the correct Participant Information Sheet and Consent Form (PICF) has been approved (as a master version) by the HREC and subsequently approved for local use by the site Research Governance Office (RGO) and is the only version used at the site
- To oversee the process of obtaining informed consent from potential participants at the site
- To obtain informed consent from potential participants for ITCC studies in accordance with applicable regulatory and ethical requirements
- To authorise other individuals (such as study nurses, site coordinators, sub-investigators) to assist in the process of obtaining consent, ensuring the delegates have undertaken suitable training in the process

- To ensure that all requirements for participant consent are met, in keeping with the NHMRC National Statement on Ethical Conduct in Human Research and ICH GCP guidelines
- To ensure that those who obtain consent also document the process of consent within the clinical record. Where the study participant may reside at home while enrolled in the study, written consent documentation is held in the site study file

The Principal Investigator may delegate the duties for the informed consent process to another suitably trained individual (e.g. Sub-Investigator, Site Study Coordinator, study nurse etc.) as documented on the Staff Signature and Delegation Log (*refer* SOP 4.2.4 Delegation of Duties) but the Principal Investigator is responsible for supervising any staff to whom they have delegated such duties:

- To ensure that consent is explained to potential participants in a manner consistent with the study protocol and the approved PICF
- To obtain consent, where approved to do so and in keeping with HREC approval and delegation on the Staff Signature and Delegation Log
- To document the process of consent in the clinical record
- To file appropriately signed consent forms

Procedure

1. Training about consent procedures

The Principal Investigator is responsible for ensuring all site team members who are delegated the task of obtaining informed consent (as documented on the Staff Signature and Delegation Log; *refer* SOP 4.2.4 Delegation of Duties) complete training in consent processes. This training must be documented (*refer* Template 3a: Individual Training Record or Template 3b: Group Training Record) and kept in the Investigator Site File.

The training in the process of obtaining consent is consistent with international and national standards and includes:

- Completion of the informed consent training session or self-review of the training slides as part of the ITCC site initiation program (*refer* SOP 5.7 Site Initiation);
- Role playing, using the study PICF as a template, 'key messages', and plain language;
- Practice explaining to a 'lay' person such as a family member or non-clinical work colleague, and answer their questions;
- Practice explaining the study to another clinician, such as a medical officer or clinical nurses, based in the potential referral area;
- Familiarisation with frequently asked questions to ensure the team member can answer questions to the participant's satisfaction.

Each session provides an opportunity to critically analyse and amend the terminology used and facilitate the understanding of the study using plain non-technical language.

2. The Consent Form

The Consent Form must meet the requirements of the approving HREC, the NHMRC National Statement on Ethical Conduct in Human Research and ICH GCP guidelines (*refer* SOP 4.8.2 Participant Information and Consent Form).

When the Participant Information Sheet and Consent Form are approved by the HREC as one document, they must remain together in the study file and clinical notes (i.e. when the signature page is page 14 of 14, then the previous 13 pages remain attached).

3. Person obtaining consent

The study team member obtaining consent from the potential participant is trained in the process of obtaining informed consent and is included on the Staff Signature and Delegation Log and assigned the specific delegation role of obtaining consent by the Principal Investigator.

Each site complies with any local restrictions and/or obligations imposed by the HREC.

The study team member obtaining consent does not have any conflict of interest with the process. For example, if a potential participant is also a relative of the team member explaining the study, it is not appropriate for that person to obtain consent as there is a conflict of interest.

4. Documentation of consent

The completed Consent Form, by itself, is not regarded as adequate documentation that consent was obtained in accordance with the relevant regulatory requirements. ITCC studies require additional documentation of the actual consent process in the medical record (*refer* SOP 4.0 Investigator Responsibilities), as confirmation that consent has been obtained correctly. This may occur during several clinical encounters, all of which require to be documented. The reasons for this additional documentation are to:

- inform all other clinicians involved in the clinical management of the participant that the correct procedures for consent are followed, including appreciation of the vulnerable position of the participant; and that consent was provided with full disclosure and full understanding.
- provide evidence of the timeline for participation in the study (i.e. consent is obtained prior to study registration and initiation of study related procedures).
- provide substantiation of the process being a dialogue and sharing of information.
- confirm the process in the event that the Consent Form cannot be located at a future time.

Any documentation in the medical record regarding the consent process is completed by the study team member who obtains the consent. A stamp can be used if approved by the HREC (*refer* SOP 6.12 Ethical Approval). See Guidance 2 for sample consent documentation considered to be appropriate.

