Human Research Seminar Series

Data and Safety Monitoring

Thursday, April 4, 2013

Presented by:
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Quality Assurance Coordinator
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Science at the heart of medicine

Einstein Institutional Review Board (IRB)

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Data and Safety Monitoring

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Overview

• Data and Safety Monitoring Plans (DSMP):
  Background & Purpose
• DSMP Requirements
  > Data and Safety Monitoring Committee (DSMC)
  > Data and Safety Monitoring Board (DSMB)
What is a Data and Safety Monitoring Plan?

- A Data and Safety Monitoring Plan (DSMP) describes how the study investigators plan to oversee research subject safety and how adverse events will be characterized and reported.
  > Monitoring is the collection, review, and analysis of data as the project progresses to ensure the appropriateness of the research, its design, and subject protections.
- The intensity and frequency of monitoring should be tailored to fit the expected risk level, complexity and size of the particular study.

What are the Requirements for a DSMP?

- The DSMP needs to address the nature of the safety monitoring and who will be conducting that monitoring.
- It may be reasonable for a single individual, e.g., the PI, to perform the data and safety monitoring in a small trial with low level risk, while an internal DSMC or external DSMB may be required for more complex, higher risk trials.
- For minimal risk studies, the PI’s compliance with the Einstein IRB’s policies is appropriate and constitutes a sufficient plan.
DSMP Elements

• The overall elements of the monitoring plan will vary depending on the potential risks, complexity, and nature of the trial.

• The monitoring plan must:
  > Define the authority of the monitoring group with regard to advising or making final decisions concerning continuation, revision or discontinuation of the research project.
  > Include the process for making such recommendations or decisions.

DSMP Elements (continued)

• The monitoring plan is to include, as appropriate:
  > The specific procedures that will be used to monitor for and report adverse events, protocol violations and deviations.
  > The timing and frequency of data analysis.
  > Periodic assessment of the following:
    • Participant recruitment and retention, to assure the feasibility of meeting recruitment projections.
    • Data quality and timeliness.
    • Participant risk versus benefit, taking into consideration the impact of new scientific or therapeutic developments.
    • Trial site performance.
    • The procedure and schedule for timely reporting to sponsors and the IRB.
DSMP Designs: PI Monitoring

• The PI’s compliance with IRB requirements constitutes a sufficient plan for studies involving no greater than minimal risk.
• Close monitoring by the PI may be adequate for:
  > single site studies presenting more than minimal risk and involving diagnostic, physiologic, biochemical, metabolic or genetic observations or interventions
  > behavioral intervention or observation studies presenting more than minimal risk
  > Phase I and Phase II drug or device studies involving a single site and small numbers of study subjects
    • Alternatively, one or two independent individuals may serve this role.
    • More intense monitoring would be appropriate if the study is blinded or employs particularly high-risk interventions or vulnerable populations.

DSMP Designs: PI Monitoring (continued)

• For Phase I and Phase II drug or device studies involving multiple sites, a Data and Safety Monitoring Committee (DSMC) would be most appropriate for performing ongoing monitoring.
• For Phase III, multiple site drug or device trials, an external Data and Safety Monitoring Board (DSMB) is generally required.
DSMP Designs: Data and Safety Monitoring Committees (DSMCs) and Boards (DSMBs)

- A group of individuals with pertinent expertise who review accumulating data from an ongoing clinical trial on a regular basis.
  - DSMCs consist of “internal” (institutionally affiliated) individuals
  - DSMBs consist of “external” (unaffiliated) individuals.
- Advises on safety of current and future participants and validity and scientific merit of the trial.

DSMC Responsibilities

- Meet and review the approved protocol prior to the enrollment of research participants.
- Evaluate the progress of the trial with periodic assessments of data quality and timeliness, participant recruitment, accrual and retention, participant risk versus benefit, and reports from related studies.
- Make recommendations to the IRB and investigators concerning continuation or conclusion of the trial.
- Record minutes of the DSMC meetings, including:
  - Attendance, summary of the discussion, and findings (e.g., research may continue, recruitment is halted, actions needed to re-open recruitment, etc.).
Additional DSMP Elements for DSMC Monitored Studies

- The DSM Plan will stipulate:
  - The composition of the DSMC.
  - The frequency of committee meetings.
  - The material to be reviewed at each meeting.
- The procedures for DSMC action are outlined in the Einstein IRB’s DSM Policy.

Review

Data and Safety Monitoring Plan (DSMP):
- Describes how the conduct of the research and the safety of the research subjects will be overseen.
- The intensity and frequency of monitoring should be tailored to fit the expected risk level, complexity, and size of the particular study.

Data and Safety Monitoring Committee/Board (DSMC/DSMB):
- A group of individuals with pertinent expertise who review the accumulating data on a regular basis from an ongoing study.
- Advises IRB/sponsors regarding safety of research subjects and scientific merit.
## Einstein IRB Contact Information

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<thead>
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<th>East Campus IRB</th>
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Website: [http://www.einstein.yu.edu/irb](http://www.einstein.yu.edu/irb)
Includes: Policies and Procedures, Submission Guidelines, Forms, and Educational Materials
I. MONITORING DEFINITION
The collection, review, and analysis of data as the project progresses to ensure the appropriateness of the research, its design, and subject protections.

II. MONITORING PRINCIPLES
A. All clinical investigation requires monitoring.
B. The CCI/IRB will generally accept the monitoring plan for externally sponsored research, and reserves the right to review the plan on an ad hoc basis. Sponsor reports must be submitted to the Primary Review Committee (CCI or IRB) within 30 days of receiving the DSM Report.
C. Monitoring should be performed according to a predetermined schedule.
D. The frequency, intensity and mechanism of monitoring depend on the level of risk and the size and complexity of the study.
E. Monitoring should provide information, as appropriate, concerning the performance of individual centers, interim results of the study for evidence of efficacy or adverse events, and possible early termination of the study because of early attainment of study objectives, safety concerns, or inadequate performance.
F. The primary responsibility of the monitoring committee is the health and safety of the research participants.

