Data Safety Monitoring and the IRB

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Commonly Used Terms:

- **DMP** – Data monitoring plan
  - describes how PD will oversee research participant’s safety and welfare and how UPs...and AEs will be characterized and reported

- **Monitoring Entity**
  - an identified individual or group assigned to conduct interim monitoring of...data from research activities
  - Sometimes called a data safety monitoring board or committee
Where Do We Get Requirements for DMP?

45 CFR 46.111 (a)(6)
When appropriate, a research study must include a plan for monitoring data to ensure safety of the subjects

Belmont Report:
Principle of Beneficence - Not just risk/benefit ratio, but also the minimization of risk

The IRB:
- ensures adequate monitoring plan is taking place
- reviews reports from the monitoring entity
- does NOT perform data monitoring
Data Monitoring Plan – When Is One Required?

HRPP 9.2
“*The IRB requires a Data Monitoring Plan for:*”

All studies considered more than low risk, including *but not limited to:*

- Phase III clinical interventions
- New, unfamiliar interventions
- Multi-site research where STANFORD is the coordinating site
- Where there is an NIH or FDA requirement for a plan
- When requested by the IRB
- Blinded studies, multiple sites, vulnerable research participants, or high-risk interventions (VA)
Data and safety monitoring is required for all types of clinical trials, including physiologic, toxicity, and dose-finding studies. The method and degree of monitoring needed is related to the degree of risk involved.
Who Does the Monitoring?

Criteria for assessing appropriateness depends on:

- Applicable regulations/policies
  - e.g., NIH requires independent data safety monitoring board for all Phase III clinical trials
- Complexity of the study
- Level of risk
- Size of study populations
- Number of sites
- Potential and method for reporting and tracking AEs/UPs
Examples of Appropriate Monitoring

Researcher monitoring

- Simple studies
e.g., blood draws/database survey

DSMBs/DSMCs

- Managed by the researcher or sponsor
e.g., Phase I or II clinical trials

Independent DSMBs

- Required for Phase III NIH trials
e.g., high risk/large multi-site studies
Data Monitoring Plans

*Plans can include information such as:

- type of data or events to be monitored
- responsibilities and roles for gathering, evaluating and monitoring data
- information about the monitoring entity
- time frame for reporting AEs/UPs to the monitoring entity

*HRPP Guidance, GUI-P20
Data Monitoring Plans, cont.

- frequency of data and event assessment
- definitions of specific triggers/stopping rules that serve as criteria for action
- as appropriate, procedures for communicating to the IRB, sponsor, and appropriate entities of the review outcomes

*HRPP Guidance, GUI-P20*
Data Monitoring Reports - Continuing Review

- Reports come back to the IRB during Continuing Review
- For staff, they ensure:
  - Reports attached?
    - As required by monitoring plan
- For IRB reviewer, in eProtocol Section 2 (Continuing Review) asks the investigator for:
  - Necessity of a report (attached in section 16)
  - Study problems/complications
  - Provides information so reviewer can make a decision regarding study continuation
Examples: DSMB or DSMC may stop a study because:

- collected data **may not support** original hypothesis
- data may reveal **new risks** not originally considered
- analysis may show that the study **may not reach** it’s defined endpoints/may reach it **earlier**
- data may suggest the **need for a change** in the protocol, procedure and/or consent form and should not continue until subjects are notified
Quiz

Which statements are accurate? Select all that apply

A. Monitoring should be commensurate with risks
B. Should be commensurate with size/complexity of the study
C. Should be performed at least 2X/year
D. All research requires monitoring by an independent DSMB

PRIMR “Ethical Oversight of Human Subject Research”
References

HRPP Chapter 9.2 - Data Monitoring Plan
GUI-P2 - FDA Guidance for Clinical Trial Sponsors
GUI-P3 - Data Monitoring Plans and Data Monitoring Committees – NIH and NCI Policies
GUI-P20 “Data Monitoring Plans – Guidance and Instructions to Investigators” on Data and Safety Monitoring
NIH Policy for Data and Safety Monitoring
VA Handbook