Pennington Biomedical Research Center
Louisiana State University

**G-006**

# Data and Safety Monitoring

Regulations and guidance

3-15-2022

# Table of Contents

# I. Overview of Data and Safety Monitoring

## A. Purpose of this guide

This document provides guidelines for writing a Data and Safety Monitoring Plan and requirements of a Data and Safety Monitoring Board.

## B. Definitions

### 1. Data and Safety Monitoring Plan (DSMP)

A DSMP describes how the investigator plans to oversee the research participant's safety and welfare and how adverse events will be characterized and reported. The intensity and frequency of monitoring should be tailored to fit the expected risk level, complexity, phase and size of the particular study.

### 2. Data and Safety Monitoring Board (DSMB)

A DSMB is a formally appointed, independent group assigned to conduct interim monitoring of accumulated data from research activities to assure the continuing safety of research participants, relevance of the study question, appropriateness of the study and integrity of the accumulated data. Membership should include expertise in the relevant field of study, statistics and research study design.

### 3. Safety Officer (or Research Monitor)

The sponsor or the IRB can require a safety officer for a portion of the project or for the life of the project, when appropriate. If the study is sponsored by the Department of the Defense (DOD), an independent research monitor is required for research involving greater than minimal risk (DoD Directive 3216.02, section 4.4.3.). In all cases, the person must be qualified and objective and must not be directly involved with design and conduct of the study.

The safety officer shall be appointed by name and generally has authority to:

- Stop a research study in progress.
- Remove individuals from a study.
- Take any steps to protect the safety and well-being of participants until the IRB can assess the research monitor's report.

# II. Regulations and Guidance

## A. Requirement

The IRB has primary responsibility for determining the level of risk to study participants. This responsibility stems from DHHS and FDA regulations, which list the following criterion for study approval: "when appropriate, the research plan makes adequate provisions for monitoring the data collected to ensure the safety of subjects" (45 CFR 46.111[a][6]). NIH policy requires data and safety monitoring for all NIH-funded clinical trials.

All protocols presenting the potential of risk to subjects, even minimal risk, should address how the investigator will monitor risk and report adverse events. The IRB requires that each new research application except those qualifying as "Exempt" will include a data and safety monitoring plan to assure the safety and welfare of participants. Research proposals should include adequate provisions for monitoring of data collected for scientific validity and safety of research subjects.

## B. Monitoring Recommendations Based on Risk

The monitoring plan for a particular research study depends on the complexity of the research study and the possibility of potential harm to subjects. Safety monitoring for a protocol must be appropriate for the level of risk identified. The combination of factors used in assessing the level of risk drives the intensity of monitoring required for a protocol.

### 1. No Greater than Minimal Risk

In this context, minimal risk means the probability and magnitude of harm or discomfort anticipated in the research are not greater than those ordinarily encountered in daily life or during the performance of routine physical and psychological examinations or tests and where confidentiality is adequately protected. However, survey research and questionnaires may present more than minimal risk to subjects if they address highly sensitive information. Inclusion of special populations (children, prisoners, pregnant women, mentally disabled persons, or economically and/or educationally disadvantaged persons) who may be more sensitive or vulnerable to the risks posed by the research, may increase the level of risk to moderate or high.

***Recommendation:*** Monitoring is the responsibility of the investigator. See the Minimal-Risk Study template as a guide to creating a data and safety monitoring plan. In most cases, these types of studies do not require an independent DSMB. **However, the sponsor or IRB may require the**

**institution of a DSMB for minimal-risk studies based on the study population or design.**

*Examples of minimal-risk studies include the following:*

- Studies that pose no more risk than expected in daily life [blood samples (venipuncture or intravenous catheter insertion), physical exam, routine psychological testing, oral glucose tolerance tests, intravenous glucose tolerance test, DXA scans, routine MRI scans, special diets, exercise testing, EKGs and anthropometric evaluations].
- Non-interventional studies (e.g., observational studies of behavior or nutrition).
- Survey/questionnaire studies of a nonsensitive nature. However, survey research and questionnaires may present more than minimal risk to subjects if they address highly sensitive information. Inclusion of special populations (children, prisoners, pregnant women, mentally disabled persons, or economically and/or educationally disadvantaged persons) who may be more sensitive or vulnerable to the risks posed by the research, regardless of the study, may increase the level of risk to moderate or high.

