Western Health

STANDARD OPERATING PROCEDURE

Site Initiation and Closeout

Standard Operating Procedure

Western Health

SOP reference	008
Version:	3.0 dated June 2019
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Next Review Date	June 2024
Approved by	Mr Bill Karanatsios, Research Program Director
Signature and date	

Amendment History

VERSION	DATE	AMENDMENT DETAILS
2.0	04 Dec 2015	
3.0	June 2019	Updated to align with MACH SOPs

1. AIM

To describe the procedures related to site initiation and close-out of a clinical trial.

2. SCOPE

Applicable to all phases of clinical investigation of medicinal products, medical devices and diagnostics.

3. APPLICABILITY

Principal Investigator (PI), Associate Investigator(s), research coordinators and other staff delegated trial-related activities by the PI.

4. PROCEDURE

For investigator initiated trials where Western Health (WH) is also the sponsor, obligations owed to or emanating from sponsor should be interpreted to mean WH.

4.1. Site initiation

The procedure outlined below refers to a "sponsored" trial. Where the investigational study is "investigator initiated" and the "sponsor" is the institution, the investigator should assign the role of monitor to a suitably qualified institution employee not involved with the study, unless an external monitor has been assigned by the institution.

Prior to initiation the investigator(s) should:

STEP	ACTION
4.1.1	Arrange with the monitor the scheduled date, time and location of the study initiation visit.
4.1.2	Review the Investigator's Brochure (IB) and any up-to-date information on the investigational product. The Investigator(s) must be familiar with the product, including pre-clinical toxicology, pharmacology, pharmacokinetics and up-to-date clinical data if applicable. **ICH GCP 4.1.2**
4.1.3	Ensure that the procedures stated in the study protocol are applicable in their study site and fully understood
4.1.4	Ensure that sub Investigator(s), pharmacist(s), research coordinators and any other relevant staff involved with the study have been advised of the meeting and are able to attend.

During the initiation the investigator(s) or delegate should:

STEP	ACTION
4.1.5	Establish that the Investigator's Trial Master File (TMF) (WH GCP SOP 002) contains all the required regulatory documents.
4.1.6	Provide a list of study personnel and functions in the study to the clinical monitor.
4.1.7	Provide Curriculum Vitae (CV) of the Associate Investigator(s) involved. **ICH GCP 8.2.14**

4.1.8	Ensure that the names and contact numbers of the relevant medical and study personnel of the sponsor are available and documented clearly.
4.1.9	Ensure that all relevant study site personnel fill out the Site Personnel/Signature Log (WH GCP SOP 001). **ICH GCP 4.1**
4.1.10	Check that the procedures and plans for storage, dispensing and return of investigational product have been agreed and finalised with the Sponsor and Pharmacist (if applicable). **ICH GCP 5.14.3**
4.1.11	Review the documents used in the shipment of the investigational products to the study site. **ICH GCP 4.6.3**
4.1.12	Check that the quantity of Case Report Forms (CRF) requested by or shipped to the trial site are sufficient for the number of participants that are likely to be recruited into the trial.
4.1.13	Check that other related supplies are available, or are to be shipped to the study site at a later date, and that they are available in sufficient quantities.
4.1.14	Check that laboratory facilities and arrangements for the dispatch of samples to the laboratory are organised and that any specialised equipment that may be required will be available throughout the period of the trial, e.g. centrifuge freezer, etc.
4.1.15	Establish who will be responsible for CRF completion and clarify the procedure for entering data in the CRF, as well as making changes and corrections and responding to data queries.
4.1.16	Ensure an understanding of the requirements that source documents and raw data will need to be available during monitoring visits to enable the monitor to perform source data verification at each monitoring visit.
4.1.17	Review the arrangements for organising and maintaining study files.
4.1.18	Ascertain that the procedures relating to the archiving of study records at the end of the study is agreeable to the sponsor.
4.1.19	Establish the next monitoring visit with the Monitor.

4.2. Premature Termination or Suspension of a Trial

STEP	ACTION
4.2.1	**If the trial is prematurely terminated or suspended for any reason, the investigator/institution should:** Promptly inform the trial participants, should assure appropriate therapy and follow-up for the participants, and, where required by the applicable regulatory requirement(s), should inform the regulatory authority(ies).

4.2.2	**If the investigator terminates or suspends a trial without prior agreement of the sponsor, the investigator should:** Inform the institution where applicable, and the investigator/institution should promptly inform the sponsor, the Human Research Ethics Committee (HREC) and Research Governance Officer (RGO). Provide the sponsor, the HREC and RGO with a detailed written explanation of the termination or suspension.
4.2.3	**If the sponsor terminates or suspends a trial, the investigator should:** Promptly inform the institution where applicable and the investigator/institution should promptly inform the HREC and provide the HREC a detailed written explanation of the termination or suspension.
4.2.4	**If the HREC terminates or suspends its approval of a trial the investigator should:** Inform the institution (RGO) and the investigator should promptly notify the sponsor and provide the sponsor with a detailed written explanation of the termination or suspension.

4.3. Site close-out

The investigator(s) should:

STEP	ACTION
4.3.1	Provide a summary report of the trial's outcome to the ethics committee and the regulatory authorities, if required.
4.3.2	Keep documentation and correspondence in the trial master file in accordance with 8.4 ICH.
4.3.3	Inform the sponsor of the completion of the study.
4.3.4	Ensure arrangements for archiving of trial documents are clarified (see WH GCP SOP 007).
4.3.5	Ensure appropriate final disposition of any investigational product. This may include return to the sponsor or destruction of remaining materials. Refer to WH GCP SOP 005 for details.

