**COMBINED RISK ASSESSMENT TOOL/REPORT**

***Study Title: (Ref: Short title & REC / EudraCT No.)***

***Chief Investigator:***

***Date of Risk Assessment: DD MMM YYYY (v1.0)***

***Attendees:***

***Study Team Attendees:***

|  |  |
| --- | --- |
| **Documents reviewed at Risk Assessment** | **Documents reviewed at Risk Assessment Sign-off** |
|  |  |

# Study Type

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Risk Adaption Categorisation** | | **Justification** | **Mitigation** | **Management Strategy Comment** |
| **1.1** | Study interventions e.g.   1. *Comparable to the risk of standard care* 2. *Risk somewhat higher than standard care* 3. *Risk markedly higher than standard care* |  |  |  |

# Investigational Product/Agent

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Risk Factor** | **ID of Risks** | **Likelihood** | **Impact** | **Mitigation** | **Management Strategy Comment** |
| **2.1** | Expected hazards related to study investigations e.g.  *- Side effects*  *- High risk dosing procedure e.g. cohort, MTD*  *- High level of treatment interception e.g. frequent PKs*  *- Interactions with concomitant/permitted medications*  *- Interactions between IMPs/NIMPs*  *- Risk carrying interventions e.g. open heart surgery*  *- Other known or anticipated safety issues*  **-** Precautions and impact on eligibility  - Congenital anomalies |  |  |  |  |  |
| **2.2** | Pharmacovigilance e.g.  *- AE reporting*  *- USMs*  *- SUSAR reporting*  *- Safety monitoring committee*  *- Oversight of dose escalation decision (DMC)*  *-Reference Safety Information (RSI) and frequency of checks* |  |  |  |  |  |
| **2.3** | Manufacture and distribution of the product(s) e.g.  *- Licence status*  *- QP certification: packaging, labelling, distribution*  *- Volume and Shelf-life of product: potential for site-site IMP transfer*  *-Device technical files* |  |  |  |  |  |

# Study Participants

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Risk Factor** | **ID of Risks** | **Likelihood** | **Impact** | **Mitigation** | **Management Strategy Comment** |
| **3.1** | Difficulties or incapacity to give consent in comparison with a fully cognisant adult e.g.  *- Language, emergency situation, age, legal incapacity, cognitive impairment. AWI, coercion*  *- Vulnerable target population e.g. babies, elderly* |  |  |  |  |  |
| **3.2** | Collection of indirectly identifying or sensitive characteristics e.g. *- Phone number, address, place of work, CHI number*  *-Sensitive characteristics, ethnic origins, sexual or religious orientation*  *- Data sent outside EU* |  |  |  |  |  |
| **3.3** | Participant well-being e.g.  *- Risk-benefit balance*  *- Burden of study visits*  *- Lifestyle requirements*  *- Study specific procedures which carry risk additional to standard care* |  |  |  |  |  |

# Study Design and Methods

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Risk Factor** | | **ID of risks** | **Likelihood** | **Impact** | **Mitigation** | **Management Strategy Comment** |
| **4.1** | Feasibility assessment of the study recruitment based on reliable sources e.g.  *- Estimation based on clinical department activity, documented pre-registry*  *-Minimum recruitment target. % PI time. Other minimum requirements* |  |  |  |  |  |
| **4.2** | Blinding of randomisation procedures e.g. *- Responsibility*  *- Blinded during allocation*  *- Centralised allocation*  *- Study double blinded*  *- Blind maintained during investigations*  *- Blind maintained throughout data analysis*  *- Testing of emergency unblinding procedures* |  |  |  |  |  |
| **4.3** | Objective assessment of primary and the main secondary outcomes and verifiability e.g. *- Source data*  *- Objective vs. subjective assessment,*  *- Independent assessor of study outcomes*  *- Location of sample analysis*  *- Data points entered straight into CRF*  *- Voluminous and/or complex data collection* |  |  |  |  |  |
| **4.4** | Complexity of study procedures e.g.  *-Study procedures: recruitment, design, follow-up*  *- Complex recruitment: cluster accrual*  *- Complex designs: crossover design, dose escalation, structured therapeutic interruption - Complex follow-up: different types of follow-up visit, additional investigations as compared to standard of care*  *- Computer systems*  *- Variable IMP dose*  *- Interim analysis plan (including reconciliation of safety / non-compliance data)*  *- Data Management Plan*  *- Use of clinical bloods prior to consent for eligibility for inpatients* |  |  |  |  |  |

