Data and Safety Monitoring Plan Guidelines

Content Applies To

Mayo Clinic Human Research Protection Program

Purpose

To provide investigators and research teams with guidelines on how to develop a Data and Safety Monitoring Plan (DSMP).

For greater than minimal risk research, the IRB requires the investigator to have a Data and Safety Monitoring Plan in place that protects the safety of subjects, the validity of the data, and the integrity of the research study. The IRB reviews the plan and determines if the plan has adequate provisions in place for monitoring the data collected to ensure the safety of participants.

A DSMP template, located on the *IRB Forms & Templates* webpage, may be used to document the investigator's plan and submit to the IRB for review.

Guidelines

What is a Data and Safety Monitoring Plan?

Data and safety monitoring provides a clinical investigation with a system for appropriate oversight and attention to the protection of human subjects by the investigator, research team, or an independent reviewer. A Data and Safety Monitoring Plan is a quality assurance plan for a research study.

A written Data and Safety Monitoring Plan (DSMP) prospectively identifies and documents monitoring activities intended to protect the safety of the subjects, the validity of the data and the integrity of the research study. The DSMP may also identify when to terminate a subject’s participation (i.e. individual stopping rules) and/or the appropriate termination of a study (i.e. study stopping rules).

What is considered when developing a Data and Safety Monitoring Plan?

Consider the following DSMP elements and their relevance to the research protocol. The nature, size, risk, and complexity of the study will determine whether and how to address the following seven elements within your plan:

- Subject Safety – monitoring is conducted to avoid or minimize risks (i.e. physical, psychological or social).
- Data Integrity – monitoring is conducted to assure data is accurate and complete. Monitoring of data assures adherence to the approved clinical study.
- Subject Privacy – monitoring is conducted to assure individual’s rights are protected.
- Data Confidentiality – monitoring is conducted to assure data is secured.

- Product Accountability – monitoring is conducted to assure drug(s) or device(s) are tracked and accounted for.
- Study Documentation – monitoring is conducted to assure that required documentation and reports are on file, accurate, and complete.
- Study Coordination – monitoring is conducted to assure that investigator delegation and communication with the research team is planned and systematic.

What are the options for developing a Data and Safety Monitoring Plan?

A data and safety monitoring plan may be incorporated within the protocol, documented within the IRB application, or attached to the IRB application. The DSMP may be developed using the template provided by the IRB (located on the *IRB Forms & Templates* webpage), or developed using an outline format or narrative summary as preferred by the investigator.

When is a Data and Safety Monitoring Plan Needed?

The criteria for approval of research states that when the research involves more than minimal risk, the research plan makes adequate provision to monitor the data collected to ensure the safety of subjects, and that adequate provisions to protect the privacy of subjects and the confidentiality of the data are maintained (45 CFR 46.111).

The IRB expects all studies that involve administration of an experimental agent or use of an experimental device, or use of an approved agent or device that has the potential for mortality or major morbidity will have a written Data and Safety Monitoring Plan. A Data and Safety Monitoring Board may also be required studies that have a high expected rate of morbidity or mortality in the study population.

If the research is considered minimal risk, then the development of a data and safety monitoring plan may be helpful, but its development is not required by the IRB unless, the IRB determines a data and safety monitoring plan is needed for the oversight of the study.

The **National Institutes of Health (NIH)** states that “oversight and monitoring of all intervention studies to ensure the safety of participants and the validity and integrity of the data” is required. NIH policy states that "monitoring should be commensurate with risks and with the size and complexity of the trials”. NIH also emphasizes “the elements of the monitoring plan may vary depending upon the potential risks, complexity, and nature of the trial”. References: http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-038.html (release date June 5, 2000) and http://grants.nih.gov/grants/guide/notice-files/not98-084.html (release date June 10, 1998).

The **Office for Human Research Protection (OHRP)** Code of Federal regulations (45 CFR 46.111) states: “When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of the subjects”. Reference: http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html.

