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| **Study title** |  |
| **Chief investigator** |  |
| **R&I reference** |  |
| **Protocol Version** |  |
| **Version of Monitoring RA and date**  |  |

**Risk Assessment Scores**;

- Low Risk < 13 (midpoint of all medium score of 26) 5% Source Data Verification (SDV) minimum will be carried out
 - Medium Risk >=13 but <= 26 (maximum of all medium score) 10% SDV minimum will be carried out
 - High Risk > 26 At least 25% SDV will be carried out, 100 per cent of ICFs, Number of Visits increased.

 - Alerts will add 3 points to any risk score.
 - SDV selection should be random except to include an appropriate level of safety reporting review depending on risk and incidence
 - Where safety analysis is a primary objective, SDV selection to be adjusted to include a representative review of SAE reporting

 Number of Monitoring visits and type of visit will be based upon the level of risk of the study and documented in the Monitoring Plan.
 - Any alerts which will adjust SDV selection and monitoring schedule to be stated specifically in the Monitoring Plan.

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| **Risk Area**  | **Question**  | **Indicator**  | **Alert****=3** | **High** **=2** | **Medium** **=1** | **Low** **=0** | **Total** | **Risk Mitigation**  |
| **STUDY**  | **1** | Phase |  |  |  |  |  |  |
| **2** | Sample size |  |  |  |  |  |  |
| **3** | Study population |  |  |  |  |  |  |
| **4** | Indication |  |  |  |  |  |  |
| **5** | Symptomatic / progressive disease |  |  |  |  |  |  |
| **6** | Emergency / Intensive care |  |  |  |  |  |  |
| **7** | Design |  |  |  |  |  |  |
| **PROTOCOL** | **8** | Complexity - treatment arms |  |  |  |  |  |  |
| **9** | Complexity - treatment dosages |  |  |  |  |  |  |
| **10** | Complexity - data |  |  |  |  |  |  |
| **11** | Experimental or non-standard investigations |  |  |  |  |  |  |

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| **PROTOCOL**  | **12** | Demands on participants |  |  |  |  |  |  |
| **13** | Equipment |  |  |  |  |  |  |
| **14** | Informed Consent e.g. vulnerable adults |  |  |  |  |  |  |
| **15** | Source Data |  |  |  |  |  |  |
| **16** | Primary and Secondary Endpoints |  |  |  |  |  |  |
| **17** | Safety endpoints and objectives |  |  |  |  |  |  |
| **IMP** | **18** | Drug - drug interactions |  |  |  |  |  |  |
| **19** | Data dependency of IMP dosages |  |  |  |  |  |  |
| **20** | Comparators and other medications |  |  |  |  |  |  |
| **21** | Medical supervision |  |  |  |  |  |  |
| **22** | IMP administration |  |  |  |  |  |  |

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| **Site Selection** | **23** | Number of sites |  |  |  |  |  |  |
| **24** | Facility requirements |  |  |  |  |  |  |
| **25** | Security |  |  |  |  |  |  |
| **26** | Off site requirements |  |  |  |  |  |  |
| **27** | Training |  |  |  |  |  |  |
| **28** | Site experience |  |  |  |  |  |  |
| **Central Labs** | **29** | Lab experience  |  |  |  |  |  |  |
| **30** | Number of research samples  |  |  |  |  |  |  |
| **31** | Vendor Assessment, any issues |  |  |  |  |  |  |
| **Medical Devices** | **32** | CE/CA for intended purpose |  |  |  |  |  |  |
| **33** | Use of data for marketing purposes |  |  |  |  |  |  |
| **Total**  |  |  |  |  |  |  |  |  |

**SIGNATURES**

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Monitor Date

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Lead Clinical Trial Monitor/

Governance Manager Date

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| **Example Questions for Indicator Risk** | **Possible Effects on Monitoring Plan and Objectives**  |  |
| **Indicator** | **Guide questions** | **Risk** | **SDV % of subjects** | **SDV selection** | **ICF %** | **Frequency of Visits**  | **Risk Mitigation** |
| 1 | Phase IIb, pre marketing, proof of concept | 1 | 20 - 30% | Early, choose from first few subjects | All | Possibly three visits |  |
| Phase I, high risk phase II, GMO, advanced therapy | 2 | 50-100% | Early, 1st subject | All | Increase Number of Visits | Possibly want to monitor subjects at an early stage but also at an advanced stage |
| 2 | Over 50 likely to need more than 1 visit | 1 | Reduce SDV or 1 additional visit | Random | 50% | Include 1 additional visit | The first 10-20 but then randomly to ensure consistency |
| Over 100 likely to need 3 or more visits | 2 | Reduce SDV or 2+ additional visits | Random | 25% | 3 or more visits | The first 10-20 but then randomly to ensure consistency |
| 3 | Non-standard demographic | 1 | None | Random | None | No increase to visits |  |
| Vulnerable group | 2 | Increase SDV | Early, targeted (consent) | Increase ICF review | Visits focused on ICFs | Possibly want to monitor subjects at an early stage but also at an advanced stage, focus on ICFs |
| 4 | Well known drug but new indication | 1 | None | Random | None | No increase to visits |  |
| New indication with little safety data | 2 | Increase SDV | Targeted (AEs) | None | Targeted visit | AE reporting is key data |

