**Monitoring Plan**

**SUMMARY**

|  |  |
| --- | --- |
| **Study Title:** |  |
| **R&D Ref:** |  |
| **Chief Investigator:** |  |
| **Study Type:** |  | **Risk Category:** |  |
| **Version:** |  | **Date:** |  |

**AUTHORISATIONS**

|  |  |  |
| --- | --- | --- |
| **Author** | **Signature** | **Date** |
|  |  |  |
| **Chief Investigator**  | **Signature** | **Date** |
|  |  |  |
| **Sponsor Representative** | **Signature** | **Date** |
|  |  |  |

**DOCUMENT REVISION HISTORY**

|  |  |  |
| --- | --- | --- |
| **Version** | **Date** | **Description of Changes**  |
| V1.0 | 04/06/2019 | Initial Version – N/A |
| V2.0 | TBD | Minor clarifications to central and off-site monitoring sections, interim monitoring requirements and escalation.Updates following ICH E6(R3): references updated,  |
|  |  |  |

Contents

[1. Purpose 3](#_Toc6999866)

[2. Trial Summary 3](#_Toc6999867)

[3. Risk Categorisation 4](#_Toc6999868)

[4. Study Management 4](#_Toc6999869)

[4.1 Trial Oversight Committees 4](#_Toc6999870)

[4.2 Study Management & Monitoring Personnel 4](#_Toc6999871)

[5. Study Data (Location of Source Data/Documentation) 5](#_Toc6999872)

[6. Monitoring Activities 6](#_Toc6999873)

[7. Protocol Deviations, Violations and Serious Breaches 7](#_Toc6999874)

[8. Communication & Escalation 7](#_Toc6999875)

[9. Risk Indicators & Triggers 8](#_Toc6999876)

[10. References 10](#_Toc6999877)

[11. Appendices 10](#_Toc6999878)

# 1. Purpose

The purpose of this monitoring plan is to specify all study specific monitoring requirements for the above study in order to ensure compliance with the protocol and regulatory requirements.For further information regarding what should be included in the Monitoring Plan, please also see NJRO-GEN-SOP-021 (Monitoring Research Sponsored by NuTH).

# 2. Trial Summary

|  |  |
| --- | --- |
| **Trial Phase** |  |
| **Trial Design** |  | Blinded? | Yes / No |
| Randomised? | Yes / No |
| **Study Type***(e.g. CTIMP, ATIMP, Clinical Investigation of non-CE marked Device etc.).*  |  |
| **Participant Population***(Disease area/patient group)* |  |
| **Planned Sample Size** |  |
| **Planned Number of Sites** |  |
| **Type of sites** *(e.g. NHS hospital)* |  |
| **Planned Trial Period** *(from opening of recruitment to end of study as defined in the protocol; specify length of recruitment & length of follow up)* |  |
| **Therapeutic Area** |  |
| **Intervention under study***(e.g. name IMP, device etc.)* |  |
| **Primary Outcome** |  | **Primary Endpoint** |  |
| **Secondary Outcome(s)** |  | **Secondary Endpoint(s)** |  |

# 3. Risk Categorisation

*(As documented in the CTRAF, Part A)*

Consider the factors critical to trial quality (ICH E6(R3) 3.11.4.3) using a risk-based approach.

|  |
| --- |
| **Risk Adaption Categorisation** |
| **Risks associated with IMP/interventions:**[ ]  **Type A** = Comparable to the risk of standard medical care[ ]  **Type B** = Somewhat higher than the risk of standard medical care[ ]  **Type C** = Markedly higher than the risk of standard medical care | **Justification:***[Justify the risk of the trial by including factors which are critical to quality and those that could impact on patient safety, rights and well-being and the reliability of the trial results. Consider trial design characteristics, the nature of the investigational product, the indication and the potential trial (if applicable), the population, its setting, and the data being collected]* |

# 4. Study Management

## 4.1 Trial Oversight Committees

*[This section can be amended to suit the oversight committee requirements for each study. Comment on the roles and responsibilities of committees; frequency of meetings; record of meetings; storage of minutes; reference to relevant charter etc.].*

