Research Compliance and Quality Assurance Program (RCQA):
Monitoring Plan
Guidance for Investigator-Initiated Research

Protocol Title

Study Title (short):
REB Reference Number:
Sponsor/Sponsor-Investigator:
Principal Investigator/Qualified Investigator (QI) :

Prepared By (print): _____ Signature: _____

Approved By (print): _____ Signature: _____

Date of Approval _____

Monitoring Plan Outline

See template on page 6 for model text

Study monitoring is a Sponsor responsibility as outlined in ICH-GCP. This outline includes a template that can be customized to your protocol.

Glossary of terms used in this document

Regulated research

Sponsor-Investigator: *An individual who both initiates and conducts, alone or with others, a clinical trial, and under whose immediate direction the investigational product is administered to, dispensed to, or used by a subject. The term does not include any person other than an individual (e.g., it does not include a corporation or an agency). The obligations of a sponsor-investigator include both those of a sponsor and those of an investigator.*

Qualified Investigator (QI): *(as defined by Health Canada)The person responsible to the sponsor for the conduct of the clinical trial at a clinical trial site, who is entitled to provide health care under the laws of the province where that clinical trial site is located, and who is*

- *in the case of a clinical trial respecting a drug to be used for dental purposes only, a physician or dentist and a member in good standing of a professional medical or dental association;*
- *in any other case, a physician and a member in good standing of a professional medical association.*

There can only be one QI per study per Canadian study site.

Non-regulated research

Sponsor: *An individual, institution, or organization which takes responsibility for the initiation, management, and/or financing of a clinical trial. Single centre/multicentre.*

Principal Investigator (PI): *A person responsible for the conduct of the clinical trial at a trial site. If a trial is conducted by a team of individuals at a trial site, the principal investigator is the responsible leader of the team.*

Choosing a Monitor

The selected Monitor must be qualified by appropriate training, education and experience (level determined by the study PI and institutional policy/SOPs (if applicable). Monitors must be trained on the study protocol/procedures prior to starting visits and must be listed on the Sponsor delegation log.

Check with your institution's administration to see if this support is provided.

1.0 Study Overview

Briefly describe the study (1-2 paragraphs), its objectives and the critical data / study procedures.

2.0 Purpose

Briefly describe the purpose of the monitoring plan.

3.0 Monitoring Scope

An overview of what the monitor will be doing when he/she performs monitoring visits. If the study is multicenter/multinational, this section will also describe how the coordinating centre is monitoring participating sites. Study monitors do not need to be independent of the study team; team members not directly involved in collecting data or recruiting participants may perform study monitoring as long as they are not monitoring their own work. Study coordinators from other trials may also monitor each other's studies.

Types of Monitoring

On-site monitoring is the most commonly used monitoring practice performed today. Monitors travel to the site to perform source-document verification (SDV) in person. The monitor has access to the required source, including identifiable personal health information (PHI) (i.e. patient medical charts, signed consent forms etc). While on-site monitoring can be costly depending on the number and locations of participating sites, visits allow the monitor to assess processes and procedures that cannot be performed remotely (i.e. consent process).
It is recommended that on-site visits be the standard monitoring format for those who are new/early career to investigator-initiated clinical research.

"Hybrid" remote monitoring is a term used for when on-site monitoring visits are performed in addition to remote source-data verification. Remote source-data verification involves sending de-identified data (i.e. direct identifiers are removed from the information and replaced with a code) off-site to a coordinating centre either through uploading into a secure validated online database) or by fax transmission.
While you cannot perform complete remote SDV on participant CRFs, partial SDV and trial management file review including date/times of test results, randomization and training of research personnel is possible. This ensures that the monitor has more time to assess critical data and/or processes while on-site.

4.0 Timing and Frequency

A "risk-based" approach to monitoring in which the degree of monitoring required per study is based on the research category (clinical phase/type of research) and risk exposure to participants and the institution is encouraged. The associated Monitoring Risk Level Tool illustrates the range of monitoring required for investigator-initiated interventional research. It is designed to be the standard monitoring platform in which the research team can customize their own plan based on protocol-specific requirements. Protocols that are more complex will require additional/more frequent monitoring than what is described in the Monitoring Risk Level Tool.

