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Guidance: Data and Safety Monitoring Plans (DSMPs), Data and Safety Monitoring Boards (DSMBs), and Data Monitoring Committees (DMCs)

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What is a Data and Safety Monitoring Plan?

A Data and Safety Monitoring Plan (DSMP) is a general plan contained in the research protocol to ensure the safety of the subjects and to ensure the validity of the data. The essential elements of a data and safety monitoring plan are:

- monitoring the progress of trial and the safety of participants;
- a description of the mechanism for reporting unanticipated problems involving risks to subjects or others (UPIRSOs), as well as adverse events, to the IRB, FDA, sponsor, and NIH, if applicable; and
- plans for assuring data accuracy and protocol compliance.

What is a Data Safety Monitoring Board or Data Monitoring Committee?

A Data Safety Monitoring Board (DSMB) or Data Monitoring Committee (DMC) is a group of individuals with pertinent scientific expertise that

- reviews, on a regular basis, the accumulated research data from an ongoing clinical trial;
- advises the sponsor and/or researcher regarding the continuing safety of trial subjects and those yet to be recruited into the research trial; and
- advises as to the continuing validity and scientific merit of the trial.

The terms DSMB and DMC are synonymous and can be used interchangeably.

Does every research protocol require a DSMP and a DSMB/DMC?

Not all research protocols require a DSMP or a DSMB/DMC. Every investigator, however, should incorporate into the research protocol

- elements of a data and safety monitoring plan to ensure subject safety (i.e. safety monitoring and periodic assessments for safety);
- methods for reporting UPIRSOs; and
- measures to protect the confidentiality of the research data (i.e. privacy, coding, and storage).

As research protocols become more complicated and the level of risk to subjects increases, the investigator and the IRB have to evaluate the need for a DSMP and/or a DSMB/DMC. The regulations require that, in order to approve the research, the IRB must determine if the research plan makes adequate provisions for monitoring the data collected to ensure the safety of participants [45 CFR 46.111(a)(6), 21 CFR 56.111 (a)(6)]. When appropriate, data and safety monitoring plans can be required for research in any discipline, including social and behavioral research.

All research protocols conducted at the Clinical Research Center (CRC) are required to have a DSMP. For additional information regarding the requirements for conducting research at the CRC refer to the CRC web site (http://www.ccts.uic.edu/repository/clinical-research-center).

When do the National Institutes of Health require DSMPs and DSMBs?

In general, the National Institutes of Health (NIH) believe that every clinical trial should have an IRB approved data and safety monitoring plan. The variety and type of monitoring plan may differ depending upon the nature, size, and complexity of the clinical trial being conducted.

A data and safety monitoring plan is required for all types of clinical trials, including physiologic, toxicity, and dose finding studies (Phase I); efficacy and safety studies (Phase II), and efficacy, effectiveness and comparative trials (Phase III).

The size and complexity of the monitoring committee or plan is also adjusted based upon the size or scope of the research. The monitoring may be conducted by the Principal Investigator or the NIH program staff for a small Phase I study, while a large Phase III clinical trial may require the establishment of an independent data and safety monitoring Board. However, even trials that pose little likelihood of harm should consider an external monitoring body.

The NIH requires the establishment of data safety monitoring boards for multi-site clinical trials involving interventions that entail potential risks to participants (generally Phase III clinical trials). For earlier phase trials (Phase I and Phase II), a DSMB may be appropriate if the studies involve multiple clinical sites, the studies are blinded or masked, or the studies involve high-risk interventions or vulnerable populations. A DSMB determines that the study is being conducted safely and effectively, and recommends early closure if significant risks have developed or if new information indicates that the trial is unlikely to be completed successfully.

Ideally, participants in monitoring the outcome of the trial are in no way associated with the trial. For trials that are conducted as part of a cooperative group, a majority of the individuals monitoring outcome data should be external to the group. Any perceived and/or potential conflicts of interest should be disclosed and evaluated to ensure the conflicts are managed in a reasonable manner.

Whatever the plan, IRBs should be provided feedback on a regular basis, usually at the time of continuing review. The feedback should include a summary of UPIRSOs, a summary of adverse events as required by NIH policy, and a copy of the DSMBs reports with any recommendations regarding the research. At a minimum, all monitoring plans must include a description of the reporting mechanisms for reporting adverse events to the IRB, the FDA, and the NIH. The investigator must ensure that the NIH is informed of any actions the IRB may take as a result of continuing review of the research.

Individual institutes within the NIH have their own policies regarding data and safety monitoring plans and data and safety monitoring boards, for example National Heart, Lung, and Blood Institute (NHLBI) revised their policy in May of 2005. For more information on the NIH Policies and IC Guidance for Data and Safety Monitoring of Clinical Trials, please refer to the following website: https://humansubjects.nih.gov/data_safety.

Does the Food and Drug Administration (FDA) require a DMC for clinical trials?

Current Food and Drug Administration (FDA) regulations do not require the use of data monitoring committees (DMC) in clinical trials except for research studies conducted in emergency settings in which the informed consent requirement is excepted [21 CFR 50.24(a)(7(iv)]. Research of this type is currently not allowed at UIC under UIC policy.

The FDA believes that all clinical trials require safety monitoring (i.e. sponsor monitoring, medical monitors, adverse event reporting), but that not all trials require monitoring by a formal committee that is external to the trial organizers, sponsors, and investigators. DMCs are generally recommended for controlled clinical trials of any size that will compare rates of mortality or major morbidity, but a DMC is not required or recommended for most clinical trials. Additionally, DMCs are not generally needed for clinical trials that address lesser outcomes such as relief of symptoms, unless the clinical trial populations are at elevated risks of more severe outcomes.

DMCs are not usually required in early Phase I and Phase II studies or pilot/feasibility studies, but formal monitoring groups may be appropriate for some early clinical studies, particularly if the risk level is higher than normal or the treatment approach is novel. These monitoring groups may be internal to the sponsor or consist of the investigators. Additionally, if the investigator is the manufacturer or the IND or IDE sponsor who presents the potential for financial or personal conflicts of interest, a DMC with independent members may provide added credibility to the oversight of subject safety and validity of the data.

REFERENCES:

NIH Policy: Policy for Data and Safety Monitoring, June 10, 1998
NIH Policy: Further Guidance on a Data and Safety Monitoring For a Phase I and Phase II Trials, June 5, 2000

NHLBI Policy: Policy on Human Subjects Research, Data and safety Monitoring Plans, National Heart, Lung, and Blood Institute (NHLBI), May 2005

FDA guidance: Guidance for Clinical Trial Sponsors, Establishment and Operation of Clinical Trial Data Monitoring Committees, March 2006

REVISION LOG:

Version (#, date)	Replaces (#, date)	Summary of changes
1.1	1.0, 4/23/07	No text changes, reformatted to new templates
1.2, 3/30/12	1.1, 1/22/09	Update of CRC to CIC, Addition of URL for CIC, changed from policy to Guidance
1.3, 6/1/13	1.2, 3/30/12	Addition of language regarding unaffiliated monitors. Removal of old hyperlinks.
1.4, 3/2/17	1.3, 6/1/13	Updating of logo and hyperlinks.