### 2. Minor Increase over Minimal Risk

There is medium to high probability of the occurrence of a low-severity event that is completely reversible (e.g., headache from lumbar puncture) or the likelihood of serious harm occurring is low (e.g., fatal anaphylaxis from allergy skin testing).

***Recommendation:*** Low-intensity monitoring. A Data and Safety Monitoring Plan is required; in most circumstances, use of the minimal-risk template is appropriate. However, the sponsor may require independent monitoring, including a DSMB, or have additional requirements.

*Examples of studies at this risk level are as follows:*

- Studies of normal volunteers using well-described research procedures with a single dose of an experimental agent.
- Post-marketing study: Phase IV drug or device (as defined by FDA) study with minor safety concerns.
- Interventions or invasive procedures that present low risks, reasonably commensurate with those expected in a medical or dental practice.
- Studies that involve sensitive information or a potential risk of breach of confidentiality.

### 3. Moderate Risk

Risks are recognized as being greater than minimal but are not considered high. There is a medium to high probability of a moderate-severity event

occurring as a result of study participation (e.g., reversible worsening of a nonfatal disease, such as seasonal allergy while receiving placebo or pneumonia from a bronchoscopy), but there are adequate surveillance and protections to identify adverse events promptly and to minimize their effects.

***Recommendation:*** Moderate-intensity monitoring. A moderate-risk study template is provided as a guide to create a data and safety monitoring plan, or use the sponsor's required template/information.

- For some strictly genetic studies in targeted populations, the investigator may serve as the monitor.
- For small, moderate-risk studies, monitoring might be performed by an independent investigator who is an expert in the agent being studied and the patient population.
- May require DSMB if the study is placebo-controlled or if an investigational agent is used.
- Sponsor may require institution of a DSMB for moderate-risk studies based on the population or study design.

*Examples of moderate-risk studies are as follows:*

- Subjects treated with placebo for a recognized disease.
- Involves subjects with serious viral, autoimmune or malignant illness in a moderate-risk Phase I or Phase II clinical trial treatment study with available safety data in humans.
- Minimal-risk studies involving vulnerable populations (e.g., subjects with impaired capacity to give informed consent).
- Studies in which blood is drawn for genetic studies in real time and/or stored for later use.

### 4. High Risk

The study presents greater than moderate risk due to the increased probability of generating serious adverse events.

***Recommendation:*** High-intensity monitoring. For some high-risk studies, monitoring might be performed by a single, independent investigator who is an expert in the agent being studied and the patient population.

- A high-risk template is provided as a guide to create a data and safety monitoring plan, or use the sponsor's required template.
- Follow the sponsor's requirements. A DSMB is generally required, but in some cases, a Safety Officer, rather than a DSMB, may be acceptable. The IRB will assess risk and must approve plan. See guidance for DSMB (in section VI of this document).
- In specific cases where an investigator is the sponsor-investigator of the test agent (i.e., holder of the Investigational New Drug (IND) application), the sponsor-investigator must submit individual adverse event reports

and IND safety reports to the FDA per FDA regulations (CFR 21 Part 312). The FDA Safety Information and Adverse Event Reporting Program may be accessed at http://www.fda.gov/medwatch/how.htm. This information must be incorporated in the DSMP.

- In specific cases where an investigator is the sponsor-investigator of the investigational device (i.e., holder of the Investigational Device Exemption (IDE) application), the sponsor-investigator must submit individual Unexpected Device Effect to the FDA per FDA regulations (CFR 21 Part 812). This information must be incorporated in the DSMP.

*Examples of high-risk studies are as follows:*

- Clinical trials of interventions to prevent or treat diseases that lead to death or irreversible morbidity.
- Involves an intervention or invasive procedure with substantial risk or potential for severe toxicity.
- An investigator-initiated IDE trial.
- Implantation of a device.
- A study involving the use of a new chemical or drug for which there is limited or no available safety data in humans.
- An investigator-initiated, Phase III clinical trial.
- Industry-sponsored, multicenter, randomized clinical trials (Phases 2b, 3 or 4).

# III. Data and Safety Monitoring Plan Templates

The following are templates that may be used for developing the study application and protocol.