# Study Organisation

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Risk Factor** | | **ID of risks** | **Likelihood** | **Impact** | **Mitigation** | **Management Strategy Comment** |
| **5.1** | Education, training, experience and resources of all investigator site staff in GCP and study procedures e.g.  *- Investigator experienced in CTIMPs/CIMDs*  *- GCP procedures, informed consent, anonymisation, SAE reporting, queries management*  *- Previous negative audit/inspection observations or other issues with the investigator(s) or investigator site*  *- Adequate resources available for the duration of the study*  *- Knowledge of study procedures: trial interventions, trial investigations*  *- Experience in the study phase and therapeutic area.*  *- Awareness of sponsor SOPs*  *- Peer reviewed,*  *- Trial Manager, experienced Research Nurse,*  *- Clinical Trial Unit/Clinical Research Facility involvement* |  |  |  |  |  |
| **5.2** | Intervention management at site e.g. *- For drugs: restocking, dispensing, accountability, expiry date, re-labelling, storage conditions*  *- Storage out with pharmacy*  *- Temperature monitoring*  *- Dispensing instructions*  *- Robustness of dose calculation*  *- Technical agreement* |  |  |  |  |  |
| **5.3** | Quickness, security and quality of data in the database e.g.  *- Quick data entry, e-CRF, electronic screening log*  *- Secure data entry: secured websites , passwords*  *- Appropriate storage of identifiable data*  *- Validation checks*  *- QC checks*  *- Audit trail*  *- IRT system in use*  *-ePRO* |  |  |  |  |  |
| **5.4** | Responsibilities e.g.  *- Trial unit involvement*  *- Clinical Research Facility involvement*  *- CI and sponsor duties defined*  *- WTCRF Phase I Committee*  *- Applicable contracts/agreements (Inclusion of safety clause for Phase I trials)* |  |  |  |  |  |
| **5.5** | Facilities, resources and vendors e.g.  *- Sufficient clinical area*  *- Clinical equipment maintenance*  *- Laboratories* |  |  |  |  |  |