*\*\* Where appropriate, sponsors may also establish an endpoint assessment/adjudication committee in certain trials to review endpoints reported by investigators to determine whether the endpoints meet protocol-specified criteria. To minimise bias, such committees should typically be blinded to the assigned treatments when performing their assessments, regardless of whether the trial itself is conducted in a blinded manner. (ICH E6(R3): 3.9.8).*

*Committees established for purposes that could impact participant safety or the reliability of trial results should include members with relevant expertise and with managed conflicts of interest, have written operating procedures (e.g., charters) and document their decisions (ICH E6(R3): 3.9.9).*

|  |
| --- |
| **Trial Management Group (TMG)** |
|  |
| **Trial Steering Committee (TSC)** |
|  |
| **Data Monitoring Committee (DMC)** |
|  |

## 4.2 Study Management & Monitoring Personnel

|  |
| --- |
| **Monitoring Responsibilities**  |
| *[Delete rows as appropriate. Comment on all monitoring related tasks (e.g. off site, central and on-site monitoring as required) and assign responsibility by role (see example table below). Provide details of who will be responsible for which monitoring activities. Consider personnel required, is PI attendance mandatory at visits?]*

|  |  |
| --- | --- |
|  | **Personnel Responsible** |
| **Monitoring Task** | [Insert job role] | [Insert job role] | [Insert job role] |
| Central Monitoring\* | e.g. Accountable\*\* | e.g. Responsible\*\* | e.g. Support\*\* |
| Off-site Monitoring\* |  |  |  |
| On site Monitoring\* |  |  |  |

*\*You should try to break down the monitoring tasks further in order to provide clarity, e.g. for central monitoring this may include running reports, raising data queries etc.* *\*\*You may also wish to specify the role of each job role within the monitoring process. For instance, a trial manger may be responsible & accountable for performing on-site monitoring but they may seek support from a database manager.*  |
| **Monitor Training & Contingency Planning for Changes in Monitors** |
| *[Include details on how monitors will be trained (including how and where this training will be documented) and how changes in monitor will be handled throughout the study.]*  |

# 5. Study Data (Location of Source Data/Documentation)

|  |
| --- |
| **Location of Source Data at Sites** |
| *[Include details of whether Source Data Agreements will be put in place with each site in place to identify the location of all source data (identify where source data agreements will be kept; e.g. TMF). Provide a summary of what will be checked during monitoring (e.g. patient’s medical records; results from routine clinical tests; consent forms; eligibility checklists/assessments; questionnaires, EDC for direct data entry etc.) and how source data will be stored at sites (will this be checked as part of monitoring) (see NJRO-GOV-SOP-003)]*  |