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| 5 | The condition is active and progressive | 1 | Increase SDV | Random | None | Targeted visit | May mean a higher rate of AEs |
| Condition active and requiring escalation of treatment or undergoing acute care | 2 | Increase SDV | Early, random | None | Possibly increase visit, targeted visit? | Will probably mean a higher rate of AEs |
| 6 | Emergency treatment commonly used to de-escalate | 1 | None | Targeted (consent) | Increase ICF review | No increase to visits | May need others to consent |
| Emergency treatment for life-threatening illness and/or requiring follow on intensive or high dependency care | 2 | Increase SDV | Targeted (consent) | Increase ICF review | Consider number of visits increasing  | Will probably need others to consent |
| 7 | Blind/double blind, placebo controlled or comparator | 1 | None | Random | None | No increase to visits | Processes for maintaining blind, unblinding |
| 8 | 3 treatment arms | 1 | None | Random | None | No increase to visits | Risk of randomisation, treatment errors |
| More than 3 treatment arms | 2 | Increase SDV | Targeted (therapy) | None | Increase number of visits  | Risk of randomisation, treatment errors |
| 9 | Consistent titration of IMP (i.e. same for all subjects) | 1 | None | Random | None | No increase to visits | Small risk of dosing errors |
| Changeable titration, data dependent titration | 2 | Increase SDV | Targeted (therapy) | None | Number of visits increase  | Heightened risk of dosing errors |

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| 10 | Blinded data, non-standard observations, non -verifiable | 1 | None | Random | None | No increase to visits | CRF might be source data, some data not available |
| Data from external sources, non-consistent subject specific data | 2 | None | Targeted (source data, process) | None | Targeted visits | Data coming in on time. Data missing. Timely assessment |
| 11 | Non-standard scans, assays, investigations as part of the study (i.e. not standard care) | 1 | None | Random | None |   No increase to visits |  |
| Experimental tests, experimental equipment | 2 | None | Targeted (source data, process) | None | Targeted visits | Can these be monitored?  |
| 12 | Frequent visits - more than 1/month, long visits, unusual travel required, source data provided by patients (diaries e.g.) | 1 | Reduce SDV | Targeted (compliance) | None | No increase to visits | Data quality, large amounts, subject complying with visits |
| Visits 1/week or more, extensive travel, overnight stays, data provided using devices or electronic equipment | 2 | Reduce SDV or additional visit | Targeted (compliance) | None | Consider an additional visit ? | Data quality, large amounts, subject complying with visits |
| 13 | Equipment requiring regular maintenance and testing (CV monitors, infusion pumps e.g.) | 1 | None | Random | None | No change to visits.  | Evidence  |
| Study specific equipment, off-site equipment, experimental equipment | 2 | None | Targeted (source data, process) | None | Targeted visits  | Evidence, quality, safety |

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| 14 | Informed Consent, eg vulnerable adults or children or use of telemedicine  | 2 | None  | None  | All | Targeted visits  | Depending on the nature of those consenting |
| 15 | Source Data verification, data fraud  | 2 | Increase SDV  | Random  | None  | May require a for cause visit if any suspicion of data fraud.  | Site specific if suspicion then a for cause visit may be arranged |
| 16 | Primary and Secondary Endpoints  | 2 | SDV to focus on the primary and Secondary Endpoints  | Targeted  | None  | Targeted monitoring visit focusing on primary and secondary endpoints. If it involves safety increase of visits may be a 2 re the risk  | Robust targeted monitoring of SDV to ensure primary and secondary data objectives are met. |
| 17 | Safety data as secondary or lesser objectives/endpoints | 1 | None | Targeted (include SAEs) | None | Targeted visit, central monitoring | Ensure accuracy and completeness of reporting |
| Safety data as primary objectives/endpoints | 2 | Increase SDV | Targeted (subjects with and without reported SAEs) | None | Visit will ensure thorough and comprehensive reporting | Ensure thorough and comprehensive reporting |

