

# *Data and Safety Monitoring at KUMC*

Understanding and navigating  
the DSM process

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## DSM Mission

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- Develop and enact procedures to monitor safety of participants and integrity of data collected in the research protocols that it oversees

# Why now for additional monitoring ?

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- **Heightened awareness about drug safety and human protection in clinical trials (i.e., Vioxx)**
- **Spotlight on FDA to be a more effective watchdog for patient safety**
- **Investor “intrusion” into clinical trials**
- **Need for risk management approach to protect against litigation**
- **Overemphasis on the monitoring ability of some groups (e.g., IRB), and under-emphasis on DMCs and Sponsors**

## When is DSM needed?

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- When investigator or the institution has a conflict of interest, added monitoring becomes part of the management plan for dealing with the conflict
- When the study is high risk – e.g., prior data suggest high potential for toxicity
- Trial is designed to provide definitive information
- Mortality is a major endpoint, such that inferiority of one study arm has safety and/or effectiveness implications
- It is ethically important to stop the trial early if the primary questions definitely answered

# Who does data and safety monitoring at KUMC?

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- **Compliance committee structure**
  - **Data and Safety Monitoring Executive Committee (DSM-EC)**
    - oversees all studies receiving this level of monitoring, and
  - **Data and Safety Monitoring Boards (DSMBs)**
    - protocol-specific

## How does the DSM-EC decide which protocols to monitor?

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- Protocols are referred to the DSM-EC for monitoring by
  - The Human Subjects Committee
  - The Conflict of Interest Committee
  - The AVC-Compliance
  - Individual investigators

## Why 2 committees: DSM-EC and DSMB ?

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- **DSMB is made up of experts 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 DSMBs
  - Ultimately responsible for oversight decisions about protocols

# DSM Review Process

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1. DSM-EC works with investigator to develop a DSM Plan (DSMP)
2. Protocol-specific DSMB is formed
  - At least two experts in relevant domain
  - A statistician
3. DSMB reviews outcome data and adverse events submitted by the investigator, submits their review to DSM-EC
4. DSM-EC makes recommendation to HSC and the referring body regarding continuation of the protocol

# The DSM Plan: required components

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- **THE RESEARCHER MUST:**
  - Nominate of at least 2 experts to serve on DSMB\*\*
  - Specify how adverse events will be documented and attributed
  - Specify stopping rules
  - Identify primary outcome variables, and indicate whether any interim analyses are planned
  - Identify a statistician who can provide interim analyses\*\*
  - Propose a frequency of monitoring

\*\*[costs of honoraria for experts and statistician are responsibility of the principal investigator]

## DSM-EC may specify additional DSMP components:

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- KUMC's RI Clinical Research Administration will conduct periodic quality indicator visits to assure data are being collected and recorded according to protocol
- DSM-EC or DSMB may identify additional variables they wish to review

## Initial review of the DSMP

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- Once a DSMP is submitted to the Office of Compliance
  - Reviewed by staff support for DSM activities, DSM-EC Chair, DSM-EC Vice-chair, and one regular DSM-EC member
  - DSM-EC chair writes a “report of initial review” with acceptance or provisos
  - Investigator can revise and resubmit

## Once plan is accepted...

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- Proposed DSMB experts will be contacted
  - To confirm willingness to participate
  - To obtain confidentiality agreement 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

# Investigator's reporting responsibilities

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- Investigator must report all adverse events
  - Within required time frame
  - On HSC or DSM forms
- At specified intervals, investigator must report
  - Current enrollment data
  - Adverse event summary data
  - Any other data requested by DSMB or DSM-EC (e.g., outcome data)

## DSMB on-going reviews

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

## DSM-EC ongoing reviews

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- DSM-EC meets regularly to consider DSMB 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: continuation, modification, termination
- Monitoring continues
  - until study is complete or
  - DSM-EC feels there is no longer a need for additional monitoring

## Other notes

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- Forms, Standard Operating Procedure document are available (or soon will be) on the Office of Compliance web site
- Office of Compliance staff and DSM-EC Chair are willing sources of assistance in developing DSMPs, understanding the DSM process, and answering questions