Overall Investigator Site File Management for Clinical Trials

BEFORE THE CLINICAL PHASE OF THE CLINICAL TRIAL COMMENCES

Investigator's Brochure (IB)

To document that relevant and current scientific information about the Investigational Drug/ Medical Device has been provided to the investigator.

- IB is approved and current (not older than 12 months or accompanied by a statement that the IB is under review or up-to-date.
- IB Receipt identifies the version number and/or date of the IB and is signed and personally dated by the Principal Investigator (PI) Superseded versions should be marked as superseded, dated and filed.

For marketed products used within the terms of its registration and for which an IB is not provided, the summary of the product characteristics / equivalent authorised in the individual country must be provided by the Sponsor.

Signed protocol (and amendments, if any) and sample case report form

To document investigator and sponsor agreement to the protocol and amendment(s) and case record form.

- Current Protocol/Amendment being signed as final i.e. not draft version and is approved for use.
- Protocol is identified by a protocol number and by a version number and/or version date.
- Protocol Signature Page is signed and personally dated by the PI.
- The name of the PI on the Protocol Signature is printed.
- Protocol Signature Page identifies the same version of the protocol approved by the IEC.
- Superseded versions should be marked as superseded, dated and filed.

Information given to clinical trial participants

- Informed Consent Form, to document the informed consent that is compliant with International Council for Harmonisation (ICH) Good Clinical Practice (GCP).
- Participant Information Sheets and any other written information – to document that participants will be given appropriate written information (content and wording) to support ability to give fully informed consent
- Advertisement for subject recruitment (if used) – to document that recruitment measures are appropriate and not coercive.
- Approved translated information provided to the participants as applicable

All approved site versions of the Information and Consent forms, correspondence and changes to the forms requested by the Human Research Ethics Committee (HREC) and Research Governance Office (RGO) should be filed appropriately.

Financial aspects of the trial
To document the financial agreement between the investigator/Site and the clinical trial Sponsor.

FDA 1572 Forms & Supplements (as applicable) and Financial Disclosure Documents required for clinical trials being conducted under an IND only

- FDA 1572 forms and Financial Disclosure Forms (FDF) must be obtained for all clinical trial investigators. Only the PI and investigator delegated to deputise in his/her absence and assume responsibility for the clinical trial should be listed on the 1572 form (Sub-PI).
  NB. Rotating general medical staff should not be included on the 1572 form. General medical staff are listed on the delegation log as e.g. haematologist, investigator and research fellow
- It is essential that the address of the PI is the exact address where the investigator is conducting the clinical trial. The address should be identical in all fields requiring information on the form.
- The 1572 lists the PI and Sub-PI, whereas the FDF is an individual form for each PI and Sub-PI.
- Addresses should include Country/ Site/ Address/ Names on FDA 1572 and FDF – this should not be handwritten. The Date of signature should not be pre-printed.
- Current version of 1572 form should always be checked on the FDA website prior to completion

Insurance statement (where required)
To document that compensation to subject(s) for clinical trial related injury will be available.

Signed agreement between involved parties
SWSLHD and the Ingham Institute accept Medicines Australia Indemnity Agreement and Clinical Trial Research Agreements (CTRA). Confident Disclosure Agreement (CDA) will be reviewed by the Research Directorate prior to execution.

All CTRA, Indemnity Agreements and CDA are to be signed by the:

- Chief Executive or Director of Research for SWSLHD
- Chief Executive Office or Chief Operating Officer for the Ingham Institute

Dated, documented favourable opinion of HREC and RGO of the following:

- Protocol and any amendments
- Case Record Forms (CRF) (if applicable)
- Informed Consent Forms
- Participant Information and Consent Forms and any other written information to be provided to the subject(s)
- Advertisement for participant recruitment (if used)
- Participant compensation (if any)
- Any other documents given approval/favourable opinion
- To document that the clinical trial has been subject to HREC review and given approval/favourable opinion. To identify version number and date(s) of the document(s)

Human Research Ethics Committee Composition
To document the HREC is constituted in agreement with ICH GCP and NH&MRC National Statement.

Regulatory authority authorisation/approval/notification of protocol
To document that appropriate authorisation/approval/notification by the regulatory authority has been obtained prior to initiation of the clinical trial in compliance with the applicable regulatory requirements – e.g. Therapeutic Goods Administration (TGA) CTN or CTX.

Curriculum vitae (CV) and other documents evidencing qualifications of investigator(s) and supporting clinical trial staff to whom investigator tasks are delegated

- Current site CVs, signed & personally dated at the beginning of the clinical trial (*current is within 2 years)*
- CVs must be collected for those listed on the Delegation of Responsibilities Log CV states current position including date of employment in current position (e.g. 01 Jan 2015 – present)
- Provides evidence of suitable training and experience to conduct the delegated tasks for the clinical trial (e.g. therapeutic expertise or technical qualification)
- Shows an affiliation with the institution / organisation where the clinical trial will be conducted i.e. name and address of institution
- States medical degree and/or other relevant professional qualifications obtained and institution where attained
- Clinical trial experience is desirable
- ICH GCP training should be listed at a minimum. SWSLHD and the Ingham Institute require refresher training every 3 years

Normal values/ranges for medical/lab/technical procedures and/or tests included in the protocol
To document normal values and/or ranges of tests

Medical/lab/technical procedures/tests
To document competence of facility to perform required tests and support reliability of results. Certification or accreditation; established quality control; external quality assessment; other validation.