The **U.S. Food and Drug Administration (FDA)** states: "Existing requirements for sponsors of clinical investigations involving new drugs for human (including biological products for human use) and medical devices under 21 CFR Parts 312 and 812 respectively, require that a sponsor monitor the progress of a clinical investigation. The monitoring functions may be delegated to a contract research organization as defined in 21 CFR 312.3. Proper monitoring is necessary to assure adequate protection of the rights of human subjects and the safety of all subjects involved in clinical investigations and the quality and integrity of the resulting data submitted to the Food and Drug Administration (FDA)". Reference: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM269919.pdf

When following the **Department of Defense** regulations and requirements, the IRB considers, when appropriate, the appointment of a research monitor for research involving greater than minimal risk. The research monitor is appointed by name and must be independent of the study team conducting the research. The monitor may be an ombudsman or a member of the data and safety monitoring board. The duties of the research monitor are determined on the basis of specific risks or concerns about the research (Reference: DoD Instruction 3216.02 http://www.dtic.mil/whs/directives/corres/pdf/321602p.pdf).

Preparing the Data and Safety Monitoring Plan

Consider the following seven Human Subject Protection elements when using the DSMP template form, developing a DSMP outline, or constructing a narrative summary for a DSMP. Select the DSMP components (as identified in the table below) depending on the level of risk and the nature of the research study.

Protection Element	DSMP Component	Examples of monitoring activities
Subject safety	Specific subject safety parameters	Vital signs, weight, safety blood tests, cardiac status, anxiety, depression scores, etc.
	Frequency of subject safety observations	Weekly telephone follow-up, monthly appointments, observations of subject while in the clinical setting, etc.

	Individual responsible for safety monitoring	Principal investigator, study coordinator, safety monitor, independent monitor, or Data/Safety Monitoring Board, etc.
	Subject stopping rules - under what conditions will a subject be removed from study participation and who will make the decision?	Exclusion criteria, including adverse response to study procedures, pregnancy, stroke, cardiac irregularity, non-compliance with medication, etc. Include procedures for analysis and interpretation of data, etc.
	Study stopping rules - under what conditions will the study be modified or stopped and who will make the decision?	Unanticipated problems involving risks to subjects or others (UPIRTSOs), unexplained adverse outcomes, life threatening adverse event, etc.
	Reporting mechanisms (i.e. deviations, adverse events, UPIRTSOs)	Plans for reporting to IRB, FDA, Sponsor, participating sites, or Data/Safety Monitoring Board, etc.
Data integrity	Specific data elements to be reviewed	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.
	Frequency of monitoring data, points in time, or after specific number of subjects	First 3 subjects and every 20th subject, monthly, quarterly, or annually, etc.
	Individual responsible for data monitoring	Principal investigator, study coordinator, safety monitor, independent monitor, etc.
Subject privacy	Under what conditions (time and place) will a subject be consented, interviewed, or telephoned?	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.
Data confidentiality	What are the conditions that will protect the confidentiality of the data?	Check for locked file cabinets, secure electronic records, secure location where protected health information is stored, etc.

Product accountability	Who is responsible for obtaining, storing, preparing, administering, or disposing of the study drug or study device? Who is responsible for overseeing product accountability?	Research Pharmacy, Principal Investigator, Central Pharmacy, Research Laboratory, Nursing, etc.
Study documentation	Study file management	Study File Management guidelines and checklists for monitoring (sampling of study files annually), etc.
Study Coordination	Roles and responsibilities are clarified, education needs are addressed, planned meetings or communications with documented meeting notes/minutes	Annual debriefing to determine if expectations are clear and if educational needs exist. Scheduled meetings are on calendar, and meeting outcomes are noted and available to staff, etc.

Related Documents

DSMP template form (*IRB Forms & Templates* webpage)

http://intranet.mayo.edu/charlie/irb/child-of-page-1/forms-library/

Effective Date

April 19, 2017

Revision History

Date	Synopsis of Change
April 19, 2017	Scheduled review. No changes made.