## A. Template for a Minimal-Risk Study

The Principal Investigator (PI) is responsible for monitoring the data, assuring protocol compliance and conducting safety reviews at the specified frequency [e.g., monthly, quarterly, etc.]. During the review process, the Principal Investigator will evaluate whether the study should continue unchanged, requires modification/amendment or should close to enrollment.

The Principal Investigator, the Institutional Review Board (IRB) or [enter the names of other oversight bodies that have this authority, e.g., OHRP, FDA] has the authority to stop or suspend the study or require modifications.

This protocol presents minimal risks to subjects, and adverse events or other problems are not anticipated. In the unlikely event that such events occur, the PI is responsible for reporting to the IRB and any appropriate funding and regulatory agencies any serious, unanticipated and related adverse events or unanticipated problems involving risks to subjects or others. The

investigator will apprise fellow investigators and study personnel of all adverse events that occur during the conduct of this research project. [Describe how the investigator will meet this obligation, e.g., through regular study meetings, via email as they are reviewed by the Principal Investigator.] [Where appropriate, modify the following sentence to apply to the specific research protocol.] The study's Research Monitor(s), study sponsor(s), funding and regulatory agencies, and decision-making bodies will be informed of [specify types of adverse events that require reporting to these oversight bodies] adverse events within 10 working days [enter other appropriate duration] of the event becoming known to the Principal Investigator. If there are unanticipated problems involving risks to subjects or others, these should be reported to the IRB per HRPP Policy 8.0.

## B. Template for a Moderate-Risk Study

### 1. Personnel responsible for the safety review and its frequency

The Principal Investigator (PI) and/or Medical Investigator (MI) will be responsible for monitoring the data, assuring protocol compliance and conducting the safety reviews at the specified frequency, at a minimum of every 6 months (including at the time of continuing review). During the review process, the Principal Investigator (or Study Monitor) will evaluate whether the study should continue unchanged, requires modification/amendment or should close to enrollment. Findings must be reported at the time of continuing review. The IRB, PI or regulatory body (e.g., FDA, OHRP, [enter the names of other oversight bodies that have this authority]) has the authority to stop or suspend the study or require modifications.

### 2. Determination of study risk

The risks associated with the current study are deemed moderate for the following reasons: (choose those that apply)

- We do not view the risks associated with the _____ as minimal.
- We do not view the risks associated with the combined use of _____and_____ as minimal.
- Given the established safety and validity of _____ in our prior work, we do not view the proposed study as high-risk.
- Given our experience with co-administration of _____ and_____, we do not view the proposed study as high-risk.

Although we have assessed the proposed study as one of moderate risk, the potential exists for anticipated and/or unanticipated adverse events, serious or otherwise, to occur since it is not possible to predict with certainty the absolute risk in any given individual or in advance of firsthand experience

with the proposed study methods. Therefore, we provide a plan for monitoring the data and safety of the proposed study as follows:

## 3. Attribution of adverse events

Adverse events for each subject participating in the study will be monitored and attributed to the study procedures/design by the Principal Investigator (PI) (Insert Investigator Name) and/or Medical Investigator (MI) (Insert Investigator Name) according to the following categories:

- Definite: Adverse event is clearly related to investigational procedure(s)/agent(s).
- Probable: Adverse event is likely related to investigational procedure(s)/agent(s).
- Possible: Adverse event may be related to investigational procedure(s)/agent(s).
- Unlikely: Adverse event is likely not related to the investigational procedure(s)/agent(s).
- Unrelated: Adverse event is clearly not related to investigational procedure(s)/agent(s).

## 4. Plan for grading adverse events

The following scale will be used in grading the severity of adverse events noted during the study:

- Mild adverse event
- Moderate adverse event
- Severe or medically significant

## 5. Plan for determining seriousness of adverse events

In addition to grading the adverse event, the PI will determine whether the adverse event meets the criteria for a Serious Adverse Event (SAE). An adverse event is considered serious if ANY of the following apply:

- It is life-threatening.
- It results in inpatient hospitalization or prolongation of existing hospitalization.
- It results in persistent or significant disability or incapacity.
- It results in a congenital anomaly or birth defect.
- It results in death.
- Based upon appropriate medical judgment, it may jeopardize the subject's health and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition.
- It adversely affects the risk/benefit ratio of the study.

An adverse event may be graded as severe but still not meet the criteria for a SAE. Similarly, an adverse event may be graded as moderate but still meet

the criteria for an SAE. It is important for the PI to consider the grade of the event as well as its seriousness when determining whether reporting to the IRB is necessary.