Instructions for handling of investigational drugs/ medical device and clinical trial related materials (if not in protocol)
To document instructions needed to ensure proper storage, packaging, dispensing and disposal of investigational products and clinical trial related materials.

Distribution records for investigational drugs / medical device and clinical trial related materials (if appropriate)
To document distribution dates, batch numbers and method of distribution, etc of investigational products and clinical trial related materials. To allow tracking of product batch, review of distribution conditions and accountability.

Decoding procedures for blinded studies
To document how, in event of an emergency, identity of blinded investigational medicinal product can be revealed without breaking the blind for the remaining participants' treatment.

Clinical Trial initiation monitoring report (externally sponsored studies)
To document that clinical trial procedures were reviewed with investigator and investigator's research staff.

DURING THE CONDUCT OF THE CLINICAL TRIAL

The following should be added to the clinical trial file during the trial:

Investigator's brochure updates
To document that investigator is informed in a timely manner of relevant information as it becomes available.

Any revision(s) to:
- Protocol
- CRF
- Informed Consent Form
- Any other written information provided to participants
- Participant Information Sheet
- Advertisement for participant recruitment (if used)
- To document any revisions of these documents during the course of the trial.

Dated, documented favourable opinion of the HREC and RGO of the following:
- Protocol amendment(s)
- Revisions of:
- Informed Consent Form
- Participant Information and Consent Form
- Any other written information to be provided to the patient
- Advertisement for patient recruitment (if used)
- Any other documents where approval required.
- To document that the amendments and/or revisions have been subject to the HREC
- Committees review and were given approval/favourable opinion. To identify the version number and date of the documents.

Regulatory authorities' approvals where required for:
- Protocol amendments and other documents.
- To document compliance with applicable regulatory requirements.

Curriculum vitae & ICH GCP certificates for new investigator(s) and/or supporting clinical trial staff to whom investigator tasks are delegated

To document that each researcher is qualified by training and experience to perform the clinical trial tasks that they have been assigned on the Delegation of Responsibilities Log.

Updates to normal value /ranges for medical/laboratory/technical procedures/tests included in the protocol
To document revisions to normal values/ranges during the course of the clinical trial.

Updates of medical/lab/technical procedures/tests
To document that tests remain adequate throughout the clinical trial period. To document that certification or accreditation or established quality control and/or external quality assessment or other validation is up-to-date.

Relevant communication

- Letters
- Emails
- Meeting reports
- Summary of telephone calls
- To document any agreements or significant discussions regarding clinical trial administration, protocol violations, clinical trial conduct and adverse event reporting.

Signed Informed Consent Forms
To document that consent is obtained in accordance with ICH GCP and the protocol and is dated prior to participation of each participant in the clinical trial. Also to document direct access permission.

Source documents
To document the existence of the participant and substantiate integrity of clinical trial data collected. To include original documents related to the clinical trial, to medical treatment, and history of each participant. Refer to SOP_CTSU_07 Source Documentation, Record Keeping, Case Report Forms and Archiving

Signed, dated and completed case report forms
If too bulky to store in the ISF they may need to be kept separately.
To document that the investigator or authorised member of investigator's staff confirms the observations recorded.

Documentation of CRF corrections
To document all changes/additions or corrections made to CRF after initial data were recorded.
Notification by originating investigator to sponsor of serious adverse events and related reports
Notification by sponsor and /or investigator, where applicable, to regulatory authorities of unexpected serious adverse drug reactions and of other safety information
Notification by sponsor to investigator(s) of safety information
Interim or annual reports by sponsor to HREC and authorities

Subject screening log
To document identification of participants who entered pre-clinical trial screening.

Subject enrolment log
To document chronological enrolment of participants by trial number.

Subject identification code list
Confidential list of names/hospital numbers of all enrolled participants and allocated clinical trial numbers to allow ease of identification of participants if required.

Investigational drug accountability at site
To document that investigational drugs have been used according to the protocol.

Delegation of Responsibilities Log

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- Delegation of Responsibilities Log – Log lists PI and all staff delegated with clinical trial responsibilities including their signatures
- Delegated tasks may only be assigned to individuals qualified to perform task described in writing and documented on CV.

Record of retained body fluids/tissue samples (if any)
To document location and identification of retained samples if assays need to be repeated.

AFTER COMPLETION OR TERMINATION OF THE CLINICAL TRIAL

All of the documents previously identified should be in the ISF together with the following:

Investigational drug(s) accountability at site (if applicable)
To document that the investigational drugs have been used according to the protocol. To document the final accounting of investigational drugs received at the site, dispensed to participants, returned by the participants and returned to sponsor.

Documentation of investigational drug destruction (if applicable)
To document destruction of unused investigational drugs by sponsor or at site.

Completed subject identification code list
To permit identification of all participants enrolled in the clinical trial in case follow-up is required. List should be kept in a confidential manner and for an agreed amount of time.

Treatment allocation and decoding documentation (if applicable)
Returned to sponsor to document any decoding that may have occurred.

Database and Statistical reports.
A copy of the CRF database should be saved to disk (if provided) and placed in the site file.
To document electronic evidence of CRF completion.

Final report by investigator to independent ethics committee where required

To document completion of the clinical trial.

Clinical trial report
To document results and interpretation of the clinical trial.

Declaration of the end of clinical trial
To document completion of the clinical trial and that notification was sent to the HREC, RGO and applicable Regulatory Authorities (See SOP 10 Clinical trial Closure).