The FDA draft guidance on the risk-based approach to monitoring is a document that outlines the principles of risk-based monitoring and may assist you in the customization of your monitoring plan: FDA Guidance on Risk-Based Approach to Monitoring.

4.1 Site Initiation

Describe how the sites will be initiated. This is usually the first visit to be performed by the monitor and focuses on training staff and research personnel on protocol-specific procedures. Oftentimes this visit occurs via teleconference. Regardless, the visit is always conducted prior to the start of recruitment.

4.2 Monitoring Process

Describe the periodic monitoring performed by the monitor including the frequency and any circumstances that would trigger additional monitoring procedures.

4.3 Close-Out Procedures

Describe the close-out process. Include any protocol-specific close out procedures. Sections 4.1 to 4.3 should contain information on the preparation, conduct and documentation/follow-up responsibilities of the monitor, site, and coordinating centre (if applicable) for this process.

5.0 Extent of Source Document Verification

Describe the extent of documentation that the monitor will review while performing monitoring procedures. The Monitoring Risk Level Tool outlines SDV requirements based on research category and associated risk exposure. Listed in the model text is typically the **minimum** SDV a monitor will perform during a visit; additional SDV may be required based on study complexity. For high-risk studies, such as phase 1, the monitor should plan to perform 100% SDV on the data points identified as critical (e.g. primary endpoint, SAE's etc.) for all patient CRFs. See the Monitoring Risk Level Tool for a more detailed explanation on the extent of SDV required.

6.0 Monitoring Plan Amendments and Communication

Describe events that may require review and revision of the monitoring plan. Additionally, this section should describe the communication process between the monitor and the site.

7.0 Non-compliance

Describe how you will address any un-resolved/significant/systemic issues identified through monitoring.

8.0 Monitoring Report

Describe the content of the monitoring report and the reporting requirements. Specify who receives the report and how you will escalate issues of non-compliance.

Investigator-Initiated Multicentre Studies

Multicentre interventional trials that are investigator-initiated and coordinated from your institution should have study monitoring in place for all participating sites. It is the **Sponsor/Sponsor-Investigator's responsibility** to ensure that all participating sites have adequate site monitoring. In order to facilitate multi-site monitoring, alternatives to on-site monitoring include the delegation of monitoring activities to a Contract Research Organization (CRO) or the performance of hybrid remote monitoring. You must describe the method(s) used and information to be collected in the REB application. The confidentiality section of the informed-consent form (ICF) should also mention what the monitor will view during the visit.

PLEASE NOTE:

If you choose to perform hybrid remote monitoring, all uploaded/faxed information **must be de-identified prior to sending**.

Examples of de-identified documents that you can fax or upload into an electronic database include:

- Laboratory assessments with patient study code only
- Electronic patient assessment forms (CRFs) with patient code only
- Randomization confirmation documents
- Unanticipated Problems/SAE reporting documentation (evidence that the SAE was reported appropriately)
- Investigational product accountability records, if the trial is not blinded
- Participant questionnaires or diaries (check for completion)
- Signed and dated training logs as well as copies of materials used to train study staff (i.e. slide presentations, hand outs)

Reference Guidelines
Use these documents in the customization of your monitoring plan

- International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) Guidelines. Section 5.18 https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/international-conference-harmonisation/efficacy/good-clinical-practice-consolidated-guideline-topic.html
- Health Canada Therapeutic Products Directorate Food and Drug Regulations for Clinical Studies. Division 5. Canada Gazette Part II, Vol. 135, No. 13, June 7,2001 http://gazette.gc.ca/rp-pr/p2/2001/2001-06-20/pdf/g2-13513.pdf
- Health Canada Natural Health Products Regulations. Canada Gazette Vol. 137 No. 13, June 18th 2003 http://archive.is/O7Fii
- Health Canada Medical Device Regulations https://www.canada.ca/en/health-canada/services/drugs-health-products/medical-devices.html
- Guidance for Industry- Oversight of Clinical Investigations — A Risk-Based Approach to Monitoring http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM269919.pdf
- Tri-Council Policy Statement 2 – Ethical Conduct for Research Involving Humans

http://www.pre.ethics.gc.ca/eng/policy-politique/initiatives/tcps2-eptc2/Default/
- Personal Health Information Protection Act, 2004. http://www.e-laws.gov.on.ca/html/statutes/english/elaws_statutes_04p03_e.htm
- Personal Information Protection and Electronic Documents Act. http://laws-lois.justice.gc.ca/eng/acts/P-8.6/index.html
- Clinical Investigation of medical devices for human subjects – ISO 14155 http://www.iso.org/iso/catalogue_detail?csnumber=45557

