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TWIST

Developing an Effective Data and Safety Monitoring Plan and Utilizing the WCM Data and Safety Monitoring Board (DSMB)

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DSMP

Data and Safety Monitoring Plan

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Utilizing the WCM DSMB

Data and Safety Monitoring Board

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DSMP

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Outline

- Purpose
- When are they needed?
- What do they contain?



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Purpose

Objective

Monitoring of:

- safety of study participants
- quality of research data
- appropriate conduct of the clinical research

Distinct from:

- IRB oversight
- scientific review



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**When is a DSMP
necessary?**

In general...

All studies that involve human subjects

Level of monitoring depends on study's

- potential risk
- size
- Complexity

Monitoring level may be decided by

- study sponsor
- IRB
- institution

Type of plans

Embedded in the protocol

- minimal risk
- monitoring done by study PI/team

Separate DSMP

- greater than minimal risk
- monitoring done by Data Safety and Monitoring Board (DSMB)

Who should write/review the plan

Study team

- PI
- study statistician
- other relevant team members

Plan written for DSMB use

- needs to be approved by DSMB
- provides guidance to study team/DSMB
- submitted to the IRB

WCM Institutional policy/guideline

Large, multi-site, randomized, blinded, and Phase III trials

Phase I and II studies for which risk to the subjects appears unusually high

Phase I and II studies for which the principal investigator is the IND/IDE sponsor or manufacturer and independent monitoring is required to maintain the integrity of the trial

Gene transfer studies

Studies with vulnerable populations or risky interventions/procedures or any other factors that might indicate high morbidity/mortality end-points

Studies with high risk of toxicity or other major medical risks

WCM Institutional policy/guideline

Always “write” a DSMP for human subjects

Determine whether the WCM DSMB is required

<http://researchintegrity.weill.cornell.edu/DSMB.html>



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Preparing a DSMP

Participant safety

DSMP Component	Examples of Monitoring Activities
specific subject safety parameters	vital signs, weight, safety blood tests, cardiac status, anxiety, depression scores, adverse events, etc.
frequency of subject safety observations	weekly telephone FU, monthly appointments, observations of participant while in clinical setting, each treatment cycle, etc.
party responsible for safety monitoring	PI, study coordinator, safety monitor, independent monitor, DSMB, etc.
subject stopping rules	exclusion criteria, including adverse response to study procedure; pregnancy; specific AE grade; cardiac irregularity; non-compliance; etc.
study stopping rules	unanticipated problems involving risk to subjects or others (UPIRTSO), unexplained adverse outcomes, life threatening adverse events,
reporting mechanisms (i.e. deviations, adverse events, UPIRTSOs)	plans for reporting to IRB, FDA, sponsor, participating sites, DSMB, etc.

Data integrity

DSMP Component	Examples of Monitoring Activities
specific data items to be reviewed	participant eligibility, data is accurate and complete, calculations are standardized and performed properly
frequency of monitoring data: points in time, or after specific number of patients	First 3 subjects and every 20 th subject, monthly, quarterly, annually, etc.
individual responsible for data monitoring	PI, study coordinator, safety monitor, independent monitor, data manager, statistician, etc.

Participation privacy

DSMP Component	Examples of Monitoring Activities
Under what conditions (time and place) will subject be consented, interviewed, or telephoned?	observations of consenting process, interviewing, or clinical visit performed quarterly on 3 subjects request input from 5 subjects related to their experiences regarding privacy expectations etc.

Data confidentiality

DSMP Component	Examples of Monitoring Activities
What are the conditions that will protect the confidentiality of the data?	Check for locked file cabinets, secure electronic records, secure location with protected health information is stored, etc.

Product accountability

DSMP Component	Examples of Monitoring Activities
Who is responsible for obtaining, storing, preparing, administering, or disposing of the study drug or study device? Who is responsible for overseeing product accountability?	research pharmacy, PI, central pharmacy, research laboratory, nursing, etc.

Study documentation

DSMP Component	Examples of Monitoring Activities
study file management	study file management guidelines and checklists for monitoring (sample of study files annually, etc.)

Study coordination

DSMP Component	Examples of Monitoring Activities
roles and responsibilities are clarified, education needs are addressed, planned meetings or communications with documented meeting notes/minutes	periodic debriefing to determine if expectations are clear and if educational needs exist scheduled meetings are on the calendar, and meeting outcomes are noted and available to staff etc.

DSMP specifics

GOAL: provide a framework by which to reduce harm or injury to participants, in order to further promote a level of conscientious conduct.

