**N2 Quality Committee Guidance for Developing Monitoring Plans**

**INTRODUCTION**

The Sponsor/Sponsor-Investigator should implement a system to manage quality throughout all stages of the trial. Ongoing quality control monitoring is one activity of a study’s overall quality management system. Study monitoring is a Sponsor responsibility as outlined in ICH GCP E6 (R2). How and when monitoring will be done should be documented in a monitoring plan prior to activation of the study.

This guidance document is intended to assist a study sponsor in developing and creating a monitoring plan for a clinical trial. Each section of a monitoring plan is outlined below and a description of the type of language (as well as some template language) that could be included in each section is provided. Sites should also review the references listed below for additional information on developing monitoring plans.

It is the Sponsor/Sponsor-Investigator’s responsibility to ensure that all participating sites have adequate site monitoring conducted by qualified monitors appointed by the Sponsor. As per ICH GCP E6 (R2) Section 5.18.2 monitors should be appropriately trained, and have the scientific and/or clinical knowledge needed to monitor the trial adequately. Monitors should be thoroughly familiar with the investigational product(s), the protocol, written informed consent form and any other written information to be provided to subjects, the sponsor’s SOPs, GCP, and the applicable regulatory requirement(s). A monitor’s qualifications should be documented. Monitors may be Investigators or site staff, but should not be directly involved in the conduct of the trial i.e., data collection, consenting participants.

In order to facilitate multi-site monitoring, alternatives to on-site monitoring include the delegation of monitoring activities to a Contract Research Organization (CRO). The Sponsor should ensure oversight of any trial-related duties and functions carried out on its behalf, including trial-related duties and functions that are subcontracted to another party by the Sponsor’s contracted CRO(s).

The Sponsor may choose on-site monitoring, a combination of on-site and centralized monitoring, or, where justified, centralized monitoring. The Sponsor should document the rationale for the chosen monitoring strategy (e.g., in the monitoring plan) and the monitoring responsibilities of all the parties involved should be clearly documented.

**Glossary of terms**

**Monitoring (As per Section 1.38 of ICH GCP E6 (R2)**

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 requirement(s).

**Monitoring Plan (As per Section 1.38.1 of ICH GCP E6 (R2)**

A monitoring plan is a description of the methods, responsibilities and requirements for monitoring the trial, which also includes the rationale for the chosen monitoring strategy.

The Sponsor should develop a monitoring plan that is tailored to the specific human subject protection and data integrity risks of the trial. The plan should describe the monitoring strategy, the monitoring responsibilities of each party involved, the various monitoring methods to be used and the rationale for their use. The plan should also emphasize the monitoring of critical data and processes. Particular attention should be given to those aspects that are not routine clinical practice and that require additional training. The monitoring plan should reference the applicable policies and procedures.

**On-site Monitoring (As per ICH GCP E6 (R2) Section 5.18.3)**

On-site monitoring is performed at the site(s) where the clinical trial is being conducted.

**Centralized Monitoring** **(As per ICH GCP E6 (R2) Section 5.18)**

Centralized monitoring is a remote evaluation of accumulating data, performed in a timely manner, supported by appropriately qualified and trained persons (e.g., project manager, data managers, biostatisticians).

**Sponsor-Investigator (As per ICH GCP E6 (R2) Section 1.54)**

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.

**Coordinating Investigator (As per ICH GCP E6 (R2) Section 1.19)**

An Investigator assigned the responsibility for the coordination of Investigators at different centres participating in a multi-centre trial.

**Qualified Investigator (QI)** **(As per Health Canada Division C.05.001)**

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.

**Sponsor (As per ICH GCP E6 (R2) Section 1.53)**

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

**Investigator (As per ICH GCP E6 (R2) Section 1.34)**

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.

**REFERENCES**

ICH Harmonized Guideline Integrated Addendum to ICH E6(R1): Guideline for Good Clinical Practice E6(R2)

Guidance for Industry. Oversight of Clinical Investigations – A Risk-Based Approach to Monitoring. U.S. Department of Health and Humans Services. Food and Drug Administration. 2013.

Health Canada Food and Drugs Act and Regulations. Division C.05.001.

1. **Administrative Details - Title Page, Approval of the Plan, Table of Contents**

Every monitoring plan should have a title page which identifies what the document is and the key contact people. Approval of the document could be included on the title page or as a separate signature page. A table of contents could also be included in the monitoring plan.