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| 18 | Prohibited medications | 1 | None | Random | None | No increase to visits | Aware of non-study care |
| Interaction analysis | 2 | None | Targeted (tests, SAEs) | None | Targeted visits  | How is this achieved? Safety analysis, PK tests, blood levels etc. |
| 19 | Data is dose dependent | 1 | None | Targeted (compliance) | None | No increase to visits | Ensure compliance and timelines are strictly adherent |
| 20 | Accountable comparators, premeds | 1 | None | Random | None | No increase to visits | Additional accountability and administration records |
| Rescue medications | 2 | None | Targeted (safety) | None | Targeted visits | Handling of meds, reporting and documenting |
| 21 | In-patient, requires medical supervision as standard | 1 | None | Random | None |   No increase to visits |  |
| Out-patient, requires medical supervision especially due to study | 2 | None | Targeted (medical oversight) | None | Targeted visits | Check delegation, appropriate documentation and safety reporting |

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| 22 | Study specific, non-standard invasive (e.g. IV) | 1 | None | Random | None |   No increase to visits |  |
| Experimental route/mode of administration (e.g. using specially designed device, route requiring additional supervision such as central line) | 2 | Increase SDV | Targeted (process, medical oversight) | None | Targeted visits  | Check delegation, appropriate documentation and safety reporting |
| 23 | Sites out with GG&C, A&A or Lanarkshire, satellite sites, PICs | 1 | None | Targeted (numbers per site) | Numbers per site, version control | Depending on recruitment sites may be remotely monitored, central monitoring | Consider resource/cost of achieving objectives |
| More than 10 sites, sites outside Scotland | 2 | Reduce SDV | Targeted (numbers per site) | Numbers per site, version control | Remote visits considered  | Consider resource/cost of achieving objectives |
| 24 | Additional clinic provision, childcare facilities, bedded units, storage of drugs, samples, non-standard equipment | 1 | None | Targeted (supplies accountability) | None | No increase to visits | Site can meet study requirements |
| Overnight accommodation, processes for the preparation of drugs, processing of samples, non-standard pre and or post procedure clinical facilities | 2 | None | Targeted (Process) | None | Targeted visits  | Supervision, documentation |
| 25 | Requirement for storage of drugs, valuable devices. Mobile site/subject files (e.g. for satellite sites) | 1 | None | Targeted (confidentiality, drug accountability, maintenance and security) | None | No increase to visits | Accountability. Processes for working between sites |
| 26 | Off-site scans or other investigation, off-site Pharmacy, 3rd party data sources | 1 | Possible additional visits | Random | None | Additional visits | Oversight of off-site provisions |
| More than 2 sites required for a visit, source data processed by multiple off-site agencies | 2 | Possible additional visits | Targeted (process) | None | Additional? | Oversight of off-site provisions |
| 27 | Additional training for non-standard/study specific non-medical processes (e.g. investigations, non-invasive procedures) | 1 | None | Random | None | No increase to visits | Training logs, materials, certificates. Oversight |
| Additional training for non-standard/study specific medical processes (e.g. invasive medical procedures) | 2 | Increase SDV | Early, targeted (delegation) | None | Targeted visits  | Training logs, materials, certificates. Oversight |
| 28 | PI/CI for first time. Small support team with little research experience. No Project Management/coordination. Multi sites with varying experience | 1 | None | Early, targeted (delegation, compliance) | Increase ICF review | . No increase to visits | Early support. May need pre-study visit. Extra intervention |
| Known previous non-compliance of site or key team members | 2 | None | Early, targeted (compliance) | Increase ICF review | Possible extra visit, targeted monitoring of issues  | Reinforcement, some degree of PM |

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| 29, 30 and 31  | Lab experience, GCP lab compliant, Number of Samples, if have been vendor assessed. | 2 | Dependent on number of samples | Will the lab samples affect the primary or secondary endpoints  | None  | Depending on Central Lab may want to monitor it separately  | Percentage of Samples to monitor, what ones if any affect Primary or secondary endpoints. |
| 32 | Medical Devices,  | 2 | Used for Intended CE marked Purpose? SDV to look at device, safety,  | None  | None  | Target monitoring  | As per a CTIMP, assess risk of Medical Device, CE marked, safety, intended purpose, risk for participants  |
| Lack of\_-Alerts | Known heightened risk in design with potential impact on safety (e.g. prophylactic drugs, exceptional safety observations/investigations | 3 | Ad hoc | Ad hoc | None |  | Need to assess on a study by study basis |

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