

Data and Safety Monitoring Plans



KUMC Office of Compliance

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Chair, Data and Safety Monitoring Executive Committee

Objectives

- ❑ Review requirements for data and safety monitoring
- ❑ Review components of a data and safety monitoring plan
- ❑ Present options for data and safety monitoring
- ❑ Provide overview of data and safety monitoring via KUMC's DSM-EC

What is a DSMP?

- Investigator's plan to ensure:
 - Safety of clinical research subjects
 - Validity and integrity of research data
 - Appropriate termination of a study
 - significant benefits identified so should be provided to all
 - significant risks have occurred, outweighing the benefits
 - study cannot be concluded successfully

When is a DSMP required?

- NIH policy requires a general description of a DSMP for clinical investigations—biomedical and behavioral intervention studies.
- KUMC HSC requires a DSMP for all studies with greater than minimal risk requiring a full HSC review.

Plan components required by HSC

- Who will review the study
 - e.g., Investigator, study team, independent safety committee
- Type of data and events that will be monitored
- Frequency of review
- Interim analyses
- Triggers or stopping rules

http://www2.kumc.edu/researchcompliance/forms/HSC_Full_Committee_Application.doc

HSC considerations

- ❑ Does the plan match the risk level?
- ❑ Does investigator need additional resources to monitor the study adequately?

COI considerations

- ❑ Is there significant conflict of interest?

If additional levels of monitoring are needed, the protocol is Referred to the Data and Safety Monitoring Executive Committee

KUMC DSM-Executive Committee

- 7-member committee
 - KUMC faculty, professional community member, statistician, patient advocate
- Organize and provide oversight for protocols referred to us
 - HSC, COI, AVC-Compliance, Investigator referrals

DSM-EC 2-component oversight

- Protocol-specific monitoring body
 - Expert(s) in the area of investigation of a specific protocol
 - Most competent to review data, adverse events
 - They review and report to the DSM-EC
- DSM-EC oversees all monitored protocols
 - Receive reports from protocol-specific monitoring bodies
 - Ultimately responsible for oversight decisions about protocols

First step in DSM-EC monitoring

- DSM Plan
 - More information required than on HSC form
 - Plan must address risk level of study as well as reason for DSM-EC referral
- DSM-EC works with investigator to develop an adequate plan
 - Plan details vary on a case-by-case basis

http://www2.kumc.edu/researchcompliance/forms/DSMB_Creating_a_Data_and_Safety_Monitoring_Plan.Template.doc

DSM Review Process

1. DSM-EC works with investigator to develop a DSM Plan (DSMP)
2. Protocol-specific monitoring body is formed

Protocol-specific monitoring body

- Appropriate body decided on a case-by-case basis

- Possible options (singly or in combination)
 - Safety monitor
 - Protocol compliance monitor
 - Clinical study oversight committee
 - Data and safety monitoring board

Options based on a model used by NIH's Institute of Dental and Craniofacial Research

<http://www.nidcr.nih.gov/GrantsAndFunding/PoliciesandGuidance/ClinicalResearch/DataandSafetyMonitoring.htm>

Independent Safety Monitor (ISM)

- a protocol-specific expert whose primary responsibility is to provide independent safety monitoring in a timely fashion. This is accomplished by review of adverse events, immediately after they occur or are reported, with follow-up through resolution. The ISM evaluates individual and cumulative participant data when making recommendations regarding the safe continuation of the study.

Protocol compliance monitoring

- The primary source documents are checked to ensure that subjects were not treated on clinical trial prior to final HSC approval, informed consent was properly obtained and executed, and pre-therapy requirements, eligibility criteria, treatment delivery, and adverse event reporting are in accordance with the approved protocol.
- Data management systems are reviewed for adequate protection of data integrity and good clinical practice.

Clinical Study Oversight Committee

- The Clinical Study Oversight Committee (CSOC) is an independent group of experts whose responsibilities are to (1) monitor human subject safety, (2) review study conduct and progress, and (3) make recommendations to the DSM-EC concerning the continuation, modification, or termination of the study. The CSOC considers study-specific data as well as relevant background information about the population under study, study procedures and progress of the study.

Data and Safety Monitoring Board

- The DSMB is an independent group of experts that advises the KUMC DSM-EC and the study investigators. The primary responsibilities of the DSMB are to (1) periodically review and evaluate the accumulated study data for participant safety, study conduct and progress, and, when appropriate, efficacy, and (2) make recommendations to DSM-EC concerning the continuation, modification, or termination of the trial. The DSMB considers study-specific data as well as relevant background knowledge about the disease, test agent, or patient population under study.

Once plan is accepted...

- Proposed PSMB experts will be contacted by Compliance Office staff
 - To confirm willingness to participate
 - To obtain confidentiality agreements and conflict of interest disclosures
- A letter of agreement is sent to the PI confirming acceptance of DSMP, and outlining reporting requirements and frequency of reviews

PSMB on-going reviews

- PSMB meets regularly to review
 - Trial progress
 - Adverse event data
 - Any other relevant information
- PSMB makes a recommendation to the DSM-EC regarding continuation of the study

DSM-EC ongoing reviews

- ❑ DSM-EC meets regularly to consider PSMB reports
- ❑ DSM-EC writes a 'report of on-going review' to the investigator, describing the outcome of their deliberations, asking for additional information if necessary
- ❑ DSM-EC report is cc'ed to referring body (e.g., HSC, COIC)
- ❑ Recommendation possibilities: continue, modify, suspend, terminate
- ❑ Monitoring continues
 - until study is complete or
 - DSM-EC feels there is no longer a need for additional monitoring