Monitoring Plan – Template for Customization

1.0 Study Overview

[Insert brief study synopsis here i.e. purpose, indication, treatment population, primary endpoint]

2.0 Purpose

[For studies conducting on-site monitoring]
The purpose of this monitoring plan is to standardize monitoring procedures for the study entitled _____. Study monitoring ensures that the rights and well-being of human subjects are protected, the reported trial data are accurate, complete, and verifiable from source documents and that the conduct of the trial complies with the protocol, GCP, and regulatory requirements. This document identifies key monitoring activities and specifies the data the monitor will review over the course of the clinical trial.

[For studies that are using hybrid remote monitoring]
The purpose of this monitoring plan is to standardize monitoring procedures for the study entitled _____. This plan identifies key documentation that the monitor will verify both on-site and remotely. This process ensures that that trial-related data are accurate, complete and verifiable from source documents and that participant rights and safety are protected. The monitor will verify compliance with the regulatory requirements, protocol, GCP, study-specific procedures and participant eligibility. In addition to evaluating the reported data for accuracy and completeness, the monitor will identify any trends in data that may be indicative of insufficient documentation or protocol deviations.

3.0 Monitoring Scope

[For studies conducting on-site monitoring]
The Sponsor/Sponsor-Investigator will assign a Monitor to monitor all participating sites. The Monitor will have training on ICH-GCP, Health Canada Division 5 Regulations, TCPS2, Protocol, Institutional SOPs and _____ (list any study-specific procedures). The Monitor will facilitate the monitoring visits with the study coordinator.

[For studies that are using hybrid remote monitoring]
In addition to on-site visits, we will also perform remote monitoring for this study. Remote monitoring will be conducted for this study because _____
*(**Note:** justification is required as to why remote monitoring is to be used – i.e. low-risk study, ease of verification, geographical issues, resources, personnel etc.)*

We will upload de-identified information electronically into a secure password-protected, validated database and/or fax de-identified information to be monitored. We will record data queries noted in the data and will inform the site of all observations in the subsequent monitoring report.

[For all studies]
The monitor will assess _____ (include all that apply):
*(Based on the Risk Level Tool, all those in bold **must** be assessed)*

- ❒ ***patient eligibility and consent***
- ❒ ***unanticipated problems/SAE's for recording and reporting completeness***
- ❒ ***protocol defined endpoints***
- ❒ ***CRF source data verification***
- ❒ ***drug accountability***
- ❒ ***regulatory documentation (for site and/or sponsor)***
- ❒ ***delegation logs***
- ❒ ***training documents***
- ❒ *study specific SOPs*
- ❒ *essential document maintenance*
- ❒ *deviation/violation recording and reporting*
- ❒ *privacy considerations*
- ❒ *any protocol-specific procedures*

During the monitoring process, the monitor will document any findings in the _____
*(**Note:** list any tools created e.g. logs, charts, templates – see Monitoring Checklist tool template)*
The monitor will address deficiencies to the appropriate study team member in order to implement corrective actions or to recommend follow-up procedures. All observations noted during the monitoring visit will appear in the monitoring report.
The monitor will assess study files and documentation against ICH-GCP, regulatory requirements, protocol, Institutional SOPs and any study-specific SOPs.

4.0 Timing and Frequency

4.1 Site Initiation

A site initiation meeting/teleconference will be conducted once the site has received all regulatory and REB approvals, but before recruitment has begun. All study team members for this site will attend in addition to the Sponsor/Sponsor-Investigator for the trial coordinating centre.
*(**Note:** This applies to multicentre studies in which the Sponsor/Sponsor-Investigator is responsible for the initiation and start-up of participating sites)*
The Sponsor/Sponsor-Investigator will conduct site initiation and will cover the items listed below in order to ensure that all study staff are aware of their delegated duties:

- *Protocol*
- *Investigational product*

- *Study-specific SOPs*
- *CRF completion*
- *ICH-GCP compliance*
- *Health Canada regulations*
- *Unanticipated Problems/SAE/AE recording and reporting*
- *Deviation and violation management*
- *QI and Co-I responsibilities*

The study monitor will generate a brief report on the material covered and any additional training required. The monitor will forward the report to the site for review and sign-off no later than _____ weeks/days from site initiation.