5. GLOSSARY

Associate Investigator

Any individual member of the project team designated and supervised by the investigator at a study site to perform critical study-related procedures and/or to make important study-related decisions (e.g., associates, residents, research fellows). Also referred to as "Sub-Investigator"

Case Report Form (CRF)

A printed, optical, or electronic document designed to record all of the protocol required information to be reported to the sponsor on each trial participant.

Delegate

A person delegated specific but appropriate tasks in relation to the conduct of a clinical trial.

Good Clinical Practice (GCP)

A standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of trial participants are protected.

Human Research Ethics Committee (HREC)

A body which reviews research proposals involving human participants to ensure that they are ethically acceptable and in accordance with relevant standards and guidelines.

The National Statement requires that all research proposals involving human participants be reviewed and approved by an HREC and sets out the requirements for the composition of an HREC.

International Conference on Harmonisation (ICH)

International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use is a joint initiative involving both regulators and research-based industry focusing on the technical requirements for medicinal products containing new drugs.

Investigator Brochure (IB)

The document containing a summary of the clinical and non-clinical data relating to an investigational medicinal product that are relevant to the study of the product in humans.

Investigator initiated trial

A clinical trial that is undertaken by the investigator whereby the investigator and/or their institution takes on the role of the sponsor in addition to their role as investigator.

Principal Investigator (PI)

An individual responsible for the conduct of a clinical trial at a trial site ensuring that it complies with GCP guidelines. If a trial is conducted by a team of individuals at a trial site, the investigator is the responsible leader of the team and may be called the Principal Investigator. In this instance they may delegate tasks to other team members.

Monitoring

The act of overseeing the progress of a clinical trial and ensuring that it is conducted, recorded, and reported in accordance with the protocol, Standard Operating Procedures (SOPs), Good Clinical Practice (GCP), and the applicable regulatory requirement(s).

Research Governance Office (RGO)

Site/institutional office that are accountable for the research activities conducted at their site to ensure that research is conducted according to established ethical principles, guidelines for responsible research conduct, relevant legislation and regulations and institutional policy.

Sponsor

An individual, company, institution or organisation which takes responsibility for the initiation, management, and/or financing of a clinical trial.

Source Documents

Original documents, data, and records (e.g. hospital records, clinical and office charts,

laboratory notes, memoranda, participants' diaries or evaluation checklists, pharmacy dispensing records, recorded data from automated instruments, copies or transcriptions certified after verification as being accurate copies, microfiches, photographic negatives, microfilm or magnetic media, x-rays, participant files, and records kept at the pharmacy, at the laboratories and at medico-technical departments involved in the clinical trial).

Trial Master File (TMF)

A file that contains all the applicable essential documents that demonstrate that the study/trial has been conducted in accordance with regulatory requirements and ICH GCP, enabling both the conduct of a project and the quality of the data produced to be evaluated. The preparation and maintenance of the Study File resides with the Site Investigator and set up at the start of a trial and is archived at the end of the trial. This may also be called the “Study Site Master File” or “Investigator Site File”.

6. REFERENCES

1. Based on VMIA GCP SOP No.008 Version1.0 Dated 17 September 2007
2. Based on MACH GCP SOP No.008 Version 1.0
3. Note for guidance on Good Clinical Practice (CPMP/ICH/135/96) annotated with TGA comments DSEB, July 2000, sections 4 and 8.4.
4. Standard Operating Procedures for Clinical Investigators, World Health Organisation, version 1.1.

7. APPENDICES

Appendix 1: Example Initiation check-list

Appendix 2: Example Close out check-list

8. AUTHORS/CONTRIBUTORS

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9. PRIMARY PERSON/DEPARTMENT RESPONSBLE FOR DOCUMENT

Western Health Office for Research

APPENDIX 1: INITIATION CHECKLIST

WH GCP SOP 008 Appendix 1 version 3 dated May 2019

ACTIVITY	COMPLETED YES/NO
Ensure the meeting is scheduled and all relevant staff are able to attend (Investigator, study coordinator, sponsor, pharmacist, other relevant people such as laboratory staff). It is usual to confirm the initiation by letter	
Review Investigational Product overview and background	
Review with investigator and relevant staff their understanding of the protocol, study procedures, investigational product, randomization procedures, unblinding procedures and timelines	
Review that site resources are adequate to conduct the trial	
Review with investigator and relevant staff Safety Reporting procedures and principles of Good Clinical Practice (ICH-GCP), including informed consent procedures, investigator responsibilities, record keeping and ethics reporting.	
Review contents of Site Master File to ensure that: • the current approved copy of the protocol, Informed consent form & Investigational Brochure are present and align with the ethics committee approval documentation • the ethics approval documentation is present and signed • a copy of the CTN/CTX form is present and complete • all necessary agreements are present and signed (Clinical trial Agreement, Indemnities, insurance) • all site staff CVs are present and signed • Laboratory normal ranges and relevant accreditation are present	
Complete staff delegations log	
Review investigational product shipment records	

APPENDIX 2: CLOSE-OUT CHECKLIST

WH GCP SOP 008 Appendix 2 version 3 dated May 2019

ACTIVITY	COMPLETED YES/NO
Ensure all protocol required data has been collected	
Finalise accountability and disposition of test drug	
Verify that all study files are complete (see Study Master File checklist)	
Discuss overall study conduct at the site	
Collect final signatures for any data queries, signature logs or reports	
Discuss archiving of original data and documents	
Dispose of or return any remaining trial specific supplies	
Formally close the site	