UNLV | Office of RESEARCH INTEGRITY HUMAN SUBJECTS

Guidance– Data and Safety Monitoring Plan (DSMP)

General Description

The purpose of this Guidance is to describe considerations for the use a Data and Safety Monitoring Plan (DSMP). The purpose of a DSMP is to ensure safety of participants and validity and integrity of data[1]; to ensure adequate protection of human subjects and of the quality and integrity of clinical trial data[7]; and to verify that rights & well-being of human subjects are protected, reported trial data are accurate, complete, & verifiable from source documents, and conduct of trial is in compliance with currently approved protocol/amendment(s), with GCP, and with applicable regulatory requirements[8]

The DSMP may be provided by a Sponsor or written by the Investigator when an Investigator is serving as the Sponsor-Investigator in Investigator-Initiated Trials (IIT), which may entail one study site or multiple sites. The IRB will consider approval of research including DSMPs when the research satisfies the conditions of 45 CFR 46.111(a)(6) and 21 CFR 56(a)(6) (when appropriate).

When it applies / context

This guidance may be used by Researchers and the IRB. Researchers should review this guidance when the PI is developing a DSMP, such as when the PI is conducting IITs and/or when the PI is the Sponsor-Investigator.

The IRB should use this guidance when determining if a DSMP is required for a protocol under review, or when reviewing a DSMP.

Considerations for Requesting or Requiring a DSMP: The following are considerations for requesting or requiring a DSMP:

- Risk level of study--greater than minimal risk may require a DSMP whereas no greater than minimal risk may not
- Complexity of Study Design--more complex study designs (e.g., adaptive or stratified designs, complex dose titrations, blinded) may require a DSMP
- Study Population—DSMP may be required due to study population, such as subjects who are vulnerable, seriously ill, or clinically complex

Generally, for research in which the level of risk is determined to be no more than minimal risk, a DSMP is not required. However, the IRB always has the option for requesting a Data and Safety Monitoring Plan.

Considerations & Best Practices

Elements of a DSMP: Data:

1. Procedures & data critical to reliability of study findings
   - Data critical to reliability of study findings
   - Primary and secondary endpoints
   - Data critical to subject safety
   - SAEs and events leading to discontinuation of treatment
   - Processes related to subject safety and ethical treatment
   - Seeking medical consultation in event specific lab finding
   - Processes related to integrity of data

- Blinding

2. Real and potential sources of error in critical data collection and reporting
   - Conduct & documentation of procedures & assessments related to
     - Critical study endpoints
     - Protocol-required safety
     - Evaluating, documenting & reporting SAEs and UPIRSOs, subject deaths, & withdrawals
   - Adherence to protocol eligibility criteria
   - Conduct & document procedure for ensuring study blind is maintained (if appropriate)
   - Verify IC was obtained appropriate & prior to any study-related procedures
   - Procedures for documenting appropriate accountability and administration of investigational product

Elements of a DSMP: Monitoring Process

1. Description of Monitoring Activities
   - Description of each monitoring activity, including how it will be used to address risks and accuracy of critical data
   - Criteria for determining timing, frequency and intensity of planned monitoring visits
   - Specific activities required at each monitoring visit, including logs, tools and/or templates
   - Definitions of events or results that trigger changes in planned monitoring activities
   - Identification of possible deviations/failures critical to study integrity and how these are recorded and reported
   - Identify who is responsible to perform monitoring activities

2. Communication of Monitoring Results
   - Format, content, timing and archiving requirements for reports and other documentation of monitoring activities
   - Process for appropriate communication
     - Of routine monitoring results to appropriate personnel
     - Of immediate reporting of significant monitoring issues to appropriate personnel
     - From study management and others used to monitor

3. Management of Noncompliance
   - Process for addressing unresolved or significant issues identified by monitoring activities
   - Processes to ensure analyses conducted when deviations are discovered and appropriate corrective and preventative actions are implemented
   - Other applicable quality management practices

4. Training
   - Description of specific training required for personnel performing monitoring activities
   - Planned quality monitoring to ensure that personnel conducting monitoring activities in accordance with monitoring plan, applicable regulations, guidance, etc.
   - Emphasis on data and procedures that are unusual and require training

5. Monitoring Plan Amendments
   - Consider, a priori, what events may require review and revision of monitoring plan and establish processes to permit timely updates when necessary (e.g., amendments)

6. Documentation of Monitoring Activities
   - Date of activity and individual(s) conducting it
   - Summary of data or activities reviewed
   - Description of any noncompliance, potential noncompliance, data irregularities, or other deficiencies identified
   - Description of any actions taken, to be taken, and/or recommended, including person responsible for completing actions & anticipated date of completion

Elements of a DSMP: Data Oversight

The DSMP should include information regarding data oversight. During the conduct of the study, the cumulative data, such as the data being monitored, should be reviewed to evaluate such things as safety and study conduct in order to protect the health, safety and welfare of study participants. The frequency the data will be reviewed, relevant statistics, and analysis and interpretation of the data should be included in the DSMP.

If a Data Monitoring Committee or Data Safety and Monitoring Board (DSMB) will be performing the data oversight, the IRB may also consider the membership, qualifications and any conflicts of interests of the members may have with the protocol. If a formal DSMB will not be used, the IRB may consider the qualifications of the individuals performing the oversight, as well as any conflicts of interests those individuals may have with the conduct and outcomes of the study.

Other Considerations

If the communication plan included in the DSMP does not include the IRB, the IRB should request the PI to include the IRB in the communication plan so that relevant monitoring results and DSMP reports are made available to the IRB.

Resources

45 CFR 46.111(a)(6)
21 CFR 56(a)(6)
21 CFR 312.53 Selecting investigators and monitors?
21 CFR 312.56 Review of ongoing investigations?
AAHRPP Element II.3.B.
AAHRPP Tip Sheet 6
Institutional Review Board Management and Function, Bankert & Amdur—Chap 5-9

NIH Policies and IC Guidance for Data and Safety Monitoring of Clinical Trials (http://grants.nih.gov/grants/policy/hs/data_safety.htm) (Link Checked March 1, 2017)

NIH POLICY FOR DATA AND SAFETY MONITORING ([1]http://grants.nih.gov/grants/guide/notice-files/not98-084.html) (Link Checked March 1, 2017)

FURTHER GUIDANCE ON A DATA AND SAFETY MONITORING FOR PHASE I AND PHASE II TRIALS (http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-038.html) (Link Checked March 1, 2017)

National Cancer Institute (https://cancercenters.cancer.gov/grantsfunding/dsmprevcriteria) (Link Checked March 1, 2017)

National Institute of Child Health and Human Development (NICHD) (http://www.nichd.nih.gov/funding/policies/upload/Final_NICHD_Clinical_Research_Monitoring_Policy.pdf (Link Checked in March 1, 2017)

FDA: Guidance for Industry Oversight of Clinical Investigations- A Risk-Based Approach to Monitoring Draft Guidance (7http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM269919.pdf)(Link Checked in March 1, 2017)

ICH HARMONISED TRIPARTITE GUIDELINE FOR GOOD CLINICAL PRACTICE E6(R1) (8http://www.ich.org/products/guidelines/efficacy/efficacy-single/article/good-clinical-practice.html (Link Check March 1, 2017; E6(R2) is current version))

National Institutes of Health (NIH)-National Institute of Dental and Craniofacial Research (NIDCR) Data and Safety Monitoring Board (DSMB) Guidelines (https://www.nidcr.nih.gov/Research/ToolsforResearchers/Toolkit/DSMBGuidelines.htm) (Link Checked March 2, 2017).