4.2 Monitoring Process

[For studies conducting on-site monitoring]
The monitor will perform the first monitoring visit shortly after the site has recruited their first participant.

> *(**Note:** The monitor performs this to ensure that research personnel have implemented the appropriate recruitment processes and procedures such as eligibility sign-off and consent. The monitor should do this visit prior to the site recruiting more participants)*

The monitor will contact the study coordinator (or designee) prior to their visit in order to arrange room bookings and visit(s) to Pharmacy (if applicable). Any corrective actions implemented in regards to discrepancies identified during the site initiation visit (or previous monitoring visits) will be assessed for completeness.

Based on the research category and participant/institute risk exposure, on-site monitoring visits will occur every _____ months/weeks following the first monitoring visit. The monitor may schedule more visits as needed.

The study coordinator (or another team member if the coordinator is unavailable) will be available to assist the monitor during the visit.

[For studies that are using hybrid remote monitoring]
For remote monitoring, research staff will fax de-identified documentation to the study monitor or will electronically upload de-identified source documentation and CRF's into a secure validated online database within _____ hours/days of receipt. The study monitor will access the online database and perform remote SDV and study master file review every _____ weeks/months. Uploaded documentation includes (include all that apply):

- *Laboratory assessments with patient study code only*
- *Electronic patient assessment forms (CRFs) with patient code only*
- *Randomization confirmation documents*
- *SAE reporting documentation (evidence that the SAE was reported appropriately)*
- *Investigational product accountability records*
- *Participant questionnaires or diaries (check for completion)*

- *Signed and dated training logs as well as copies of materials used to train study staff (e.g. slide presentations, hand outs)*

4.3 Close Out Procedures

The monitor will conduct close-out procedures once the last enrolled participant has completed his/her final study visit. During close-out, the monitor will perform the following:

- *Ensure the completion of outstanding case report forms and queries*
- *Ensure all previous monitoring corrections have been addressed*
- *Return or destruction of study drug (if applicable)*
- *Collect outstanding patient data forms and study forms such as the screening and monitoring logs*
- *Perform a final review of the study file documents*
- *Review the plans for record retention*
- *Ensure all SAE's have been reported appropriately*
- *Ensure that the QI has notified the local REB of the site closure*

The monitor will prepare the final monitoring report and send it to the site for their records. The site will address all monitoring observations (including observations from previous monitoring reports) prior to final study closeout.

5.0 Extent of Source Document Verification

[For studies conducting on-site monitoring]
During the on-site monitoring visit(s), the monitor will perform the following source document verification and study master file review:

- *100% of patients' Informed Consent Forms (ICFs) and Eligibility Criteria*
- *100% of the Unanticipated Problems/Serious Adverse Events (SAEs) that have been reported since the previous monitoring visit will be SDV*
- *100% of protocol-related endpoints will be assessed for all applicable participants*
- *X% of patients' drug accountability records will be verified 100%*
  *(**Note:** This will vary depending on target accrual numbers. This number usually varies between 10-20%. This may not be feasible for blinded trials)*
- *X% of patients' CRFs will be source-document verified 100%*
  *(**Note:** This will vary depending on target accrual numbers. This number usually varies between 10-20%)*
- *Any training documentation/records and delegation log*
- *Any regulatory documentation including Health Canada approvals/amendments*

If the monitor notices a large number of discrepancies during the visit, they may perform additional SDV and/or monitoring visits as needed.

[For studies that are using hybrid remote monitoring]
During each remote monitoring review, the monitor will perform the following source document verification and study master file review:

- *100% of participant randomization confirmation documentation*
- *100% of the Unanticipated Problems/Serious Adverse Events (SAEs) that have been reported since the previous monitoring review*
- *100% of protocol-related endpoints will be assessed for all applicable participants*
- *X% of patients' CRFs will be source-document verified 100%*
- *X% of patients' drug accountability records will be verified 100%*
- *Any training documentation/records and delegation log*
- *Any regulatory documentation including Health Canada approvals/amendments*

If the monitor notices a large number of discrepancies during the visit, they may perform additional SDV and/or on-site monitoring visits as needed.