# Outcome

| **Topic** | **Monitoring strategy** | | **Facilitation/Sponsorship** | **Audit** |
| --- | --- | --- | --- | --- |
| Investigational product/agent | | **Dose assessments** (RA section 4.4, 5.2) – level of monitoring according to appendix 2  **AE assessment** (RA section 2.1, 2.2) – level of monitoring according to appendix 2  **IMP accountability** (RA section 2.3, 5.2) – level of monitoring according to appendix 2  **IMP storage** (RA section 2.3, 5.2) – level of monitoring according to appendix 2 | **IMP management** (RA section 2.3, 5.2) **–** Risk adaption according to appendix 1  **Labelling** (RA section 2.3) – Risk adaption according to appendix 1  **Submission & approval** (RA section 1.1) – Type | *Select 1 of 3:*  *1) No audit required unless cause arises.*  *2) Monitoring reports and feedback will be reviewed and/or discussed regularly with the Senior Clinical Trials Monitor, to ascertain if audit is required*  *3) An audit plan will be prepared and agreed with the monitors and the sponsor(s), and will include the following (where applicable);*  *Study management*  *Database assessment*  *Vendor (facility/laboratory) assessment* |
| *State strategy towards each area. Intensity and nature of monitoring will be greater if for a type C study compared with type B and greater for a type B study compared with a type A study. Intensity and nature of monitoring will also be increased depending on the likelihood associated with identified risks and mitigation strategies.* | *State strategy towards each area. Requirements will be reduced for type A studies compared with type B and reduced for type B studies compared with type C studies in accordance with competent authority guidelines. Type A studies will qualify for reduced submission (MHRA notification scheme) and reduced labelling requirements. Facilitation/sponsorship actions will be increased depending on the likelihood associated with identified risks and mitigation strategies. For phase I studies at the WTCRF, the role of the WTCRF phase I committee should be considered.* |
| Study participants | | **Participant eligibility** (RA section 3.3, 4.4) – level of monitoring according to appendix 2  **Participant calendar** (RA section 3.3, 4.4) – level of monitoring according to appendix 2  **Participant consent** (RA section 3.1) - level of monitoring according to appendix 2 | n/a |
| *State strategy towards each area. Intensity and nature of monitoring will be increased depending on the likelihood associated with identified risks and mitigation strategies.* |
| Study design and methods | | **Data QC checks** (RA section 4.4, 5.3) – level of monitoring according to appendix 2  **CRF completion** (RA section 4.3, 4.4, 5.3) – level of monitoring according to appendix 2  **Protocol/regulatory compliance** (RA section 4.1, 4.4, 5.4) – level of monitoring according to appendix 2  **SDV of Outcomes** (RA section 4.3, 4.4, 5.3) – level of monitoring according to appendix 2 | **Safety surveillance** (RA section 2.1, 2.2) – Risk adaption according to appendix 1 |
| *State strategy towards each area. Intensity and nature of monitoring will be increased depending on the likelihood associated with identified risks and mitigation strategies.* | *State strategy. Facilitation/sponsorship actions and surveillance requirements will be determined depending on the likelihood associated with identified risks and mitigation strategies.* |
| Study organisation | | **Staff training** (RA section 4.1, 5.1) – level of monitoring according to appendix 2  **Recruitment reporting** (RA section 4.1, 4.4) – level of monitoring according to appendix 2  **Facilities & resources** (RA section 4.1, 5.4, 5.5) – level of monitoring according to appendix 2  **Records and delegation** (RA section 3.2, 4.4, 5.4) – level of monitoring according to appendix 2 | **Documentation** – (RA section 2.2, 3.1, 3.2) Risk adaption according to appendix 1  **Archiving** (RA section 1.1) – Risk adaption for non- regulated studies only |
| *State strategy towards each area. Intensity and nature of monitoring will be increased depending on the likelihood associated with identified risks and mitigation strategies.* | *State strategy towards each area. Facilitation/sponsorship actions and documentation/archiving requirements will be determined depending on the likelihood associated with identified risks and mitigation strategies. Type A studies can qualify for reduced requirements* |

# Combined Risk Assessment Contributor Signatures

Sponsor Representative (UoE): Print Name: Date:

Sponsor Representative (NHSL): Print Name: Date:

QA Representative: Print Name: Date:

Monitoring Representative: Print Name: Date:

Pharmacovigilance Representative: Print Name: Date:

Add Contributors (state sections contributed to, department and title):

Sign: Print Name: Date:

(Title)

# Risk Assessment Appraisal History

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Risk Assessment Version Number** | **Amendment / Protocol Number** | **Reason for Risk Assessment Appraisal** | **Sections updated** | **Issue Date** |
|  |  |  |  |  |