# 6. Monitoring Activities

|  |
| --- |
| **Summary and Rationale**  |
| *[Insert here a brief introduction to the monitoring methods that have been selected for use – include justification for the decision to include or exclude certain monitoring methods. Include references to the relevant sections of the study risk assessment where appropriate. (See NJRO-REG-T-026)]*  |
| **Blinded Study Considerations** |
| *[For blinded studies, are aspects of the study unblinded (e.g pharmacy or IMP administration)? If yes, detail study specific monitoring requirements to prevent bias]* |
| **Central Monitoring**  |
| *[Describe the content and frequency of central monitoring. With regards to content, examples may include: TMF & ISF maintenance; review of enrolment against site and study targets; protocol deviation & safety reporting trends/outliers; data entry and query resolution metrics; error rates in critical data processes; discontinuation trends etc. Consider the stage at which central monitoring of sites would be required/trigger points (see NJRO-GEN-SOP-021]* |
| **Off Site Monitoring**  |
| *[Describe the content and frequency of off-site monitoring. With regards to content, examples may include: TMF & ISF maintenance; review of conformation of capacity & capability at sites; confirmation of fully executed CTAg; review of screening and enrolment logs; review of deviation logs including CAPA review & identification of important deviations potential violations/breaches; timeliness and quality of data entry; review query resolution; review eCRFs to assess protocol compliance at sites; confirm completion of actions; review essential documents; review consent & eligibility; review SAE reports and safety reporting; review sample tracking logs; review delegation logs for completeness, accuracy and to monitor changes in personnel; conduct remote training; track recruitment per site; review CVs & GCPs; GMC registration checks etc. Consider the stage at which off-site monitoring of sites would be required/trigger points]* |
| **On Site Monitoring**  |
| *[Describe the content and frequency of on-site monitoring, if required. With regards to content to be reviewed, this may include: TMF & ISF maintenance; verification of the existence of participants; checks for valid informed consent; study conduct and protocol adherence; subject eligibility; checks relating to safety reporting and adverse events; IMP accountability; supplies management requirements, temperature logs; personnel delegation & signature logs; patient medical records; protocol deviations, violations & serious breaches; follow up of outstanding issues; source data verification; checks for data quality and completeness etc. Consider the stage at which on-site monitoring of sites would be required/trigger points.]* |
| **Site Initiation Visits (SIVs):** | *[List the purpose of the SIV; whether this will take place at all sites; format; content; personnel required; documentation of SIV attendance etc.]*The purpose of the SIV is to train investigators and site personnel on the specific requirements and procedures needed to perform the clinical trial. For studies requiring regulatory green light (see NJRO-REG-SOP-005), the SIV report must be submitted to Sponsor for review alongside the request for green light. At a minimum, the SIV agenda must include:* [list all items here *– examples include: Protocol review; GCP regulations; SAE reporting requirements; IMP handling; sample handling; EDC system; maintenance of the ISF etc.]*
 |
| **Interim Monitoring Visits:** | *[List the purpose of the interim monitoring visits; whether these will take place at all sites; frequency; format; content; documentation of visit etc. Consider personnel required, is PI attendance mandatory at visits?] (See NJRO-GEN-SOP-021)*The purpose of interim monitoring visits is to ensure:1. that the rights, safety and wellbeing of each subject is protected;
2. trial data are accurate, reliable, complete & verifiable;
3. the trial is conducted in accordance with GCP and the protocol;
4. and that the trial site and staff remain appropriately trained and qualified.
 |
| **Support Department Monitoring (e.g. Pharmacy & laboratories etc.):** | *[List the purpose of support department monitoring; whether these will take place at all sites during interim monitoring visits; frequency; format; content; personnel required; documentation of visit etc.]* |
| **Triggered Monitoring Visits:** | *[List the purpose of triggered monitoring visits; when these will take place at sites; format; content; personnel required; documentation of visit etc.]*A triggered monitoring visit will be conducted where an issue is identified by the Sponsor, trial team or during remote monitoring which cannot be resolved without onsite investigation. |
| **Close Out Visits:** | *[List the purpose of close out visits; when these will take place at sites; format; content; arrangements for the retention of the essential records; personnel required; documentation of visit etc.]*The purpose of the close out visit is to bring to official completion all trial related activities at each site. Remote close out visits may be conducted where all requirements can be verified remotely. |
|  |

# 7. Protocol Deviations, Violations and Serious Breaches

|  |
| --- |
| **Recording & Reporting of Deviations, Violations and Serious Breaches** |
| *Comment on how deviations/violations/breaches will be reported by monitors; documentation used to document these; timelines for reporting etc. Is there a rationale for handling important deviations? Is it stated that actions taken in relation to deviations should be proportionate to their importance?* |

# 8. Communication & Escalation

|  |
| --- |
| **Communication & Escalation Plan** |
| *Comment on how monitoring reports will be reported to Sponsor; communication of data queries; frequency of communication where applicable. Are there clear mechanisms in place to ensure actions are followed up on in a timely manner?* |

# 9. Risk Indicators & Triggers

*The risk indicators and triggers will be study specific; some examples are shown below for different risk categories:*

*\* Risk Indicator –*Critical data and other trial variables (including compliance to monitoring plan) to be assessed in order to monitor the occurrence of identified potential risks as outlined in the CTRAF (Parts A & B).