5. Filing of the Consent Form

The **original** signed Consent Form is filed in the participant's study file or investigator folder and is considered the source document. One copy of the signed Consent Form is provided to the person who provided consent (this must be confirmed as part of the documentation of consent in the clinical record), and a second copy is filed in the medical record, clinic record, outreach records, or other file as appropriate so that other clinicians involved in the care of the participant are aware of their participation in the study.

6. Changes to the Consent Form

Changes to the approved Participant Information Sheet and/or Consent Form must be approved by the HREC (*refer* SOP 6.12 Ethical Approval) and the local Research Governance Office (RGO) and contain the appropriate track changes and version changes. Changes to a Consent Form may occur under the following circumstances:

- A protocol amendment;
- Changes of study personnel, requiring changes to contact details on the Consent Form;
- An error is discovered on the Consent Form.

When changes are made to the Consent Form while a participant is still enrolled in the study, either during intervention or during follow-up, the participant will be informed of the changes in a timely manner if new information becomes available that may be relevant to the participant's willingness to continue their participation in the study. Communication of this information must be documented in the medical record. Re-consent will be obtained, the

updated consent form will be signed at the next scheduled study visit and a copy provided to the participant, except if the changes are only administrative or where a new protocol amendment has been approved but not yet applied (to the current participants). In the event a new version of the approved consent form is not signed by an enrolled participant due to the reasons listed above, a comment must be added to the medical record to confirm that the participant was informed of the changes to the consent form and to document the reason why the new approved version of the consent form was not signed.

7. Obtaining consent when the potential participant is unable to read or write English

If a potential participant is unable to read or write and if the legally acceptable representative is unable to read or write, an Impartial Witness must be present during the entire informed consent discussion. This must also be documented as part of the consent documentation in the medical record. The Impartial Witness must be a person who is independent from the trial and who cannot be unfairly influenced by the people involved in the trial. The Impartial Witness signs the Consent Form after:

- the Participant Information Sheet and Consent Form (and any other written material supplied) is read and explained to the potential participant and/or their legally acceptable representative;
- the potential participant (or their legally acceptable representative) consents verbally to participation in the study;
- if able to do so, the potential participant (or their legally acceptable representative) signs and dates the Consent Form.

By signing the Consent Form, the Impartial Witness attests that the information in the Consent Form and any other written information was accurately explained to, and apparently understood by, the participant or the participant's legally acceptable representative, and that informed consent was freely given by the participant or the participant’s legally acceptable representative.

Where an impartial witness is not required, but there is space on the consent form for ‘Witness Signature’, this section is struck through by the study staff with their initials and date, to indicate this section is not required to be completed as part of the informed consent process.

8. Obtaining proxy (third party) consent

In certain circumstances the medical condition of the intended participant precludes their capacity to consent to the study in their own right (e.g. when studying conditions such as delirium). Such studies require informed consent to be provided by a ‘responsible person’, ‘proxy’ or ‘third party’.
Obtaining consent for these studies is still a process of information exchange between the study staff, the potential third party and any other person the potential third party believes should be included in the discussion, including the participant (a health care interpreter can be used to assist if English is not the primary language). In such cases, the HREC approved third party information sheet is used as a basis for the discussion, which covers all procedures, benefits, burdens and side effects that may be possible during the study. The

study team ensures the third party has been given sufficient time and opportunity to consider the study and discuss with other family members.
It is critical that the third party is made aware that consent for the study must be in keeping with what the potential participant would want if they had capacity to consent in their own right, and that the consent is not based on the personal views of the third party.
Written informed proxy consent is to be obtained from a responsible person. No information collected for this study is to be released to the proxy consent person.
The definition of third party for consent to participate in clinical trials varies across Australia, with state specific directions on the identification of an appropriate third party. These state definitions and any associated approvals must be strictly adhered to and the identification of the third party must be documented within the medical record.

9. Declining consent/Withdrawal of consent

People who elect not to participate in an ITCC/PaCCSC/CST study are not required to provide any reason for their decision. The site study team must do everything possible to ensure that people who decline to participate will suffer no disadvantage and that a participant's refusal to participate will not affect the provision or quality of care they receive in any way.

Participants are entitled to withdraw from the study at any time and will be informed about any consequences of such withdrawal during the informed consent discussion.

10. Electronic consent (E-Consent)

E-Consent, or electronic consent, involves the process of obtaining participant consent for a clinical trial using electronic means, and may include passive and interactive systems and webpages, and the use 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.

