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| Sponsor |  |
| **Investigational product** |  |
| **Protocol number** |  |
| **Principal Investigator (PI)** |  |
| **Study sites** |  |

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| --- | --- | --- | --- | --- |
| Signature/date Sponsor | |  | | |
| Signature/date Monitor | |  | | |
| Personnel consulted during the drafting of this monitoring plan | | | | |
| **Name** | **Affiliation** | | **Role** | **Section consulted on** |
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# Introduction

The Monitoring Plan (MP) establishes how a risk based monitoring approach will be applied for [protocol number, title], including the monitoring methods, requirements and responsibilities of parties involved. The plan was developed in collaboration with the personnel mentioned above and has been informed by a corresponding risk assessment. A monitor will perform tasks in accordance with the, ICH GCP, applicable regulatory requirements and relevant standard operating procedures (SOPs). The monitor is familiar with the investigational product, protocol, informed consent form(s)/assents and the SOPs the site and/or coordinating centre staff will be working within. Major protocol amendments will require this monitoring plan be revisited.

## Description of the study

## Study objectives

*List study objectives as per protocol*

## Critical data

*Define the critical data and processes*

# Monitoring activities

### Monitor’s role in communication with the site

The monitor acts as the main line of communication between the sponsor and the investigator. As each trial team is structured differently, including instances where the PI is not based at a site for field trials, it should be clear to all involved as to how site staff is privy to important information necessary for their role and vice versa. If necessary, a note to file or other documentation may be used when assigning communication responsibilities.

**Monitor’s role in essential documentation (ED) maintenance and/or review**

EDs will be maintained according to [SOP(s)].

*Delete not applicable options or use text to describe the process for this particular study if required:*

* This is a single site study where the Sponsor file and ISF are combined. Note(s) to file will specify which ED, if any, are not located in the hardcopy file, and indicate where they are located and why. The monitor will periodically review EDs for completeness and accuracy and alert the study staff to discrepancies and upcoming expiration dates etc.
* This is a multi-centre study where the Sponsor file and ISF are not combined. [Site] acts as a co-ordinating centre, holding and maintaining the Sponsor file on its behalf, and provides each site with their ISF at site initiation. The monitor will periodically collect original documents from the sites, ensuring that a copy of such are then placed in the relevant ISF, ensuring that EDs are maintained at the site as per [SOP] in collaboration with an appropriate member of the site team.

### Monitor’s role in site initiation and interim monitoring visits

An initiation visit will take place at each site before the enrolment of any study participants, according to [SOP]. Interim monitoring visits will then be conducted to confirm that participants’ rights are being protected, and the study is being conducted according to the protocol, applicable regulations (including GCP) and relevant SOPs.

*Adapt/remove the text below as appropriate:*

A risk-based approach has been used to determine the frequency and timing of monitoring visits, the following factors have been taken into account.

* Complexity of study design
* Number of study visits
* Types of study endpoints
* Clinical complexity of study population and target enrolment
* Geography
* Relative experience of the PI and of the sponsor with the PI
* Electronic data capture
* Relative safety of the investigational product
* Stage of the study
* Quantity of data

1. The first monitoring visit will be conducted at each site after approximately [number of participants] have been [screened, enrolled, randomised].
2. Subsequent monitoring visits will be scheduled at [frequency]. *More specific metrics may be used if a tapered approach to monitoring will be used, with more regular monitoring initially and decreasing if no non-compliance issues have been detected.*
3. Metrics for activities during each monitoring visit are detailed in Appendix 1

The monitor will discuss findings and planned follow up procedures with the sponsor/PI. The site must provide the monitor with opportunities to meet with the study staff periodically during the visit to ask questions and provide clarification where needed.

### Monitor’s role at close-out of a clinical trial

The monitor will conduct the close visit according to [SOP]. All monitoring findings will be addressed prior to study close out. The final report is prepared and sent to the sponsor PI for their records.

# Non-compliance

Non-compliance with the protocol, procedures, GCP guidelines and/or applicable regulatory requirement(s) must be documented and retained, and lead to prompt action to ensure compliance. If the monitor encounters a serious issue, negative performance trend, or general non-compliance, contact will be made with the sponsor to determine the appropriate course of action. A decision will be made on whether to initiate a corrective and preventive action (CAPA) to assess the root cause of problem. This process of escalation, investigation and resulting decisions need to be documented in the ISF/Sponsor file and clinical study report.

# References

EMA Reflection paper on risk-based quality management in clinical trials, 18 November 2013.

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MRC/DH/MHRA Joint Project Risk-adapted Approaches to the Management of Clinical Trials of Investigational Medicinal Products, 10 October 2011, <https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/343677/Risk-adapted_approaches_to_the_management_of_clinical_trials_of_investigational_medicinal_products.pdf>

University of Oxford, Core Standard Operating Procedure: No.012, Monitoring, 24 June 2014, <https://www.admin.ox.ac.uk/media/global/wwwadminoxacuk/localsites/researchsupport/documents/ctrg/downloads/newsops/University_Core_SOP_012_v1.0_Monitoring.pdf>

**Appendix 1: Metrics for activities during monitoring visits**

*<This list can be expanded and edited based on the risk assessment, if centralised monitoring is utilised add column 4 with appropriate calculations>*

| **Area of review** | **Percent/number/description of review needed** | **Potential triggers to change planned monitoring percentage** |
| --- | --- | --- |
| Safety | X % of suspected SAEs  X % of non-serious AEs  X % of SAEs  X % of AEs | PI/designee’s ability to access and assess safety documents  Timelines of reporting of safety information to sites IRB  Outliers/trends in number of events per participant or per site  Outliers/trends in number of events per participant or per site  Timelines of reporting (date of data entry versus date of event)  Incidence of potentially unreported SAEs based on information from data review |
| IP | x % of drug accountability records of participants dosed | Receipt and site and acknowledge send to coordinating centre  Dispensing (Calculate error rate by comparing (medical notes source data date -clinical) against (Medication/Dispensing date –pharmacy records)  Compliance (amount assigned versus administered)  Incidence and/or severity of temperature excursions |
| Subject recruitment and discontinuation | X % checked for eligibility | Level of screen failures  Inconsistent recruitment  Planned versus actual enrolment  Ratio of randomised to discontinued |
| Consent documents | X % of consent or re-consent documents |  |
| CRFs | X % of critical data (detail) | Missing data/per participant/site  Visit date versus completion date  Number of queries, overdue, query redressing, query response time |
| Protocol non-compliance | Outliers/trends in number or type of deviations | Number of deviations (e.g. per subject per site)  Significant versus non-significant |

**When conducting source data verification**

* Ensure that corrections on the CRFs are signed, dated (and an explanation if required)
* Work with site to resolve queries while on-site and request resolution of any remaining queries that cannot be resolved during the visit in a follow-up letter
* Provide the site staff with copies of data clarification forms once completed
* Verify that previously outstanding data queries have been resolved, signed and dated by the appropriate designated study team member
* Address any protocol deviations with the study team and identify ways to prevent a recurrence of similar issues

**Monitor**

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Name Signature Date

**Sponsor representative**

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Name Signature Date

**Principal investigator**

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Name Signature Date