Minimum required

Assessment of level of risk

A plan for safety review

- anticipated AEs
- AE grading and attribution
- unanticipated and/or serious AE reporting
- periodic reporting of AEs

Ensure compliance with principles of informed consent

Assessment of protocol compliance, including violations/deviations

A plan for compliance with privacy related regulations (e.g., HIPAA)

Additional considerations

Prospective stopping rules

- unacceptable risk (toxicity stopping rule)
- strong evidence of futility/efficacy (interim analyses)

Plan for on-going review

- information to be provided
- review frequency
- rationale for info provided and frequency

Study enrollment

- observed accrual rate compared to expected accrual rate
- eligibility rate

Safety review questions

- reasons for drop-outs
- AEs too frequent or severe?
- should the protocol be modified?



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Utilizing the WCM Data and Safety Monitoring Board

Nida Cassim, MPH

Assistant Director, Quality Assurance Unit

January 20, 2016

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General Information

1 DSMB, 2 Co-Chairs:

- General Clinical Trials: David Behrman, D.M.D
- Cancer Clinical Trials: Tomer M. Mark, M.D., M.Sc.

Membership:

- 12 Investigators across a variety of specialties (i.e. neurology, oncology, infectious disease, etc.)
- 3 Statisticians
- Institutional Official
- Director of Human Research Protections Program
- Director of Clinical Trials, Joint Clinical Trials Office
- 2 DSMB Coordinators
- Assistant Director of Quality Assurance Unit

Meeting Schedule:

- Regular monthly meetings, scheduled as posted on the DSMB website

Meeting Format:

- Open/closed sessions
- Review of new protocols, existing protocols and preliminary DSMP review

DSMB Webpage

<http://researchintegrity.weill.cornell.edu/DSMB.html>

THE OFFICE OF
**RESEARCH
INTEGRITY**

- ORI Staff
- Institutional Review Board (IRB) [MORE](#)
- WCMC-Qatar IRB
- Data Safety Monitoring Board (WCM DSMB)**
- Institutional Biosafety Committee (IBC) [MORE](#)
- Institutional Animal Care and Use Committee (IACUC)
- HIPAA In Research [MORE](#)
- Conflicts Management Office (CMO) [MORE](#)
- Educational Programs
- Human Embryonic Stem Cell Research
- Research Archive Storage
- Clinical Study Evaluation Committee (CSEC)

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[Office of Research Integrity > DSMB](#)

Weill Cornell Medicine Data Safety Monitoring Board

The Weill Cornell Medicine (WCM) DSMB is available to aid WCM principal investigators and the Institutional Review Board (IRB) in providing an independent means of data and safety monitoring for clinical trials that involve significant risk to research subjects. The WCM DSMB reviews interim data on a schedule commensurate with the needs of a given protocol to evaluate research subject safety, rates of accrual, and efficacy of experimental intervention. After each evaluation, the Board provides the principal investigator with recommendations for protocol modification, continuation or termination.

Studies for which the WCM DSMB is appropriate as an independent method of monitoring include:

- Large, multi-site, randomized, blinded, and Phase III trials
- Phase I and II studies for which risk to the subjects appears unusually high
- Phase I and II studies for which the principal investigator is the IND/IDE sponsor or manufacturer and independent monitoring is required to maintain the integrity of the trial
- Gene transfer studies
- Studies with vulnerable populations or risky interventions/procedures or any other factors that might indicate high morbidity/mortality end-points
- Studies with high risk of toxicity or other major medical risks

Downloads

WCM DSMB Periodic Report Form	Microsoft Word
WCM DSMB Roster	Adobe PDF
A Guide to Understanding Data Safety Monitoring Procedures	Adobe PDF



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Initial Submission

Initial Submission: *The Basics*

CSEC Review

- If you know that your study will be utilizing the WCM DSMB or if you are unsure whether your study needs a DSMB, contact the Quality Assurance Unit (JCTOQAU@med.cornell.edu) for assistance.
- Investigator-Initiated Trial Template:
<http://jcto.weill.cornell.edu/investigators/study-activation-and-conduct/researchers-toolbox>

When to Submit

- Prior to IRB review or concurrently **AND**
- At least 3 weeks prior to DSMB meeting date

What to Submit

- Protocol (with Data and Safety Monitoring Plan)
- Informed Consent Form
- Investigators Brochure (if available)
- Any IRB correspondence (if available)

How to Submit

- Email: DSMB@med.cornell.edu

Initial Submission: *Open Session*



PI's are invited and *highly* encouraged to attend the DSMB meeting to present their protocol and address any questions during the open session.