The introduction of e-Consent has been gaining increasing momentum with the advancement of technology to improve efficiencies in clinical trials and recent changes in trial processes and practices due to social distancing in response to the COVID-19 pandemic and changes in patient expectations.

Whilst GCP does not explicitly address or comment on the use of e-Consent, there are currently many systems in place for the conduct of obtaining e-Consent, much of which is new within the Australian clinical trials context. These range from a digital consent form with hand-signed consent to sophisticated systems integrating multimedia, translation and other technologies.

ITCC has investigated the potential of e-Consent within the conduct of UTS sponsored and ITCC coordinated clinical trials. Recent feedback from ITCC recruiting sites regarding the use and capabilities of REDCap has identified that many users would like to see e-Consent adopted in standard practice.

The REDCap Electronic Data Capture (EDC) system is a secure, web-based application for building and managing online surveys and databases. It serves as a GCP compliant and validated tool to collect and disseminate research data.

The ITCC team has set up a process to enable e-Consent for participants using the REDCap EDC system. This includes:

- The development of guidelines and project templates to enable the use of the e-Consent framework on a study-by-study and site-by-site basis.
- An e-Consent project template will be developed for each site individually, which includes uploading the locally approved, site-specific PICF.

The use of e-Consent will be implemented for future studies considering:

- Details of the proposed consent process, the study population, and the appropriateness of the electronic platform for each study overall.
- Prior HREC and local RGO approval of the proposed e-Consent process.

Following training delivered by the ITCC:

- The tailored e-Consent project will be completely handed over to the Principal Investigator and the delegated site staff to manage.
- All ITCC staff will be removed from the project by the Principal Investigator after the handover, completely disabling access to ITCC.
- The site study team can then assign their own participants to the e-Consent platform, present the HREC approved PICF, and manage signatures and storage of the signed PICF directly in the system as per GCP and other applicable clinical trial regulations.

This site managed process enhances the capacity of sites to obtain written consent remotely, thus reducing the number of face-to-face visits and potentially enabling more consultation and consideration time for participants during this critical process (*See* Manual 4: E-Consent Site Manual for an outline of the structure of the feature and instructional document for site training).

The informed consent elements encompassed by this SOP also extend to the application of e-Consent, such as training, person obtaining consent, documentation of consent, use of impartial witness and obtaining proxy consent.

Related SOPs

4.0 Investigator Responsibilities
4.2.4 Delegation of Duties
4.8.2 Participant Information and Consent Form
5.7 Site Initiation
6.10 Version Tracking
6.12 Ethical Approval Review and Reporting
8.0 Essential Documents

Related documents

Template 3a: Individual Training Record
Template 3b: Group Training Record
Guidance 2: Documentation of Consent (example)
Manual 4: E-Consent Site Manual

References

COSA Standard Operating Procedures for Investigational Sites, Centre for Clinical Research Practice, Clinical Oncology Society of Australia, March 2006

International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH). Integrated Addendum to ICH E6(R1): Guideline for Good Clinical Practice E6(R2). November 2016 (accessed 28/02/2022) https://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E6/E6_R2__Step_4.pdf

National Statement on Ethical Conduct in Human Research (2007) - Updated 2018- (accessed 28/02/2022) https://www.nhmrc.gov.au/about-us/publications/national-statement-ethical-conduct-human-research-2007-updated-2018

Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95). Annotated with TGA comments 2000 (accessed 17/10/2017) https://www.tga.gov.au/sites/default/files/ich13595an.pdf

eConsent Initiative, eConsent: Implementation Guidance V1.0, Transcelerate Biopharma Inc., February 2021 (accessed 28/02/2022) https://www.transceleratebiopharmainc.com/wp-content/uploads/2021/02/eConsent-Implementation-Guidance_February-2021.pdf

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Acknowledgments

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History			
Version	Date	Author	Reason
1.1	8/10/2013	B Fazekas	New procedure
1.2	18/05/2015	C Hope	Periodic review
1.3	28/02/2018	B Fazekas, S Kochovska	Periodic review Publication of the ICH GCP E6 (R2)
1.4	16/03/2020	C Strauss	Periodic review Publication of the National Statement on Ethical Conduct in Human Research (2007) - updated 2018
1.5	01/03/2022	C Strauss	Periodic review Incorporation of eConsent procedures

Approval		
Version	Approval Name	Approval Signature
1.5	Meera Agar