*\* \* Threshold* – The level, point, or value associated with a Risk Indicator that will trigger an action.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Risk Indicator Category** | **\*Risk Indicator** | **Route of Measurement** | **\*\*Threshold** | **Actions to be taken when threshold is breached** |
| **STUDY MONITORING** |
| Monitoring Plan Compliance | Compliance with monitoring schedule | Comparison of monitoring activities vs. those listed in monitoring plan | [insert monitoring timelines as per monitoring plan]  | E.g. Schedule monitoring visit / remote training. |
| Monitoring plan compliance | Compliance with SDV % | % SDV completed vs. monitoring plan | <75% of required SDV completed | Implement plan to increase the completion of SDV for critical data taking upcoming milestones (e.g. interim analysis) into account. |
| **ESSENTIAL DOCUMENTS** |
| Essential documents – site compliance | Delegation log not received or issues identified with completed delegation logs (i.e. inappropriate delegation). | Delegation log receipt and completion | Missing delegation log for siteAny error found on delegation logs | Contact made with site; if no response following 2 emails and/or telephone calls this will be escalated to the site PI and the CI will be informed.Sponsor will be made aware of any GMC registration issues as soon as possible (within 24 hours).Deviation logs/ violation forms will be completed as required for any delegation issues identified.Monitoring visit may be triggered, if issues arise again and no appropriate CAPAs have been implemented, following discussion with the TMG, including Sponsor. |
| **SAFETY** |
| SAEs / SARs | Time from site being aware of SAE/SAR occurrence to Sponsor being informed | Comparison of reporting timeframe against protocol. | After 1 SAE/SAR being reported outside of protocol timeframe | Site will be asked to document the late report on a deviation log and complete a violation report if patient safety is impacted. CI will be informed.If late reporting becomes a consistent issue, site will be re-trained. If issues continue after the site have been retrained, a triggered monitoring visit may be appropriate if agreed by the TMG, including Sponsor. |
| **DATA MANAGEMENT** |
| CRF Completion | Accuracy of data entry in to EDC | On site SDV | Errors in >5% of data checked | If errors occur consistently in a particular measure, site staff will undergo further training in data entry of this measure. If errors found more generally, this will be escalated to site PI and site staff may be asked to undergo further training and SDV may be carried out on a further % of data. An action plan may be created for site staff to perform further QC and correct any data which do not match source. |
| **DEVIATIONS** |
| Site Compliance  | Completed deviation log or email to confirm that no deviations have occurred not received | Receipt of deviation log or confirmation email | If site fails to send log or a confirmation email every 4weeks that no deviations have occurred | If triggered the site will be contacted. If no response following 2 emails and / or telephone calls, this will be escalated to the PI and the CI will be informed. A triggered monitoring visit may be appropriate if the site fail to send the deviation log or confirmation email after escalation to PI, or if PI has not responded, if agreed by the TMG including Sponsor. |
| **IMP / Device** |
| Drug Accountability | Site not following process to ensure receipt/storage/use/ return/destruction of IMP | IMP Accountability Log and storage of IMP at site | Accountability or storage issues identified | Discuss with site during visit/monitoring report action. Complete deviation log/violation form as appropriate. Where a deviation has occurred, a deviation log will be sent to sponsor.  A monitoring visit may be triggered if issues arise again and no appropriate CAPAs have been implemented, following discussion with the TMG. |
| **FACILITIES, RESOURCE & STAFFING** |
| Site Compliance | Completion of site actions identified at monitoring visits | Review of lag time between monitoring visit letter being sent to site and site completion of the required actions. | 3 consecutive attempts of contacting sites about their actions within 3 months with no response | Escalated to Sponsor and another monitoring visit considered. Sponsor may consider auditing the site. |

# 10. References

The Medicines and Healthcare products Regulatory Agency (2012) Good Clinical Practice Guide.

ICH GCP Guidelines with Integrated Addendum E6(R3) Step 4, January 2025.

# 11. Appendices

Appendix 1 – Refer to current CTRAF (Parts A & B) via [NJRO-REG-SOP-004](https://g14784.ideagenqpulse.com/QPulseDocumentService/Documents.svc/documents/active/attachment?number=NJRO-REG-SOP-004).