Initial Submission: *Closed Session*

DSMB Reviewer

- Assess overall appropriateness of DSMP, including:
 - Frequency of periodic reports
 - Review of any safety concerns
 - Interim analysis
 - Criteria for study discontinuation (stopping rules)

Outcomes

- DSMB votes to:
 - Approve the DSMP
 - OR
 - Modify the DSMP
 - OR
 - Request for additional information or clarification



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Periodic Reviews

Periodic Reviews: *The Basics*

When to Submit

- Periodic Reports are due based on the DSMB approved review schedule (i.e. annually, semiannually, quarterly, etc.)
- Reminders are sent 1 month prior to the DSMB meeting date
- Submissions are due 2 weeks prior to DSMB meeting date
- If your protocol requires a certain threshold be met prior to a review, it is the **PI's responsibility** to ensure the report is submitted on time

What to Submit

- Periodic Report Form
 - **AE and IND Safety Reporting Cumulative Table for Subjects on Study**
 - **AE Narratives**
 - **Enrollment Tables (by Arm and by Site)**
- Interim data as planned in the DSMP
- Protocol (with DSMP)
- Informed Consent Form
- Investigators Brochure (if available)
- Any relevant IRB correspondence (if available)

How to Submit

- Email: DSMB@med.cornell.edu

Periodic Reviews: *Open/Closed Session*

Open Session

- At the request of the DSMB, the PI or designee may be invited to attend the open session and present any relevant data/outcomes

Closed Session

- General conduct of the trial
- Accrual
- Review outcomes/results, including SAEs and toxicities

Outcomes

- DSMB votes to:
 - Continue without modifications

OR

 - Modify the DSMP
- OR**
- Request for additional information or clarification



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Immediate Reports and Amendments

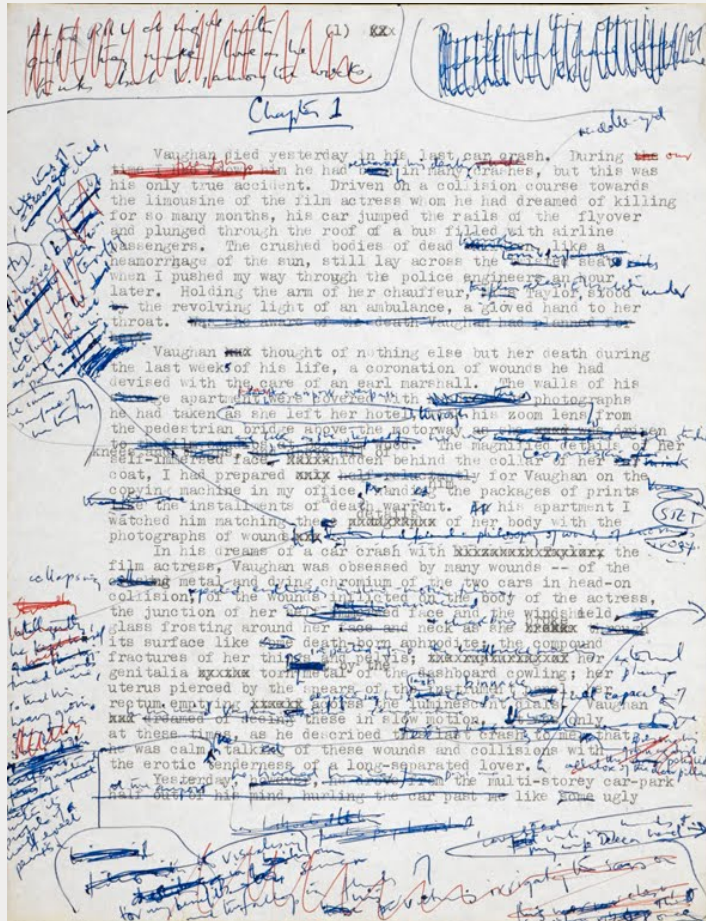
Immediate Reports



Institutional Policy

- If you are using the WCM DSMB you must also CC your Immediate Report to DSMB@med.cornell.edu
- The WCM DSMB will review the immediate report via email and provide an acknowledgment letter or request for additional information

Amendments



- Notify the WCM DSMB as soon as you are aware of any potential amendments to your protocol
- The WCM DSMB can provide guidance and make recommendations for any changes prior to IRB review



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Common Mistakes

Common Mistakes

- Protocol and eIRB application do not match
- Interim analysis is not submitted according to DSMP
- Protocol is submitted before/after threshold is met
- Enrollment tables do not include accrual from all sites participating in the study
- PIs signature is missing on AE/IND Cumulative Table and/or Periodic Report Form
- Missing attachments



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Questions?

Please direct any questions to DSMB@med.cornell.edu for a prompt response!