
Yale University Institutional Review Boards

IRB Policy 420 Data and Safety Monitoring

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Scope

This policy describes requirements related to data and safety monitoring of research, thereby contributing to the safety and well-being of research participants who are a part of the proposed research protocol. This policy applies to all investigators at Yale or its research affiliates who conduct human research.

Policy Statement

All non-exempt human subjects research protocols submitted to the IRB for review must include an explicit Data and Safety Monitoring Plan (DSMP). The plan must detail how the Principal Investigator (PI) will conduct monitoring of human research participants' data and safety commensurate with the risks associated with their participation in Yale research. In addition, for multi-center clinical trials in which the Yale (or research affiliate) PI serves as the overall PI, the DSMP must include a detailed plan describing how the PI will conduct data and safety monitoring for the subjects at all other sites.

The formation and use of a Data and Safety Monitoring Board (DSMB) may be required by the IRB in certain circumstances depending on the level of risk to research participants or when a real or potential interest of a study investigator or the University involves a new invention or poses, or may pose, a significant conflict of interest. When a DSMB exists, the DSMP must include plans for submitting DSMB reports to the IRB and other research oversight committees.

The IRB is responsible for evaluating the appropriateness of the DSMP when it performs initial and continuing protocol reviews.

Reason for the Policy

Data and safety monitoring is considered to be an essential component in the protection of human research participants. Investigators and the IRB must ensure that an adequate and appropriate data and safety monitoring plan is proposed and approved prior to the commencement of any human research. By doing so, both the investigators and the IRB ensure that any events or problems which may present a risk to study participants are monitored, reported and resolved. By examining the accruing data for indications of benefits or harm (including physical, psychological, economic or social harm), the investigator, the IRB or the DSMB can assess new risks and determine if the study should progress, be altered for more protections, or be terminated.

Definitions

Adverse Event

An undesirable and unintended, although not necessarily unexpected, result of therapy or other intervention.

Data and Safety Monitoring Board or Committee (DSMB/DSMC)

A group charged by the sponsor, investigator, or steering committee of a study with protecting subject safety by examining the accruing data for indications of benefit or harm. The DSMB/DSMC makes a judgment as to whether the trial should continue. The DSMB/DSMC usually looks at global data, as investigators forward all adverse event reports and safety data to a data coordinating center, which compiles the data for the DSMB/DSMC to review at predefined intervals. Data presented to the DSMB/DSMC is either completely unblinded, or categorized by treatment arm. As such, the DSMB/DSMC is able to determine whether a clear effect exists in one arm of the study versus the other(s).

Data and Safety Monitoring Plan (DSMP)

A plan, tailored to a particular protocol, that describes who has the responsibility to monitor study data and at which frequency study data is monitored to ensure the safety of human subjects and integrity of study data.

Related Event

An event is “related” if it is possibly, probably, or definitely caused by the research procedures.

Risk

associated with participating in a study can be categorized as:

Minimal Risk

Risk commensurate with ordinary daily life or with risks encountered in the performance of routine physical or psychological examinations. Examples may include blood draws of small volumes for research purposes, the collection of biological specimens for research purposes by noninvasive means, the collection of data from medical records, and most research employing surveys, interviews, or focus groups.

Moderate Risk

Risk that is greater than minimal, but not high and where there is adequate surveillance and protection to minimize risks and discover adverse events promptly. Examples include insulin clamp studies, Phase II and some Phase III trials, and some biopsies.

High Risk

Studies that pose potential significant harm to a subject because of the nature of the study or because there is significant uncertainty about the possible occurrence or nature of the risks. Examples may include most Phase I investigational drug or device trials that aim to establish a safety profile, and that have not yet been conducted in humans (so-called First in Man Trials – FiMT).

Serious Adverse Event

Any adverse event that results in any of the following outcomes: death, a life-threatening experience, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant disability/incapacity, or a congenital anomaly/birth defect, or any other adverse event that, based upon appropriate medical judgment, may jeopardize the subject’s health and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition.

Unanticipated Event

Problems, risks or events that occur during the conduct of the research, but were not expected and therefore are not cited in the written protocol, the consent form(s) or the Investigator’s Brochure.

Unanticipated Problems Involving Risks to Subjects or Others

See IRB Policy 710, Reporting Adverse Events and Unanticipated Problems

Policy Sections

420.1 Required Elements of the DSMP

The DSMP must document the procedures and means to protect the welfare and safety of subjects and to protect the integrity of the data. When the study sponsor is performing data and safety monitoring activities, the Yale investigator must provide a brief plan that describes how the local monitoring responsibilities will be integrated into the sponsor's DSMP and accomplished by the Yale investigator and how the IRB reporting requirements will be met.