6.0 Monitoring Plan Amendments and Communication

This study monitoring plan will be reviewed every _____ (timeline in which plan will be reviewed i.e. quarterly, bi-annually etc.) in order to ensure that the processes and procedures outlined herein remain applicable to the conduct of the study. Additionally, if amendments are made to the protocol that affect the study procedures and/or patient safety, a review of the monitoring plan will be performed in order to revise the plan as needed.

The monitor will remain in communication with the site during the entire course of the study. All monitoring communications between the site and the monitor will be printed and saved in the study communication binder. If the monitoring visit needs to be re-scheduled, the monitor will give the site ample notice of the new monitoring visit date and vice versa.

7.0 Non-compliance

If the monitor identifies significant/recurring/systemic issues during monitoring procedures, the monitor will communicate these issues immediately to the study coordinator and QI/PI in order to secure compliance. It is the QI/PI's responsibility to ensure that they have implemented corrective actions appropriately. For multicenter trials, escalation to the Sponsor/Sponsor-Investigator may be necessary if non-compliance at the site-level persists.
If these issues continue with no corrective action implemented within a reasonable period, the monitor will communicate these findings directly to the institution's clinical research administration for risk escalation.

8.0 Monitoring Report

The study monitor will generate monitoring reports after the completion of every monitoring event (i.e. completing an on-site visit or remote monitoring). The trial-coordinating centre will review reports prior to sending a copy of the report to the monitored site. The trial-coordinating centre will retain the original report.

*(**Note:** This applies for multicenter studies in which the coordinating centre's QI takes responsibility for monitoring participating sites)*

The report will give a brief overview of the status of the study and will include a list of all the documentation reviewed by the monitor, any observations noted, corrective actions implemented and any follow-up required.

The study monitor will communicate findings to the site in a timely manner. The site will respond to any queries, observations and/or comments listed in the monitoring report. The Site QI/PI will sign, date and return a signed copy of the monitoring report to the monitor. The monitored site will keep a signed monitoring report in the site files for their records and will use the report as a reference in any subsequent monitoring visits.

*(**Note:** See monitoring report template)*

ATTACHMENT # 1

Monitoring Checklist Template

ESSENTIAL DOCUMENT AND RECORD MANAGEMENT

Document Type	Document Date	Date of REB Approval / Acknowl.	In Study File? Yes	No	N/A
Copy of REB Initial Application			☐	☐	☐
Health Canada No Objection Letter - for international sites, other regulatory bodies approvals if applicable (FDA, Europe)			☐	☐	☐
Clinical Trial Agreement(s)		N/A	☐	☐	☐
Qualified Investigator Undertaking Form (Canadian sites)		N/A	☐	☐	☐
REB Attestation or equivalent (Canadian sites)		N/A	☐	☐	☐
Clinical Trial Site Information Form (all Canadian sites)		N/A	☐	☐	☐
FDA 1572 form (if applicable)		N/A	☐	☐	☐
Investigator Brochure/ Product Monograph Version			☐	☐	☐
Original Approved Protocol			☐	☐	☐
Protocol Amendments:			☐	☐	☐
Original Approved ICF version			☐	☐	☐
Approved ICF versions:			☐	☐	☐
Annual Renewals:			☐	☐	☐

Component of Review	Findings:
REB documentation	

Component of Review	Findings:
Essential documentation	

REB DOCUMENTATION

REB Documentation Review	In Study File? Yes	No	N/A
All REB communications on file	☐	☐	☐
Timely submission of changes to REB (amendment reports, updated product monographs/protocols/ICF etc.)	☐	☐	☐
All SAE's submitted to the REB in a timely manner	☐	☐	☐
All annual renewals submitted on time	☐	☐	☐

REGULATORY DOCUMENTATION

Regulatory Document	Document Date	In Study File? Yes	No	N/A
Approved QOL (if applicable)		☐	☐	☐
REB Correspondence	various	☐	☐	☐
REB Membership List		☐	☐	☐
Investigator/QI's Licence		☐	☐	☐
Sub-Investigator's CV		☐	☐	☐
Other Personnel's CV		☐	☐	☐
Laboratory Certification		☐	☐	☐
Lab normal ranges		☐	☐	☐