**Example of a Title Page:**

|  |
| --- |
| Monitoring Plan for Protocol # |
| Study Title (Full Title):  |
| REB Reference Number (if applicable):  |
| Sponsor/Sponsor-Investigator: |
| Study Chair/Medical Monitor/Senior Medical Officer/(Responsible for Monitoring Plan):  |

Prepared By (print): \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Role \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_Signature: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Date: \_\_\_\_\_\_\_\_

Approved By (print): \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Role\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Signature: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Date:\_\_\_\_\_\_\_\_\_

Date of Approval: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Monitoring Plan Version Date/number: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

1. **Study Overview**

A brief synopsis of the study protocol should be outlined including the purpose, indication, treatment population, primary endpoint, objectives and the critical data/study procedures. Much of this information can be taken from the synopsis within the study protocol.

1. **Purpose**

This section should describe the purpose of the monitoring plan including the general purpose of monitoring as outlined in ICH GCP E6 (R2) and the regulations.

**Example of text that could be included in the purpose:**

*The purpose of this monitoring plan is to standardize monitoring procedures for the study entitled <Protocol name>. 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. 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 and/or protocol deviations. This document identifies key monitoring activities, (particular attention should be given to those aspects that are not routine clinical practice and that require additional training) and specifies the data the monitor will review over the course of the clinical trial.*

1. **Monitoring Scope**

The determination of the extent and nature of monitoring should be based on considerations such as the objective, purpose, design, complexity, blinding, size, and endpoints of the trial. The Sponsor should develop a systematic, prioritized, risk-based approach to monitoring a clinical trial. The monitoring plan should be tailored to the specific human subject protection and data integrity risks of the trial. Varied approaches to monitoring are acceptable, and there should be flexibility in the extent and nature of monitoring to ensure effectiveness and efficiency of the monitoring process. The rationale for the chosen monitoring strategy should be documented in the plan.

The scope of the monitoring plan should be an overview of what the monitor will be doing when conducting a monitoring visit. If the study is multicentre/multinational, this section should also describe how the coordinating centre is monitoring participating sites. Areas to be monitored need to be outlined and could include: the Trial Master File/Investigator Site File and all required essential documents. This may include training documentation, regulatory documents, study task delegation log, participant logs, signed consents, investigational product handling and participant data.

**Types of Monitoring**

**On-site monitoring**. Monitors travel to the site to conduct a review of documents and facilities 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, pharmacy processes, laboratory processes). Additionally, on-site monitoring allows for verification of the existence of enrolled participants and that data are real and accurate (i.e., view signed consent(s), view original/identifiable source documents).

**Centralized monitoring**. Centralized monitoring is a remote evaluation of accumulating data, performed in a timely manner, supported by appropriately qualified and trained persons (e.g., project manager, data managers, biostatisticians). Remote monitoring could involve the review of regulatory documents and/or de-identified data. All direct identifiers are removed from the information and replaced with a code before transmitting the data to a coordinating centre. This can be done either through uploading into a secure validated online study database or by secure email.

Centralized monitoring processes provide additional monitoring capabilities that can complement and reduce the extent and/or frequency of on-site monitoring and help distinguish between reliable data and potentially unreliable data.

Review of accumulating data from centralized monitoring, which may also include statistical analyses, can be used to:

(a) Routinely review submitted data;

(b) Identify missing data, inconsistent data, data outliers or unexpected lack of variability;

(c) Identify protocol deviations that may be indicative of systematic or significant errors in data collection and require reporting at a site or across sites, or may be indicative of potential data manipulation or data integrity problems;

(d) Identify data trends such as the range, consistency and variability of data within and across sites;

(e) Analyze site characteristics and performance metrics;

(f) Select sites and/or processes for targeted on-site monitoring.

The monitoring plan can also be made up of a combination of on-site and centralized monitoring when on-site monitoring visits are performed in addition to remote monitoring.