**Appendix 1**

**Facilitation/Sponsorship Risk Adaptations (Clinical Trials of Investigational Medicinal Products)**

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| --- | --- | --- | --- |
| **DOCUMENT** | **RISK ADAPTATION POSSIBLE** | | |
| **TYPE A** | **TYPE B** | **TYPE C** |
| Investigators Brochure | Yes | (Yes) | No |
| IB annual update | No | No | No |
| Sample label | Yes | (Yes) | No |
| Certificate(s) of analysis | Yes | (Yes) | No |
| IMP shipments | Yes | Yes | No |
| IMP handling instructions | Yes | (Yes) | No |
| Master randomisation list | No | No | No |
| Unblinding procedures | No | No | No |
| Site IMP accountability | Yes | (Yes) | No |
| IMP return/destruction | Yes | (Yes) | No |
| IMP dossier | Yes | (Yes) | No |
| MIA for IMP | Yes | (Yes) | No |
| Manufacturing Authorisation | (Yes) | No | No |
| IMP importation authorisation | No | No | No |
| QP certification | N.A. | (Yes) | No |
| GMP compliance statement | Yes | (Yes) | No |
| AE/AR recording | Yes | (Yes) | (Yes) |
| AE/AR reporting to sponsor | Yes | (Yes) | (Yes) |
| SAE/SAR reporting to sponsor | (Yes) | (Yes) | (Yes) |
| SUSAR reporting to MHRA/REC/investigators | No | No | No |
| Annual safety report | Yes | No | No |
| Trial level IMP accountability | Yes | (Yes) | No |
| Subject level IMP accountability | Yes | (Yes) | No |
| Storage conditions records | (Yes) | (Yes) | No |
| Deviation impact assessment | (Yes) | (Yes) | No |
| Combined/centrally held documentation | (Yes) | (Yes) | (Yes) |
| Document retention time | No | No | No |
| Reduced MHRA role for approval | Yes | No | No |

N.A. = not applicable

Yes = risk adaption possible

(Yes) = risk adaption may be possible on case by case basis

No = little, if any flexibility in requirements**Appendix 2**

**Monitoring Strategy Template**

|  |  |  |  |
| --- | --- | --- | --- |
| **Reduced Level of Monitoring** | | | |
| **IMP / Agent (A)** | **Study Participants** | **Study Design and Methods** | **Study Organisation** |
| Dose Assessment: Study dose may be assessed remotely by clinical monitors.  Example of when reduced level may be applied: IMP used within the licenced indication with no additional risks identified | Participant Eligibility: Eligibility can be confirmed remotely via eligibility checklists by a trial manager or clinical monitor.  Example of when reduced level may be applied: cluster randomisation with simplified eligibility criteria | Data QC Checks: May be checked remotely by a data monitor/clinical monitor.  Example of when reduced level may be applied: no electronic database required for data analysis or non-complex data collection where checks can be conducted remotely | Staff Training: Study team will receive training in the sponsor’s SOPs, and conducting a study to GCP and study protocol as required.  Example of when reduced level may be applied: non-complex protocol, CI and Study Team experienced and no additional risks identified |
| AE Assessment: DSURs will describe safety information to maintain oversight. DMC may review safety information  Example of when reduced level may be applied: IMP used within the licenced indication and well known safety profile therefore risk adapted for safety reporting. No additional risks identified | Participant Calendar: Participant attendance may be checked remotely by a trial manager/clinical monitor.  