Trial initiation documentation (start up meeting agenda / attendance)		☐ ☐ ☐
Training records		☐ ☐ ☐
Delegation log		☐ ☐ ☐
Screening log		☐ ☐ ☐
Patient Identification Code List		☐ ☐ ☐
Randomization / Registration log		☐ ☐ ☐
Trial Closure Documentation		☐ ☐ ☐

Component of Review	**Findings:**
Regulatory documentation	

PRIVACY RECOMMENDATIONS

PHI (personal health information) REB/ICF components	**Yes**	**No**
Which organizations and/or individuals will have access to PHI		
Data containing PHI will be protected against breaches of privacy (ie: locked cabinets, password protected, encrypted)?		
Indicates what patient identifiers will be used.		
Indicate how information will be stored (paper or electronic or both).		
Indicate how long information will be kept after the close of the study?		
Indicate how data will be destroyed once the storage date has expired?		

Component of Review	**Findings:**
Privacy issues	

PHARMACY REVIEW

ASSESSMENT/DEFICIENCIES		
Number of patients cross-checked with accountability records:		
1. DRUG ACCOUNTABILITY LOG (DAL) COMPLETED & CORRECTLY FILLED OUT	**Yes**	**No**
Able to track the receipt, use and disposition of supplied agent		
Data on DAL is correct: (dose/agent/route/date/initials/ID)		
Discrepancies between DAL and patient data on CRF		
DAL not kept on timely basis chronological order		
There are erasures or “whiteouts”; Corrections are not lined out, dated and initialled		
Comments:		
3. DRUG ACCOUNTABILITY LOGS KEPT AS RECORD OF RECEIPT / DISPENSING	**Yes**	**No**
All transactions documented on DAL		
Balance on DAL matches inventory balance		
Comments:		
4. DRUG ORDER/SHIPMENT RECEIPTS KEPT	**Yes**	**No**
All drug orders kept as required		
All drug temperature monitoring kept as required		
All shipment receipts kept as required		
Comments:		
5. RETURN OF DRUG TO RELEVANT ORGANIZATION (or destruction)	**Yes**	**No**
Agent returned/destroyed as required		
Agent destroyed before authorized		
Agent drug return/destruction receipts / DALs kept as required		
Comments:		

Component of Review	Findings:
Pharmacy	

PATIENT ASSESSMENT/ DEFICIENCIES

INFORMED CONSENT RESPONSE SHOULD BE **"YES"**	**Yes**	**No**
1. Original consent (not copy) present on site / All pages present		
2. ICF current REB approved version when signed		
3. Re-consenting if applicable in a timely manner		
4. Copy of signed consent provided to each patient		
5. Local privacy requirements followed		
Comments:		
ELIGIBILITY RESPONSE SHOULD BE **"YES"**	**Yes**	**No**
6. Patient eligible		
7. Able to confirm eligibility		
8. Sufficient documentation		
Comments:		
INVESTIGATIONS RESPONSE SHOULD BE **"YES"**	**Yes**	**No**
9. Reported protocol mandated lab tests		
10. Reported protocol mandated radiology or other investigations		
Comments:		
TREATMENT RESPONSE SHOULD BE **"YES"**	**Yes**	**No**
11. Correct dose administration		
12. Dose modifications as per protocol		
13. Compliancy		
Comments:		
ADVERSE EVENTS / SERIOUS ADVERSE EVENTS / UNANTICIPATED PROBLEMS RESPONSE SHOULD BE **"NO"**	**Yes**	**No**
14. Unreported SAE		
15. Unreported grade 1 / 2 adverse event (as defined by the protocol and/or study AE grading criteria)		

16. Unreported grade 3 / 4 adverse event and/or significant lab values (as defined by the protocol and/or study AE grading criteria)		
Comments:		
GENERAL RESPONSE SHOULD BE **"NO"**	**Yes**	**No**
17. Data could not be verified (source documentation)		
18. Transcription errors (errors in submitted data)		

Component of Review	**Findings:**
Patient documentation	