III. MONITORING PLAN - ELEMENTS AND DESIGNS
The CCI/IRB will review and approve the monitoring plan, as well as the appropriateness of the individuals for Data Safety Monitoring activities on a case-by-case basis. Consideration will be given to the need for expertise and independence from the investigator, the department or the institution.
A. ELEMENTS:
   i. The overall elements of the monitoring plan will vary depending on the potential risks, complexity, and nature of the trial.
   ii. The monitoring plan must:
      1. Define the authority of the monitoring group with regard to advising or making final decisions concerning continuation, revision or discontinuation of the research project.
      2. Include the process for making such recommendations or decisions.
      3. The monitoring plan is to include, as appropriate:
         a. The specific procedures that will be used to monitor for and report adverse events, protocol violations and deviations.
         b. The timing and frequency of data analysis.
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c. Periodic Assessment of the following:
   i. Participant recruitment and retention, to assure the feasibility of meeting recruitment projections.
   ii. Data quality and timeliness.
   iii. Participant risk versus benefit, taking into consideration the impact of new scientific or therapeutic developments.
   iv. Trial site performance.
   v. The procedure and schedule for timely reporting to sponsors and the CCI/IRB.

B. DESIGNS:
   i. For studies involving no greater than minimal risk, the signed assurances of the PI included in the CCI/IRB Research Application form, including the policy for reporting internal and external adverse events, constitute a sufficient plan.
   ii. For Phase I and Phase II drug or device studies involving a single site and small numbers of study subjects, close monitoring by the study investigator may be adequate. Alternatively, one or two independent individuals may serve this role. More intense monitoring would be appropriate if the study is blinded or employs particularly high-risk interventions or vulnerable populations.
   iii. For Phase I and Phase II drug or device studies involving multiple sites, a central DSM entity would be most appropriate for performing ongoing monitoring.
   iv. For Phase III, multiple site drug or device trials, an external Data and Safety Monitoring Board is generally required.
   v. For single site studies presenting more than minimal risk and involving diagnostic, physiologic, biochemical, metabolic or genetic observations or interventions, close monitoring by the study investigator may be adequate.
   vi. For behavioral intervention or observation studies presenting more than minimal risk, close monitoring by the study investigator may be adequate.
   vii. For high risk and complex studies, the CCI/IRB may require additional monitoring, such as:
      1. The addition of one or two individuals not involved in the study who would join the PI as a monitoring committee.
      2. An internal Data Safety Monitoring Committee.
      3. A full External Data Safety Monitoring Board.
      4. An external Data and Safety Monitoring Board for multiple sites studied.
IV. PROCEDURAL GUIDELINES FOR PROTOCOLS REQUIRING THE ESTABLISHMENT OF A DATA SAFETY MONITORING COMMITTEE FOR RESEARCHER-INITIATED PROTOCOLS AND EXTERNALLY SPONSORED PROTOCOLS HAVING NO MONITORING COMMITTEE:

The DSM Committee is required to meet and review the approved protocol prior to enrolling research participants.

A. The DSM Plan will stipulate:
   i. The composition of the DSM Committee.
   ii. The frequency of committee meetings.
   iii. The material to be reviewed at each meeting.

B. The DSM Committee is required to record minutes of the meetings. The minutes are to include the following:
   i. Attendance.
   ii. Summary of the discussion.
   iii. Findings, (e.g., research may begin or continue, recruitment is halted, actions needed to re-open recruitment, etc.).

C. When the DSM Committee concludes that the protocol should continue, unmodified, the DSM Committee will send the investigator and the CCI/IRB the minutes. No further action is required.

D. When the DSM Committee concludes that recruitment should be stopped:
   i. The DSM Committee will send the investigator and the CCI/IRB the minutes with directive to suspend recruitment immediately.
   ii. The DSM Committee and the CCI/IRB will copy each other on all written and electronic communications.
   iii. The CCI/IRB Chair or designee will review the DSM Committee recommendations, and if in agreement, the CCI/IRB will notify the investigator, in writing, affirming the DSM Committee action, and directing the investigator to submit an amendment to implement the required changes.
   iv. Depending on the nature of the changes, the amendment will receive expedited or full committee review.

E. When the DSM Committee concludes that changes to the protocol and/or the informed consent are required, but recruitment may continue:
   i. The DSM Committee will send the investigator and the CCI/IRB the minutes.
   ii. The CCI/IRB Chair or designee will review the DSM Committee recommendations, and if in agreement, the CCI/IRB will notify the
investigator, in writing, to submit an amendment to implement the required changes.

iii. Depending on the nature of the changes, the amendment will receive expedited or full committee review.

F. The researcher is required to include all DSM Committee reports as attachments to the Progress Report at the time of recertification.

G. GREATER THAN MINIMAL RISK STUDIES HAVING NO DSM COMMITTEE:

In the rare instance in which the CCI/IRB has determined that a protocol that is slightly greater than minimal risk does not require a DSM Committee, the researcher must submit a DSM Plan for review and approval by the CCI/IRB.

References:
General Clinical Research Center: http://ictr.aecom.yu.edu/
http://www.niaid.nih.gov/dmid/clinresearch/policy.htm

Approved 9/7/04
Revised 12/6/04, 3/07
CCI/IRB Joint Policy - approved
Administrative revision 10/22/07