Data and Safety Monitoring Plan Requirements

Every study requires a plan with some level of data and safety monitoring. Monitoring, an ongoing process of overseeing the progress of a study from start to finish, is a quality control tool for determining whether study activities are being carried out as planned and whether there are any unexpected safety concerns. Monitoring enables study teams to identify and correct any deficiencies in the conduct, record keeping, or reporting. The Data and Safety Monitoring Plan (DSMP) should be based on a risk assessment of critical data and processes that are necessary for human participant protection and integrity of the investigation.

Studies That Involve No More than Minimal Risk

The protocol should include a DSMP to protect data and ensure the safety and confidentiality of research participants. Paper forms should be secured. Digital data should be encrypted and password-protected and should only be collected and stored using encrypted devices. Participant protections should be appropriate for the population and research procedures and typically focus on ensuring participant privacy and the confidentiality of any data, as physical harms are not reasonably foreseeable.

Studies That Involve More Than Minimal Risk

Complexity and Risk

Besides the requirements described above to protect data confidentiality and participants’ privacy, additional requirements apply to all studies involving more than minimal risk. The IRB will consider the level of risk and burden a participant may experience in a study when determining additional requirements for a plan.

Based on NIH guidance, the Emory IRB defines study complexity as follows:

- **Medium-complexity**: This includes behavioral interventions and studies involving sample collection or imaging done during a single interaction with a study participant or when the probability of harm is limited to the immediate circumstances of the research encounter. For example, studies involving an MRI with contrast, bone marrow sample collection for research purposes, or CSF or biopsy material collection in the context of a clinical encounter or when the remainder of the study-related activities are considered to be no more than minimal risk.

- **High-complexity**: (1) Phase I –III interventional studies, and all studies under an Investigational New Drug [IND] or Investigational Device Exemption [IDE] with the FDA. (2) Other studies that may not be under an IND or IDE, where a participant is exposed to risk for an extended period or for which the risk might change with time.

**DSMP plan**

After reviewing the complexity of a study, the IRB will require the following for medium and high-complexity studies:

- **Data Safety Monitoring Plan (DSMP)**: Must include a plan for both (1) review of participant safety, welfare, and data integrity; and (2) site monitoring conducted to ensure data accuracy and protocol compliance.
• **(1) Review of participant’s data for safety, welfare, and data integrity:** Study teams should have a process to review data during initial data collection.
  
  o Information obtained directly from participants should be reviewed in real-time. For example, when obtaining consent from a participant, the person obtaining consent should check the consent document to ensure the participant has signed in the right place(s) and the documentation of the consent process is adequate.
  
  o The study team should have a standard operating procedure to review other data at pre-determined intervals to ensure there is adequate documentation of critical elements such as eligibility criteria. For example, the plan may include a review of participant data after the first 2 participants are enrolled and then at specified intervals based on enrollment rate. At a minimum, a review of some pre-defined proportion of designated data is required annually, while study data is being collected.

• **(2) Site Monitoring:** study teams should ensure that the study is following the protocol, including study procedures, study intervention, and data collection processes.
  
  o For high-complexity studies, monitoring should be conducted by a designated study monitor, an experienced, knowledgeable person who is independent of the study team. The responsibility for site monitoring may be delegated by the study sponsor to a Contract Research Organization (CRO).
  
  o For medium-complexity studies, the IRB may approve a monitoring plan relying on self-monitoring
    
    ▪ **Site Monitoring conducted via Self-monitoring:** a process for self-assessment of protocol compliance and data integrity which can be part of an overall DSMP. [Click here for a Self-Monitoring Tool](#)

The site monitoring plan should specify who will serve as study monitor and should specify the frequency and percentage of the files to be reviewed, including the following items. The site monitoring should be more frequent and more comprehensive as study complexity increases:

- Consent form review (for example, a high-complexity study should plan to review 100% of consent forms)
- Review of credentials, training records, the delegation of responsibility logs (if applicable)
- Comparison of case report forms (CRF) to source documentation for accuracy and completion
- Review of documentation of adverse event
- Monitoring of critical data points (eligibility, study endpoints, etc.)
- A monitoring schedule that includes monitoring at study initiation and early in enrollment and interim monitoring, based on the site activity and study complexity

Note: An inadequate monitoring plan will result in a study deferral. See appendix 1 for more examples.

### Additional considerations for FDA regulated trials

Depending on the procedures affecting risks to participants, the site monitoring plan should include:

- Monitoring methods (may include centralized/remote, on-site, and self-monitoring)
- Timing, frequency, and intensity of monitoring
- Reference to any tools used (i.e. checklists)
- Identification of events that may trigger changes
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- Identification of deviations or failures that would be critical to study integrity
- Categorization of activities done centrally and those on-site

Please ensure you read the FDA documents referenced at the end of the document for more detailed information.