**Example of Text that could be included in the 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 the applicable regulations <Include all regulations that apply to the specific study i.e., ICH-GCP, Health Canada Division 5 Regulations, TCPS2>, the study protocol and <list any study-specific procedures>. The Monitor will facilitate the monitoring visits with the study coordinator.*

**[For studies that are using centralized monitoring only]**

 *Centralized monitoring will be conducted for this study because [justification is required as to why centralized monitoring is to be used – i.e., nature of study, low-risk study, etc.].*

*Sites will be asked to upload de-identified information electronically into a secure password-protected, validated database and/or email de-identified information to be monitored. A confidential/secure process must be in place when email is to be used. Data queries will be recorded and the site will be informed of all observations in the monitoring report.*

***[For all studies]***

*The monitor will assess \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ (include all that apply):*

* + - *participant eligibility and consent*
		- *unanticipated problems/SAE’s for recording and reporting completeness*
		- *protocol defined endpoints*
		- *CRF source data verification*
		- *pharmacy documents, drug accountability logs (if applicable)*
		- *documentation of intervention (e.g. therapy, procedure)(if applicable)*
		- *randomization process (if applicable)*
		- *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*
		- *biospecimens, sample management documents*
		- *specify:*

*During the monitoring process, the monitor will document any findings. The monitor will address deficiencies to the appropriate study team member in order to implement corrective actions and/or preventative actions or to recommend follow-up procedures. All observations noted during the monitoring visit will appear in the monitoring report or letter. The monitor will assess study files and documentation against ICH-GCP, regulatory requirements, the study protocol, any study-specific SOPs and any applicable Institutional SOPs.*

1. **Monitoring Process**

The periodic monitoring performed by the monitor including the frequency and any circumstances that would trigger additional monitoring procedures should be described. Selection of monitors should also be addressed. This section should contain information on the preparation, conduct and documentation/follow-up responsibilities of the monitor, site, and coordinating centre (if applicable) for this process.

* 1. **Timing and Frequency**

The timing and frequency of the monitoring should be outlined in the monitoring plan. Health Canada requires a minimum of annual monitoring regardless of enrollment. A “risk-based” approach to monitoring in which the degree of monitoring required 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 Sponsor can customize their own plan based on protocol-specific requirements. A high-risk study should undergo monitoring at a greater frequency than lower-risk studies. The frequency of monitoring could be based on calendar dates (i.e., every six months) or participant enrolment (i.e., after the first enrolment). Note: If a site is a high-enroller then more frequent monitoring visits may be needed.

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 in the customization of a monitoring plan: [FDA Guidance on Risk-Based Approach to Monitoring](http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM269919.pdf).

**5.2 Choosing a Monitor**

The selected monitor must be qualified by appropriate training, education and experience (level determined by the Sponsor and institutional policy/SOPs (if applicable).The monitor should have a good understanding of the study protocol, any study-specific SOPs, GCP and any other applicable regulations and guidelines. Study monitors need to be independent of the areas of the study which they are monitoring. 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, who are qualified by training, from other trials may also monitor studies they are not involved with. In addition, some institutions have a quality department that can provide monitors for on-site monitoring.

* 1. **Extent of Source Document Verification (SDV)**

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 participant CRFs. See the Monitoring Risk Level Tool for a more detailed explanation on the extent of SDV required.

**5.4 Communication**

Describe the communication process between the monitor and the site. Monitoring results should be provided to the sponsor (including appropriate management and staff responsible for trial and site oversight) in a timely manner for review and follow up as indicated. Results of monitoring activities should be documented in sufficient detail to allow verification of compliance with the monitoring plan.

**5.5 Close-Out Procedures**

The close-out process should be described including any protocol-specific close-out procedures.

**Example of text that could be included in the Monitoring Process:**

***[For studies conducting on-site monitoring]***

*The monitor will perform the first monitoring visit within 2 weeks after the site has recruited their first participant. The monitor will contact the study coordinator (or designee) prior to their visit in order to arrange room bookings, visit(s) to Pharmacy (if applicable), and access to patient charts (as required for source data verification).*

*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 based on results of monitoring visits or the number of participants enrolled. Any corrective actions implemented in regard to discrepancies identified during previous monitoring visits will be assessed for completeness.*

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

* *100% of participants’ 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 participants’ 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 participants’ 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 authorizations, correspondence*

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 centralized monitoring]***

*For centralized monitoring, site research staff will be requested to send de-identified documentation to the study monitor or coordinating centre 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 de-identified documentation includes (include all that apply):*

* + *Laboratory assessments with participant study code only*
	+ *Electronic patient assessment forms (CRFs) with participant 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, handouts)*
	+ *Regulatory documents – ethics approval letters, ethics submission documents*
	+ *Delegation logs*
	+ *Approved consents*

