



1. Purpose

The purpose of this operating procedure is to outline the procedures involved in monitoring research sites involved in CERU trials.

2. Responsibilities

CERU: The Project Leader, or delegate, at CERU will be responsible for conducting monitoring visits. CERU is responsible for verifying that the study is conducting according to the protocol and amendments, applicable regulatory requirements, GCP and study procedures. CERU is responsible for ensuring that the rights and safety of study participants are protected and that the data is accurate and verifiable.

Qualified Investigator (QI): The QI at the research site, or delegate, will ensure the research site accommodates requests for a monitoring visit regarding a CERU trial. This includes but is not limited to: providing access to source data/documents, providing a location to work, and being available to discuss issues.

3. Procedures

3.1 Monitoring is *“the act of overseeing the progress of a clinical trial, and of 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 requirements.”*

-ICH GCP section 1.38

Qualification and Selection of Monitors

3.2 Monitors should be appointed by the the Sponsor of the trial.

3.3 Individuals delegated the responsibility of conducting study monitoring should have their qualifications documented.

3.4 The monitor should be familiar with the investigational product, written informed consent form (and any other written information provided to participants), CERU SOPs, GCP and any governing regulations.

Extent and Nature Site Monitoring Visits

3.5 CERU should ensure the extent and nature of monitoring is proportionate to the following:

3.5.1 Objectives and purpose;

3.5.2 Design and sample size;

3.5.3 Complexity;

3.5.4 Blinding;



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3.5.5 Associated risks;

3.5.6 Endpoints.

3.6 In general, on-site monitoring should be conducted before, during and after the study. However in the context of academic (Investigator initiated) studies, the Sponsor and CERU may decide central monitoring supplemented with training, meetings, written guidance is sufficient to ensure compliance with trial procedures, ICH GCP and governing regulations.

3.7 The specific details concerning site monitoring visit activities for a particular trial will be documented in a study specific work instruction (WI). The WI should include the following details:

3.7.1 Selection of data elements to be verified

3.7.2 Frequency of monitoring

3.7.3 Scheduling monitoring visits (including requests for access to source documentation)

3.7.4 Communications with research sites

3.7.5 Monitoring queries and follow-up

3.7.6 Monitor documentation

3.7.7 If applicable, details concerning central monitoring and associated training, meetings and procedures

Monitor's Responsibilities

3.8 As per Sponsor and CERU requirements, the monitor should ensure the study is conducted and documented properly through the following activities (refer to ICH GCP section 5.18.4 for full details):

3.8.1 Facilitating communication between the research site and CERU.

3.8.2 Verifying research site personnel, including the qualified investigator and facilities (i.e. pharmacy, laboratory) are adequately qualified to conduct the study (and remain adequate for the duration of the study).

3.8.3 Research site follows study procedures and data collection is carried out in compliance with the study protocol and ICH GCP.

3.8.4 Data is collected and entered into case report forms by appropriately delegated personnel.

3.8.5 Data is free of omissions and is correct.

3.8.6 Confirm each participant has provided written informed consent.

3.8.7 Verifying for the investigational product that:

3.8.7.1 Supplies are sufficient and storage conditions are acceptable.

3.8.7.2 Administration of investigational product follows study procedures (i.e. frequency and dosage).

3.8.7.3 Accountability is performed

3.8.8 Verifying all enrolled participants met eligibility criteria

3.8.9 Verifying that all source documents and other study records, including regulatory documents, are accurate, complete, kept up-to-date and maintained.



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3.8.10 Determining whether all adverse events are appropriately reported and within the time frame required by ICH GCP and governing regulations.

3.8.11 Communicating protocol violations/deviations and taking appropriate action to prevent recurrence of the violation/deviation.

3.9 A comprehensive list of monitor responsibilities can be found in ICH GCP section 5.18.4.

Monitoring Procedures

3.10 The monitor should follow the study specific WI for monitoring a specific study.

Monitoring Report

3.11 Following the monitoring visit, the monitor should provide the Sponsor with a written report. Written reports should include:

3.11.1 Institution, qualified investigator, research site personnel in attendance

3.11.2 Date visit conducted, name of monitor

3.11.3 Summary of documents the monitor has reviewed, along with a statement of findings, violations/deviations, deficiencies, conclusions, actions taken or recommended.

3.12 Refer to appendix 4.1 for the Site Monitoring Visit Report template.

4. Appendix

4.1 Site Monitoring Visit Report

5. References

5.1 ICH GCP Section 1.38: Monitoring

5.2 ICH GCP section 5.18: Monitoring

5.3 Food and Drug Regulations, Division 5: Drugs for Clinical Trials Involving Human Subjects section C.05.010.

5.4 Network of Networks Standard Operating Procedures for Clinical Research (N₂ organization).



Site Monitoring Report

Study Title:	
Principal Investigator:	
Research Site:	
Qualified Investigator:	
Date Monitoring Performed:	
Site Monitoring Performed By:	

Key Research Site Personnel Present for Monitoring Visit

Name	Title	Available During Discussions (Y/N)
	Qualified Investigator	
	Research Coordinator	
	Pharmacist	
	Etc...	

Activity	Y	N	N/A	Comments
Study Team Meeting				
1. Review of the site visit agenda with the Investigator and study staff	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
2. Review of previous site visit outstanding items to addressed for the next visit	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
3. Review of subject accrual status and enrollment objectives	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
4. Review of protocol and any amendments	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Facilities				
1. Tour of study facilities (i.e. clinic, laboratory, pharmacy)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
2. Collection and storage of biological samples	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
3. Shipping of samples	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
4. Investigational product storage (i.e. secure, locked place with proper storage conditions, if applicable)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
5. Investigational product accountability	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
6. Ensure the site has adequate supplies	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	



Data Review			
1. Informed Consent Review (if the ICF has been updated ensure active patients are re-consented with updated ICF)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2. Review of screening log	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3. Enrolled participants meet inclusion/exclusion criteria	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
4. Visits and procedures are performed at the correct times	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
5. Randomization order and assignment of subjects to treatment are maintained	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
6. Source Documentation	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
7. CRF Review	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Regulatory Documentation Review			
1. Ensure regulatory compliance with the applicable regulations (i.e. ICH, IRB, Health Canada)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2. Verify the protocol and all amendments have approval granted from the IRB	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3. Verify the ICF has been approved by the IRB (as well as any amendments)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
4. Review study staff CVs and licenses	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
5. Review Laboratory Accreditation	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
6. Review regulatory agency documentation (Health Canada, FDA)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
7. Ensure all adverse events and serious adverse events have been reported to the IRB and Sponsor as per applicable regulations and guidelines.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Safety Review			
1. Evaluate the accurate reporting for all safety measures (i.e. abnormal lab values, physical exam findings, abnormal findings on any procedure report)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2. Review all adverse event data	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3. Review all serious adverse event data	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>



4. Ensure notifications to the IRB are filed for all adverse events and serious adverse events	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Record Retention				
Provide instructions and confirm the research site has a plan for record retention.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Ensure record retention storage documentation is filed.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	

Summary

Post monitoring visit summary including:

- *Site recruitment activities (screening, enrolment)*
- *SAEs*
- *Protocol violations, deviations*
- *deficiencies, including actions taken and resolution*

Written by:

Name

Date