### 6. Plan for reporting adverse events

#### *a) Reporting adverse events to the IRB*

The investigator will report the following types of adverse events to the IRB:

- Serious AND unanticipated AND possibly, probably or definitely related events.
- Anticipated adverse events occurring with a greater frequency than expected.
- Other unanticipated problems involving risks to subjects or others.

These adverse events or unanticipated problems involving risks to subjects or others will be reported to the IRB within 10 working days of becoming known to the investigator, using the appropriate forms found in IRB Manager.

#### *b) Reporting adverse events to co-investigators*

The following individuals and funding and/or regulatory agencies will be notified of adverse events (choose those that apply):

- All co-investigators listed on the protocol.
- Study sponsor(s).
- National Institutes of Health.
- Food and Drug Administration (Physician-Sponsored IND #_____).
- Foundation (Grant_____).

The Principal Investigator (Insert Investigator Name) and/or Medical Investigator (MI) (Insert Investigator Name) will conduct a review of all adverse events upon completion of every study subject. The Principal Investigator will evaluate the frequency and severity of the adverse events and determine if modifications to the protocol or consent form are required.

## C. Template for a High-Risk Study

## 1. Personnel responsible for the safety review and its frequency

The Principal Investigator (PI) and/or Medical Investigator (MI) will be responsible for monitoring the data, assuring protocol compliance, and conducting the safety reviews at the specified frequency, at a minimum of every 6 months (including at the time of continuing review). During the review process, the Principal Investigator (or Study Monitor) will evaluate whether the study should continue unchanged, requires modification/amendment or should close to enrollment. Findings must be reported at the time of continuing review. The IRB, PI or [enter name of any regulatory body (e.g., FDA, OHRP) that has this authority] has the authority to stop or suspend the study or require modifications.

## 2. Determination of study risk

The risks associated with the current study are deemed high for the following reasons: (choose those that apply)

- We do not view the risks associated with _____ as minimal/moderate.
- We do not view the risks associated with the combined use of _____ and _____ as minimal/moderate.
- Given the established safety and validity of _____ in our prior work, we do not view the proposed study risk as minimal/moderate.
- Given our experience with co-administration of _____ and _____, we do not view the proposed study risk as minimal/moderate.

Since it is not possible to predict with certainty the absolute risk in any given individual or in advance of firsthand experience with the proposed study methods, we provide a plan for monitoring the data and safety of the proposed study as follows:

## 3. Attribution of adverse events

Adverse events for every subject participating in the study will be monitored and attributed to the study procedures/design by the Principal Investigator (PI) (Insert Investigator Name) and/or Medical Investigator (MI) (Insert Investigator Name) according to the following categories:

- Definite: Adverse event is clearly related to investigational procedure(s)/agent(s).
- Probable: Adverse event is likely related to investigational procedure(s)/agent(s).
- Possible: Adverse event may be related to investigational procedure(s)/agent(s).
- Unlikely: Adverse event is likely not related to investigational procedure(s)/agent(s).
- Unrelated: Adverse event is clearly not related to investigational procedure(s)/agent(s).

## 4. Plan for grading adverse events

The following scale will be used in grading the severity of adverse events noted during the study:

- Mild adverse event.
- Moderate adverse event.
- Severe adverse event.

## 5. Plan for determining seriousness of adverse events

In addition to grading the adverse event, the PI will determine whether the adverse event meets the criteria for a Serious Adverse Event (SAE). An adverse event is considered serious if ANY of the following apply:

- It is life-threatening.
- It results in inpatient hospitalization or prolongation of existing hospitalization.
- It results in persistent or significant disability or incapacity.
- It results in a congenital anomaly or birth defect.
- It results in death.
- Based upon appropriate medical judgment, it may jeopardize the subject's health and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition
- It adversely affects the risk/benefit ratio of the study.

An adverse event may be graded as severe but still not meet the criteria for a SAE. Similarly, an adverse event may be graded as moderate but still meet the criteria for an SAE. It is important for the PI to consider the criteria described on the Reportable Event Form before submitting the event to the IRB.

## 6. Plan for reporting adverse events

### *a) Reporting adverse events to the IRB*

The investigator will report the following types of adverse events to the IRB:

- Serious AND unanticipated AND possibly, probably or definitely related events.
- Anticipated adverse events occurring with a greater frequency than expected.
- Other unanticipated problems involving risks to subjects or others.