Deviation logs can be used to capture when participants have not attended visits and sent to the Sponsor periodically  Example of when reduced level may be applied: simplified study schedule with no potential to significantly impact outcomes if not met | CRF Completion: May be checked, by the DMC/data monitor/clinical monitor remotely if applicable.  Clinical monitors can be alerted of poor completion of data by DMC, data monitor and study team.  Example of when reduced level may be applied: non-complex data collection where missing data can be monitored remotely | Recruitment and Reporting: Levels of recruitment discussed between the study team and the sponsor as necessary.  Example of when reduced level may be applied: recruitment data is not essential for study analysis and recruitment reporting is not required |
| IMP Accountability: IMP accountability may be conducted remotely by the monitors or by delegated study team members and pharmacy and reported to monitors.  Batch numbers and expiry dates may be checked remotely or by delegated study team members and reported to monitors.  Example of when reduced level may be applied: where risk adaption has been identified as possible in the risk assessment e.g. generic, off the shelf stock with no study specific labelling | Participant Consent: Forms may be reviewed remotely by clinical monitors. Process can be discussed at SIV and at other time if necessary.  Example of when reduced level may be applied: cluster randomisation with risk adapted consent approach | Protocol / Regulatory Compliance: Deviations will be sent to the Sponsor for review at intervals agreed with study team. Violations will be Sent to the Sponsor as per SOP.  Study teams able to contact clinical monitors via telephone/email during the study to discuss compliance.  Example of when reduced level may be applied: non-complex study design where compliance can be confirmed remotely | Facilities and Resources: Appropriateness of facilities and resources can be confirmed remotely.  Example of when reduced level may be applied: no supporting department involvement or routine support e.g. lab sample analysis via local, accredited NHS labs only. No additional risks identified. |
| IMP Storage: Review of temperature logs and storage may be performed remotely by monitor or by delegated study team members and reported to clinical monitors where required.  Example of when reduced level may be applied: where risk adaption has been identified as possible in the risk assessment e.g. stable IMP stored as standard clinical stock according to local practice |  | SDV of Outcomes: SDV for primary and secondary endpoints will be carried out remotely where possible and necessary by monitors.  Example of when reduced level may be applied: where risk adaption has been identified as possible in the risk assessment e.g. non-complex study endpoints which can be SDV’ed remotely | Records & Delegation: Guidance on Investigator Site File provided by clinical monitors.  Delegation logs provided by clinical monitors, for completion by the PI.  Example of when reduced level may be applied: where risk adaption for documentation has been identified as possible in the risk assessment |
| Reduced Monitoring Guide: For studies with Reduced as the maximum level of monitoring: Remote SIV and close out as standard. Monitoring will be conducted as described in the study specific monitoring and SDV plan. Onsite monitoring visits will only be conducted if issues are identified during central monitoring that require resolution/investigation via on-site monitoring. | | | |