*During each centralized 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 participants’ CRFs will be source-document verified 100%*
* *X% of participants’ drug accountability records will be verified 100%*
* Any training documentation/records and delegation log
* *Any regulatory documentation including Health Canada authorizations, correspondence*

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

*The monitor will conduct close-out procedures once the last enrolled participant has completed the final study visit, all queries have been addressed, and individual patient files will no longer be accessed. Data analysis may be ongoing or complete. 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 participant data forms and study forms*
* *Perform a final review of the study file documents*
* *Review the plans for record retention*
* *Ensure all SAEs 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/letter 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. The site Investigator must acknowledge receipt/review of the report.*

1. **Monitoring Plan Amendments**

Describe events that may require review and revision of the monitoring plan.

**Example of Text that could be included in the Monitoring Plan Amendments:**

*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 participant safety, a review of the monitoring plan will be performed to revise the plan as needed.*

1. **Non-compliance**

A description of how any un-resolved/significant/systemic issues identified through monitoring will be addressed should be provided. See Section 5.20 of ICH GCP E6 (R2). Also refer to your institutional SOPs.

**Example of text that could be included in the Non-Compliance Section:**

*If the monitor identifies significant/recurring/systemic issues during monitoring procedures, the monitor will communicate these issues immediately to the Sponsor, study coordinator and the Principal Investigator (PI)in order to secure compliance. It is the PI’s responsibility to ensure that corrective actions have been implemented appropriately. If these issues continue with no corrective action implemented within a reasonable period, the Sponsor may take additional action to ensure compliance including temporarily or permanently terminating the site from participating in the conduct of the trial.*

1. **Monitoring Report/Follow-up letter**

The content of the monitoring report, reporting requirements and who receives the report in this section.

**Example of text that could be included in the Monitoring Report Section:**

*The study monitor will generate monitoring reports/letters after the completion of every monitoring visit (i.e., completing an on-site visit or centralized 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.*

*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 within a specified timeframe. 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.*

**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(s) - 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; original and amendment)  |  | N/A | [ ]  [ ]  [ ]  |
| FDA 1572 form (if applicable) |  | N/A | [ ]  [ ]  [ ]  |
| Investigator Brochure/ Product Monograph Version  |  |  | [ ]  [ ]  [ ]  |
| Original Approved Protocol  |  |   | [ ]  [ ]  [ ]  |
| Protocol Amendments:  |  |   | [ ]  [ ]  [ ]  |
| Original Approved ICF version(s) |  |  | [ ]  [ ]  [ ]  |
| Approved ICF version(s): |  |  | [ ]  [ ]  [ ]  |
| Annual Renewals:  |  |  | [ ]  [ ]  [ ]  |
| Patient information materials |  |  | [ ]  [ ]  [ ]  |

|  |  |
| --- | --- |
| **Component of Review** | Findings: |
| Essential documentation |  |

**REB DOCUMENTATION**

|  |  |
| --- | --- |
| **REB Documentation Review** | **In Study File?****Yes No N/A** |
| All REB communications on file (submissions, approvals, etc) | [ ]  [ ]  [ ]  |
| Timely submission of changes to REB (amendment reports, updated product monographs/protocols/ICF etc.)  | [ ]  [ ]  [ ]  |
| SAE’s submitted to the REB in a timely manner | [ ]  [ ]  [ ]  |
| Annual renewals submitted on time | [ ]  [ ]  [ ]  |

**REGULATORY DOCUMENTATION**

|  |  |  |
| --- | --- | --- |
| **Regulatory Document**  | **Document Date** | **In Study File?****Yes No N/A** |
| Approved QOL(s) (if applicable)  |  | [ ]  [ ]  [ ]  |
| REB Membership List |  | [ ]  [ ]  [ ]  |
| Investigator/QIs License |  | [ ]  [ ]  [ ]   |
| Sub-Investigators CV |  | [ ]  [ ]  [ ]  |
| Other Study Personnel’s CV/documentation of qualifications |  | [ ]  [ ]  [ ]  |
| Laboratory Certification(s)  |  | [ ]  [ ]  [ ]  |
| Lab normal ranges |  |  [ ]  [ ]  [ ]  |
| Trial initiation documentation (start-up meeting agenda / attendance) |  | [ ]  [ ]  [ ]   |
| Training records (protocols/amendments; GCP, Div 5, site SOPs) |  | [ ]  [ ]  [ ]  |
| Delegation log |  | [ ]  [ ]  [ ]   |
| Screening log |  | [ ]  [ ]  [ ]  |
| Patient Identification Code List(Master List)  |  | [ ]  [ ]  [ ]  |
| Enrollment/Randomization / Registration log |  | [ ]  [ ]  [ ]  |
| Trial Closure Documentation(Archival information) |  |  [ ]  [ ]  [ ]  |