The DSMP must include:

- A description of the monitoring of the progress of the trial, the safety of participants, data accuracy and assuring protocol compliance.
- A description of the mechanism and timeframe for appropriate reporting of adverse events, unanticipated problems, protocol noncompliance and protocol deviations to the IRB, the FDA, or the government agency program official or sponsor representative responsible for the grant or contract.
- An explicit statement of risk level determination. Overall risk assessment associated with the protocol may be assessed by the investigator as minimal, moderate or high.

DSMP Requirements Based on Risk:

Minimal Risk

The DSMP for Minimal Risk studies must include:

1. Identification of the individual(s) who will be responsible for monitoring the data, assuring protocol compliance, conducting the safety reviews, and the required frequency of the reviews
2. Explicit statement of Minimal Risk(s), and, if applicable, a description of any expected adverse events such as bruising or minor infection from a blood draw, or breach of confidentiality; or
3. A statement that adverse events are not anticipated
4. A plan for reporting to the IRB serious unanticipated adverse events and unanticipated problems involving risks to subjects or others at Yale or other sites, when applicable for multi-center trials.

Moderate or High Risk

The DSMP for Moderate or High risk studies must, at a minimum, include:

1. Identification of the individual(s) who will be responsible for monitoring the data, assuring protocol compliance, reporting protocol non-compliance, conducting the safety reviews, and the specified frequency of the reviews.
2. Explicit statement of Moderate or High risk and a description of any expected adverse events
3. Plan for attribution of adverse events
4. Plan for grading adverse events (See Guide 420 GD.1 Data and Safety Monitoring Plan for grading instructions)
5. Plan for reporting serious unanticipated adverse events, anticipated adverse events occurring at a greater frequency than expected, and unanticipated problems involving risks to subjects or others at Yale or other sites, when applicable for multi-center trials to the IRB.
6. Plan for reporting adverse events and unanticipated problems to co-investigators on the study, and, as appropriate, to the protocol's research monitor(s), e.g., industrial sponsor, Yale Cancer

Center monitors, the Yale Center for Clinical Investigation (YCCI) Research Subject Advocates (RSAs), Cancer Center's Quality Assurance, Compliance and Safety Committee (QUACS), DSMBs, study sponsors, funding and regulatory agencies, and regulatory and decision-making bodies.

420.2 Investigator Responsibilities

The DSMP must describe how the investigator intends to provide ongoing supervision and evaluation of the activities of the study, including the frequency and severity of adverse events and whether new risks have been identified and whether appropriate progress is being made. The DSMP must describe how the investigator will evaluate the progress of the trial, including periodic assessments of data quality and timeliness, participant recruitment, accrual and retention, participant risk versus benefit, and other factors that can affect study outcome. Ongoing oversight should also involve consideration of factors external to the study when interpreting the data, such as scientific or therapeutic developments that may have an impact on the safety of the participants or the ethics of the study.

Multi-Center Clinical Trials

An Investigator who serves as the sponsor of a multi-center trial has additional responsibilities of coordinating the trial across all sites. These responsibilities include, but are not limited to, ensuring ongoing IRB approval at other study sites, monitoring adverse events and reporting to the IRB, the FDA, the Sponsor, and other bodies that monitor the conduct of the study, and retaining copies of this documentation. A multi-center clinical trial may require a central monitoring entity to perform these functions.

Related Information

- 420 GD.1: Guidance on Data and Safety Monitoring
- 420 FR.1: Data and Safety Monitoring Plan Template
- 700 FR1: Protocol Deviation or Unanticipated Problem Involving Risks to Participants or Others Report Form
- IRB Policy 710: Reporting Adverse Events and Unanticipated Problems
- 710 PR1: Reporting Adverse Events to the IRB
- 710 PR2: Reporting Unanticipated Problems Involving Risks to Research Participants or Others to the IRB
- 710 PR.3: IRB Review of Adverse Events and Unanticipated Problems Involving Risks to Participants or Others
- 710 FR2: Reports of Adverse Events (AEs) under a Yale PI
- 710 FR3: Reports of Adverse Events (AEs) under a Non -Yale PI

Contacts

Subject	Contact	Phone
Data and Safety Monitoring Plans: Biomedical Research	Human Investigation Committees	203-785-4688
Data and Safety Monitoring Plans: Social and Behavioral Research	Human Subjects Committee	203-436-3650

Roles and Responsibilities

Human Investigation Committees

HIC I, HIC II, HIC III and HIC IV serve as the Institutional Review Boards or IRBs for human subjects biomedical research conducted at Yale University.

Human Subjects Committee

The HSC is responsible for review and oversight of social and behavioral research involving human subjects.

Revision History: 5/30/2007, 11/19/2009

References

National Institutes of Health: NIH POLICY FOR DATA AND SAFETY MONITORING (<http://grants.nih.gov/grants/guide/notice-files/NOT98-084.html>)

National Institutes of Health: 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>)

NCI Guidelines at <http://www.cancer.gov/clinicaltrials/conducting/dsm-guidelines>