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| --- | --- | --- | --- | --- | --- | --- |
| **Regular Level of Monitoring**  **(Regular is the default level of monitoring)** | | | | | | |
| **IMP / Agent (B)** | | **Study Participants** | | **Study Design and Methods** | | **Study Organisation** |
| Dose Assessment: Actions described in “reduced level” in addition to:  Onsite monitoring: selected participants will have their batch numbers traced from their medical notes to pharmacy. Study dose of IMP will be compared with medical notes and any randomisation documentation for those.  Of those participants whose notes are reviewed, it will be confirmed that 100% of the dose was correct. | | Participant Eligibility: Actions described in “reduced level” in addition to:  Onsite monitoring: for selected participants monitors will SDV 100% of eligiblility criteria where possible or unless otherwise stated in the monitoring plan. | | Data QC Checks: Actions described in “reduced level” in addition to:  Onsite monitoring: sample of CRFs checked during routine monitoring visits. | | Staff Training: Actions described in “reduced level” in addition to:  Onsite monitoring: additional training needs will be reviewed during the course of routine monitoring and addition training will be provided to the study team as necessary. |
| AE Assessment: Actions described in “reduced level” in addition to:  Onsite monitoring: for selected participants monitors will review medical records and any other applicable records onsite for adverse events and will ensure that they are noted. | | Participant Calendar: Actions described in “reduced level” in addition to:  Onsite monitoring: for those participants selected for monitoring monitors will check 100% of attendance data where possible or unless otherwise stated in the monitoring plan. | | CRF Completion: Actions described in “reduced level” in addition to:  Onsite monitoring: CRFs will be checked for completion. | | Recruitment and Reporting: Actions described in “reduced level” in addition to:  Onsite monitoring: Screening / pre-screening logs will be checked during monitoring visits.  Recruitment will be recorded and discussed during any monitoring visits. |
| IMP Accountability: Actions described in “reduced level” in addition to:  Onsite monitoring: during routine onsite monitoring, a visit to pharmacy may be conducted to carry out an accountability check of the IMP.  Batch numbers and expiry dates of any IMP will also be checked for a sample of participants. | | Participant Consent: Actions described in “reduced level” in addition to:  Onsite monitoring: It will be checked that a consent form exists for all participants.  Selected participant consent forms will be checked for completeness and accuracy during monitoring visits.  For those participants selected for monitoring medical notes will also be checked to ensure all the correct documentation has been completed and the person taking consent is delegated to do so. Process can be reviewed at monitoring visits and in dialogue. | | Protocol / Regulatory Compliance: Actions described in “reduced level” in addition to:  Onsite monitoring: confirm/observe compliance with study team. For participants selected for monitoring data and medical notes will be reviewed to identify deviations/violations and ensure correct recording/reporting. . | | Facilities and Resources: Appropriateness of facilities and resources will be discussed with the team and confirmed during onsite visits. |
| IMP Storage: Actions described in “reduced level” in addition to:  Onsite monitoring: temperature logs and storage conditions will be reviewed at routine monitoring visits to pharmacy/alternative agreed storage area. | |  | | SDV of Outcomes: Actions described in “reduced level” in addition to:  SDV will be carried out for primary and secondary endpoints’. These will be checked for 100% of selected participants where possible or unless otherwise stated in the monitoring plan. | | Records & Delegation: Actions described in “reduced level” in addition to:  Onsite monitoring: study team may be provided with prepared Investigator Site file by the clinical monitors if possible.  Delegation log checked at monitoring visit along with ISF |
| Regular Monitoring Guide: For studies with Regular as the maximum level of monitoring: Onsite SIV and COV as standard. Remote SIV and/or close out should be justified. Remote close-out standard if no participants recruited.. Monitoring will be conducted as described in the study specific monitoring and SDV plan e.g.at least 1 monitoring visit (per site) will be conducted during the trial. Further triggered visits will be conducted where required by the Sponsor or if issues are identified during central/onsite monitoring which require resolution/investigation via on-site monitoring. | | | | | | |
| **Increased Level of Monitoring** | | | | | | |
| **IMP / Agent (C)** | **Study Participants** | | **Study Design and Methods** | | **Study Organisation** | |
| Dose Assessment: Actions described in “reduced level” in addition to:  Onsite monitoring: selected participants will have their batch numbers traced from their medical notes to pharmacy. Study dose of IMP will be compared with medical notes and any randomisation documentation for those.  Of those participants whose notes are reviewed, it will be confirmed that 100% of the dose was correct.  Example of when increased level may be applied: complex dosing procedure e.g. dose escalation design | Participant Eligibility: Actions described in “reduced level” in addition to:  Onsite monitoring: for selected participants monitors will SDV 100% of eligibility criteria unless otherwise stated in the monitoring plan.    Example of when increased level may be applied: complex eligibility criteria where multiple risks requiring additional mitigation are identified at risk assessment | | Data QC Checks: Actions described in “reduced level” in addition to:  Onsite monitoring: sample of CRFs checked during routine monitoring visits.  Example of when increased level may be applied: 100% QC check of data used for dose escalation decision making required | | Staff Training: Actions described in “reduced level” in addition to:  Onsite monitoring: additional training needs will be reviewed during the course of routine monitoring and additional training will be provided to the study team as necessary.  Example of when increased level may be applied: complex protocol, inexperienced CI and Study Team or additional specific training required e.g ATIMP requirements | |