These adverse events and unanticipated problems involving risks to subjects or others will be reported to the IRB within 10 working days of becoming known to the investigator, using the appropriate forms found in IRB Manager.

### *b) Reporting adverse events to co-investigators*

The following individuals and funding and/or regulatory agencies will be notified of adverse events (choose those that apply):

- All co-Investigators listed on the protocol.
- Study sponsor(s).
- National Institutes of Health.
- Food and Drug Administration (Physician-Sponsored IND #_____).
- Medical Research Foundation (Grant_____).

The Principal Investigator (Insert Investigator Name) and/or Medical Investigator (MI) (Insert Investigator Name) will conduct a review of all adverse events upon completion of every study subject. The Principal Investigator will evaluate the frequency and severity of the adverse events and determine if modifications to the protocol or consent form are required.

# IV. Data and Safety Monitoring Board Guidelines

## A. Requirement for DSMB

As a general guideline, DSMBs are needed for research studies of diseases with high mortality or morbidity, for research studies involving high risks, and for multicenter clinical trials. The involvement of a DSMB may be requested for low-risk studies if the studies are exceptionally large, long-term, and/or involve vulnerable subjects. For this discussion, "high-risk" refers to studies of interventions associated with substantial side effects to subjects (e.g., side effects that could result in serious morbidity or death, or are irreversible), trials of diseases associated with high mortality or morbidity, and trials of highly experimental therapies (e.g., gene therapy).

## B. DSMB Structure

### 1. Independence of DSMB

DSMB members should not have conflicts of interest with regard to the research study. While the most obvious type of conflict of interest is financial, there can also be professional, intellectual and emotional conflicts. DSMB members and the key personnel of the study must not be professional supervisors or mentors of each other, and must not be current co-investigators or collaborators. Representatives of the manufacturer of the drug(s) or device(s) being tested, and other

individuals with vested interests in the outcomes of the study, are not permitted to serve on the DSMB.

Each DSMB member will be asked about potential conflicts at the first meeting of the DSMB, and any such conflicts will be discussed and acted on as appropriate. At each subsequent meeting, members will be asked if they have any new conflicts to disclose. A DSMB may decide that each member should submit written conflict of interest disclosures for documentation and to raise the level of awareness of this important issue. Complete elimination of all real and perceived conflicts of interest is generally impossible if DSMB members are to be knowledgeable and experienced in the medical subject being studied. PBRC may institute a plan to mitigate risks.

## 2. Financial Conflict of Interest Guidelines

Members of the DSMB will not buy, sell, or hold stock options in the Sponsor for at least the following periods and in accordance with applicable laws:
From the first meeting of the DSMB until the last meeting and after the study results are made public; OR
From the first meeting until the member's active personal involvement in the DSMB ends.

Each member agrees not to serve as a paid consultant to the Sponsor during these same periods. The guidelines also will apply to the member's spouse and dependents.

Certain other activities are not viewed as constituting conflicts of interest but must be reported annually to the DSMB chairman. These include:

- Participation of a member in educational activities supported by the study sponsor.
- Participation of members in other research projects supported by the study sponsor.
- Occasional scientific consulting to the study sponsor on issues not related to the product in the trial and for which there is no financial payment or other compensation.

## 3. Payment of DSMB Members

DSMB members may receive an honorarium or nominal pay for their time and effort in the DSMB meetings.

## 4. Composition of a DSMB and Roles of Members

A DSMB ordinarily will be multidisciplinary and should always include members with relevant clinical and statistical expertise in order to correctly interpret the data and ensure patient safety. A DSMB may consist of as few as three members, but this number should be large enough to include a representation of all needed skills and experience. The desired clinical expertise of the DSMB members should be dictated by the particular disease and patient population being studied. Ad hoc specialists may be invited to participate as nonvoting members at any time if additional expertise is needed. Individuals with financial or other conflicts of interest should not be members. Members should be independent from the direct management of the study. Ideally, all DSMB members should have experience with the design, conduct and interpretation of clinical trials and study monitoring.