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| --- | --- |
| **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** | **Yes No** |
| --- | --- |
| **Pharmacists listed on delegation logs** | [ ]  [ ]  |
| **Appropriate licensure, GCP/Div 5 & SOP training records; Pharmacy training on protocol & amendments** | [ ]  [ ]  |
| **Protocol/NOL/Pharmacy manual available in Pharmacy** | [ ]  [ ]  |
| **Number of participants cross-checked with accountability records:** | [ ]  [ ]  |
| **1. DRUG ACCOUNTABILITY LOG (DAL) COMPLETED & CORRECTLY FILLED OUT**  |  |
| Able to track the receipt, use and disposition of supplied agent(investigational product) | [ ]  [ ]  |
| Investigational Product labelling (as per Health Canada Div 5, if applicable) | [ ]  [ ]  |
| 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 | [ ]  [ ]  |
| Good documentation practices followed. There are no erasures or “whiteouts”; Corrections are lined out, dated and initialled.  | [ ]  [ ]  |
| Comments: |  |
| **3. DRUG ACCOUNTABILITY LOGS KEPT AS RECORD OF RECEIPT / DISPENSING** | Yes No |
| All transactions documented on DAL (log accurate and up to date) | [ ]  [ ]  |
| Balance on DAL matches inventory balance (shelf count accurate) | [ ]  [ ]  |
| Comments: |  |
| **4. DRUG ORDER/SHIPMENTRECEIPTS/STORAGE CONDITIONS** | Yes No |
| All drug orders/shipment receipts kept as required | [ ]  [ ]  |
| All drug temperature monitoring kept as required | [ ]  [ ]  |
|  Temperature excursions documented appropriately and followed up? | [ ]  [ ]  |
| 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 participant | [ ]  [ ]  |
|  |  |
| Comments: |  |
| **ELIGIBILITY** RESPONSE SHOULD BE **“YES”**  | **Yes No** |
| 5. Participant eligible / sufficient documentation  | [ ]  [ ]  |
| 6. Able to confirm eligibility; eligibility confirmed by Investigator  | [ ]  [ ]  |
|  | [ ]  [ ]  |
| Comments: |  |
| **INVESTIGATIONS** RESPONSE SHOULD BE **“YES”**  | **Yes No** |
| 7. Reported protocol mandated lab tests  | [ ]  [ ]  |
| 8. Reported protocol mandated radiology or other investigations  | [ ]  [ ]  |
| Comments: |  |
| **TREATMENT** RESPONSE SHOULD BE **“YES”** |  **Yes No** |
| 10. Correct dose administration  | [ ]  [ ]  |
| 11. Dose modifications as per protocol  | [ ]  [ ]  |
| 12. Compliancy (? Oral?)  | [ ]  [ ]  |
| Comments: |  |
| **ADVERSE EVENTS / SERIOUS ADVERSE EVENTS / UNANTICIPATED PROBLEMS** RESPONSE SHOULD BE **“NO”** | **Yes No** |
| 13. Unreported SAE  |  [ ]  [ ]   |
| 14. Unreported grade 1 / 2 adverse event (as defined by the protocol and/or study AE grading criteria)  | [ ]  [ ]  |
| 15. Unreported grade 3 / 4 adverse event and/or significant lab values (as defined by the protocol and/or study AE grading criteria)  | [ ]  [ ]  |
| 16. Causality assigned by Investigator  | [ ]  [ ]  |
| Comments: |  |
| **GENERAL** RESPONSE SHOULD BE **“NO”** | **Yes No** |
| 17. Data could not be verified (inadequate source documentation)  | [ ]  [ ]  |
| 18. Transcription errors (errors in submitted data)  | [ ]  [ ]  |
| 19. Timeliness of data entered on CRF/eCRF.  | [ ]  [ ]  |

|  |  |
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| **Component of Review** | Findings: |
| Patient documentation |  |