Appendix 2: Trial Risk Based Monitoring Strategy

CTIMP Studies

<table>
<thead>
<tr>
<th>Risk Level</th>
<th>Examples of Types of Clinical Trials</th>
<th>Minimum Monitoring</th>
<th>Minimum SDV</th>
</tr>
</thead>
</table>
| Type A: No higher than that of standard medical care | Trials involving medicinal products licenced in the EU member state if:  
- They relate to the licensed range of indications dosage and form  
- Or they involve off-label use (such as in paediatrics and in oncology etc.) if this off label use is established practice and supported by sufficient published evidence and/or guidelines.  
  e.g. Phase 4 studies | SIV  
- Trial specific Interim Monitoring visits after first 3 patients recruited  
- Close Out | 100% consent  
100% SAE reporting  
20% eligibility  
20% SDV on primary endpoints |
| Type B: Somewhat higher than that of standard medical care | Trials involving medicinal products licensed in any EU member state if:  
- Such products are used for a new indication (different patient population/disease group) or  
- Substantial dosage modifications are made for the licence indication or  
- If they are used in combinations for which interactions are suspected  
Trials involving medicinal products not licensed in any EU member state if:  
- The active substance is part of a medicinal product licensed in the EU (A grading of TYPE A may be justified if there is extensive clinical experience with the product and no reason to suspect a different safety profile in the trial population)  
  e.g. Phase 3, Phase 2b studies (may include some phase 1/2a studies of licensed products in new indications) | SIV  
- Trial specific Interim Monitoring visits after first 1-2 patients recruited  
- QC of dose escalation data  
- Close Out | 100% consent  
100% SAE reporting  
50% eligibility  
50% SDV on primary & secondary endpoints |
| Type C: Markedly higher than that of standard medical care | Trials involving a medicinal product not licensed in any EU Member State.  
(A grading other than Type C may be justified if there is extensive class data or pre-clinical and clinical evidence)  
  e.g. Phase 1, phase 2a studies | SIV  
- Trial specific Interim monitoring visits after 1st patient recruited  
- QC of dose escalation data  
- Close Out | 100% consent  
100% SAE reporting  
100% eligibility  
Trial specific SDV on primary & secondary endpoints |

*Note: Capacity for monitoring multi-centre centre studies will be ascertained on a case by case basis during sponsor review.*
Non-CTIMP Studies

<table>
<thead>
<tr>
<th>Type of Non-CTIMP study</th>
<th>Risk Level *</th>
<th>Examples of Types of Non-CTIMP studies</th>
<th>Minimum Monitoring</th>
<th>Minimum SDV</th>
</tr>
</thead>
</table>
| Interventional:  
Procedure | High         | High e.g. Invasive procedure, high risk patient population | Aim to monitor 10% of interventional p.a.  
Different clinical areas to be equally monitored unless triggered monitoring deemed necessary | Assessed on case by case basis |
|                         | Medium       | Medium e.g. Non-invasive procedure, diagnostic procedures | High risk studies should be monitored within first 6 months of sponsor green light.  
SIV if deemed necessary for high risk studies or new investigators only. | |
| Interventional:  
Tissue | Medium       | Sample /Tissue collection studies | Aim to monitor 10% of interventional p.a.  
Different clinical areas to be equally monitored unless triggered monitoring deemed necessary | Assessed on case by case basis |
| Non-interventional | Low          | Questionnaires  
Interviews  
Qualitative Data Collection | One study per quarter, with triggered monitoring as necessary. | Assessed on case by case basis |

- Ascertained during sponsor review