The DSMB should meet prior to enrollment of the first subject to review the research protocol, informed consent documents, and plans for data and safety monitoring of the study. This review is to determine the risks and benefits to research subjects, protection and safety of the subjects, and to offer suggestions for improving the study design. In addition, the board should reach agreement on the data that will be required for review. Determination of the schedule of future meetings, appointment of the chairman and voting members, confirmation of who receives minutes, and the signing of conflict of interest statements occur during the pre-enrollment meeting.

## 5. Purpose of DSMB

Appropriate goals of a DSMB include ensuring safety of trial participants and ensuring overall integrity of the trial through periodic review and evaluation of accumulated study data for study conduct and progress, participant safety and, when appropriate, efficacy. Based on these considerations, the board makes recommendations to the study investigators concerning continuation, modification or termination of a study.

### *a) Study assessment*

In order to achieve these goals, a DSMB will typically:

- Review major modifications to the study protocol before their implementation.
- Review safety data, ordinarily in the form of summary statistics, although a DSMB may decide to review individual adverse event reports.

- Review subject accrual and timeliness of study completion.
- Evaluate the quality of study conduct including compliance with the protocol or treatment, timeliness, retention and quality of the data collected.
- Assess participant risk versus benefit based on interim analyses.
- Evaluate interim analysis results in light of protocol-specified early stopping rules.
- Consider whether any modifications in the protocol are warranted, including possibly terminating the study early.
- Be available to the investigator for consultation concerning any adverse study events.
- Consider 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.

### *b) Stopping a study*

Early stopping may be warranted if there is strong evidence of either of the following:

- A treatment benefit such that it is considered unethical not to make the treatment available to all patients.
- A lack of a treatment difference with a low likelihood of reversing this finding with further accrual and/or follow-up.

Ordinarily, the protocol will have pre-specified stopping rules giving guidelines for reaching these decisions. Other reasons for early stopping include:

- Unintended harm due to study participation.
- Inability to answer the study questions (e.g., because of low accrual, high rate of unanticipated problems, poor study conduct, high dropout rate, etc.).
- Evidence external to the study rendering it unethical to continue the study.

### *c) Reporting findings*

After each meeting, the DSMB should make a written statement within four weeks of meeting regarding the quality of the study and safety of participants and a brief recommendation either to continue the study without changes or to modify the study in specified ways with appropriate justification. Suggested modifications may include:

- Addressing safety concerns.
- Suspension or early termination due to inadequate performance or rate of enrollment, or according to pre-established statistical guidelines.

- Optional approaches to consider, such as adding study centers or extending recruitment due to unsatisfactory or suspicious performance.

## C. DSMB Structure

### 1. Timing and Frequency of Meetings

DSMB meetings will take place at least annually. The board may meet more often (quarterly, semiannually or annually) if the risk to subjects is high, the population is vulnerable, there is a large volume of data to review, and/or after a predetermined number of subjects have been accrued in the study. The chairman may also call ad hoc meetings depending on safety or efficacy concerns. Meetings may be conducted by teleconference at the request of board members. Members may meet in person or by email or teleconference.

### 2. Meeting Agenda Template

a) The investigator will provide the board with the information that was determined at the pre-enrollment meeting.
b) As per the Data and Safety Monitoring Plan, the board will:
   (1) Determine adherence to treatment plan
   (2) Review interim analysis, if applicable, and determine specific data to be analyzed
   (3) Evaluate end point/stop point rules
   (4) Review protocol violations and deviations to assess adequacy of study
   (5) Ensure documentation of informed consent
   (6) Enrollment:
      (a) Followed eligibility criteria
      (b) Enrollment numbers
      (c) Visit compliance
      (d) Screening failure information
   (7) Review IND/IDE information
   (8) Discuss investigator or key personnel changes
   (9) Review completeness and quality of data collection forms
   (10) Evaluate the aggregate analysis of adverse events/serious adverse events
   (11) Review confidentiality
   (12) Additional assessments as mandated by committee e.g. review vital signs, clinical tests, etc.

### 3. Meeting Outcome

The major outcomes following data review include:

a) Continuing the trial unchanged
b) Modify the protocols and/or consent form (It may be unethical to continue giving a placebo after a new treatment has been proven to be effective or to continue a new treatment when there is no chance the trial will be positive.)
c) Terminate the trial

### 4. Minutes

Minutes from the meeting will be maintained. Following the board meeting, a report should be provided to the investigator, the IRB and the study sponsor documenting major points of discussions and recommendations of the board.