| AE Assessment: Actions described in “reduced level” in addition to:  Onsite monitoring: for selected participants monitors will review medical records and any other applicable records onsite for adverse events and will ensure that they are noted.  All adverse events will be reviewed for medical oversight and follow up.  Example of when increased level may be applied: first in human studies or complex safety reporting requirements e.g. AE of special interest (AESI) | Participant Calendar: Actions described in “reduced level” in addition to:  Deviation logs will be forwarded to Sponsor at a greater frequency  Onsite monitoring: for those participants selected for monitoring monitors will check 100% of attendance data unless otherwise stated in the monitoring plan.  Example of when increased level may be applied: first in human post dosing safety assessments required within a specific timeframe | | CRF Completion: Actions described in “reduced level” in addition to:  Onsite monitoring: CRFs will be checked for completion.  Example of when increased level may be applied: complex data collection where multiple risks relating to missing data requiring additional mitigation are identified at risk assessment | | Recruitment and Reporting: Actions described in “reduced level” in addition to:  Onsite monitoring: Screening / pre-Screening logs will be checked during monitoring visits.  Recruitment will be recorded and discussed during any monitoring visits.  Example of when increased level may be applied: an explicit risk is identified at risk assessment which requires an increase in frequency of monitoring of recruitment reporting | |
| IMP Accountability: Actions described in “reduced level” in addition to:  Onsite monitoring: during routine onsite monitoring, a visit to pharmacy may be conducted to carry out an accountability check of the IMP. Record of receipt, dispensation, return and destruction will be reviewed. Batch numbers and expiry dates of any IMP will also be checked for a sample of participants.  Example of when increased level may be applied: first in human or ATIMP trial where traceability of product must be confirmed | Participant Consent: Actions described in “reduced level” in addition to:  Onsite monitoring: all participant consent forms will be checked during monitoring visits for completeness and accuracy.  All participants’ medical notes will also be checked to ensure all the correct documentation has been completed and the person taking consent is delegated to do so. Process can be reviewed at monitoring visits and in dialogue.  Example of when increased level may be applied: vulnerable participant population e.g AWI consent | | Protocol / Regulatory Compliance: Actions described in “reduced level” in addition to:  Onsite monitoring: confirm/observe compliance with study team. For participants selected for monitoring data and medical notes will be reviewed to identify deviations/violations and ensure correct recording/reporting.  Example of when increased level may be applied: complex study design where multiple risks relating to compliance requiring additional mitigation are identified at risk assessment | | Facilities and Resources: Appropriateness of facilities and resources will be discussed with the team and confirmed during onsite visits  Example of when increased level may be applied: complex non-routine requirements for supporting departments with multiple risks requiring additional mitigation identified at risk assessment | |
| IMP Storage: Actions described in “reduced level” in addition to:  Onsite monitoring: temperature logs and storage conditions will be reviewed at routine monitoring visits to pharmacy/alternative agreed storage area.  Example of when increased level may be applied: non-stable IMP with specific storage conditions required, unless otherwise specified in the risk assessment |  | | SDV of Outcomes: Actions described in “reduced level” in addition to:  SDV will be carried out for primary and secondary endpoints. These will be checked for 100% of selected participants unless otherwise stated in the monitoring plan.  Example of when increased level may be applied: complex endpoints where multiple risks relating to endpoint data requiring additional mitigation are identified at risk assessment or endpoint data used for dose escalation decision making | | Records & Delegation: Actions described in “reduced level” in addition to:  Onsite monitoring: study team may be provided with prepared Investigator Site file by the clinical monitors if possible. Delegation log checked at monitoring visit along with ISF  Example of when increased level may be applied: when multiple risks relating to documentation requiring additional mitigation are identified at risk assessment | |
| Increased monitoring guide: For studies with Increased as the highest level of monitoring: Onsite SIV and close-out as standard. Monitoring will be conducted as described in the study specific monitoring and SDV plan e.g.at least 1 monitoring visit (per site) will be conducted every 6 months during the active stage of the trial. Further triggered visits will be conducted where required by the Sponsor and if issues are identified during central/onsite monitoring that require resolution/investigation via on-site monitoring. | | | | | | |