Additional requirements for high-complexity studies
The monitoring plan should include these additional requirements:

- 100% review of investigator regulatory files, reviewed at first and close-out visits
- Laboratory review of processing and storage of specimens at first and close-out visits and at least biannually
- Assessment of laboratory specimens stored locally
- Interim monitoring based on the site activity.
- Drug and Device accountability procedures

For studies using drugs or biologics, test article accountability is managed by IDS per Emory policy 7.14. See this decision tree for more information.

Data and Safety Monitoring Board (DSMB)
Not all studies require a DSMB. The following questions are designed to help determine whether a DSMB may be needed.

- Are there plans for any predetermined actions outlined, for example stopping rules?
- Is there a large study population, or are there multiple study sites?
- Is this a study where investigators are blinded to the treatment arm?
- Is the trial intended to provide definitive information about the effectiveness and/or safety of medical intervention?
- Do prior data suggest that the intervention being studied has the potential to induce unacceptable toxicity?
- Does the trial evaluate mortality or another major endpoint, such that inferiority of one treatment arm has safety and effectiveness implications?
- Would it be ethically important for the trial to stop early if the primary question addressed has been definitively answered, even if secondary questions or complete safety information were not yet fully addressed?

A DSMB should usually be implemented if answers to two or more of the above questions are ‘yes’.

High-complexity clinical trials with international sites
In addition to all the above, as applicable, these studies are required to engage a CRO working in the study country, and/or to consult with legal counsel regarding compliance with the country’s clinical research regulations.


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Appendix 1

<table>
<thead>
<tr>
<th>Protection Element</th>
<th>DSMP Component</th>
<th>Examples of monitoring activities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subject safety</td>
<td>Specific subject safety parameters</td>
<td>Vital signs, weight, safety blood tests, cardiac status, anxiety, depression scores, etc.</td>
</tr>
<tr>
<td></td>
<td>Frequency of subject safety observations</td>
<td>Weekly telephone follow-up, monthly appointments, observations of subject while in the clinical setting, etc.</td>
</tr>
<tr>
<td></td>
<td>Individual responsible for safety monitoring</td>
<td>Principal investigator, safety monitor, independent monitor, or Data/Safety Monitoring Board, etc.</td>
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<tr>
<td></td>
<td>Subject stopping rules - under what conditions will a subject be removed from study participation and who will make the decision?</td>
<td>Adverse response to study procedures, pregnancy, stroke, cardiac irregularity, non-compliance with medication, etc. Decision made by sponsor, investigator, medical monitor</td>
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<tr>
<td></td>
<td>Study stopping rules - under what conditions will the study be modified or stopped and who will make the decision?</td>
<td>Unanticipated problems (UPs) involving risks to subjects or others, unexplained adverse outcomes, life threatening adverse event, etc., futility</td>
</tr>
<tr>
<td></td>
<td>Reporting mechanisms (i.e. deviations, adverse events, UPs)</td>
<td>Plans for reporting to IRB, FDA, Sponsor, participating sites, or Data/Safety Monitoring Board, etc.</td>
</tr>
<tr>
<td>Data integrity</td>
<td>Specific data elements to be reviewed</td>
<td>Subject inclusion criteria being met, transcription of data is accurate and complete, units of measure are recorded appropriately, calculations are standardized and performed accurately, etc.</td>
</tr>
<tr>
<td></td>
<td>Frequency of monitoring data, points in time, or after specific number of subjects</td>
<td>First 3 subjects and every 10th subject, monthly, quarterly, or annually, according to study complexity.</td>
</tr>
<tr>
<td></td>
<td>Individual responsible for data monitoring</td>
<td>Principal investigator, study coordinator, safety monitor, independent monitor, etc.</td>
</tr>
<tr>
<td>Subject privacy</td>
<td>Conditions (time and place) under which a subject will be consented, interviewed, or telephoned</td>
<td>Observations of consenting process, interviewing, or clinical visit performed quarterly on 3 subjects. Request input from 5 subjects related to their experiences regarding privacy expectations, etc.</td>
</tr>
<tr>
<td>Data confidentiality</td>
<td>Conditions that will protect the confidentiality of the data</td>
<td>Check for locked file cabinets, secure electronic records, secure location where protected health information is stored, etc.</td>
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<tr>
<td>Product accountability</td>
<td>Responsibility for obtaining, storing, preparing, administering, or disposing of the study drug or study device. Responsibility for overseeing product accountability</td>
<td>Research Pharmacy, Principal Investigator, Central Pharmacy, Research Laboratory, Nursing, etc.</td>
</tr>
<tr>
<td>Study documentation</td>
<td>Study file management</td>
<td>Study File Management guidelines and checklists for monitoring (sampling of study files annually), etc.</td>
</tr>
</tbody>
</table>