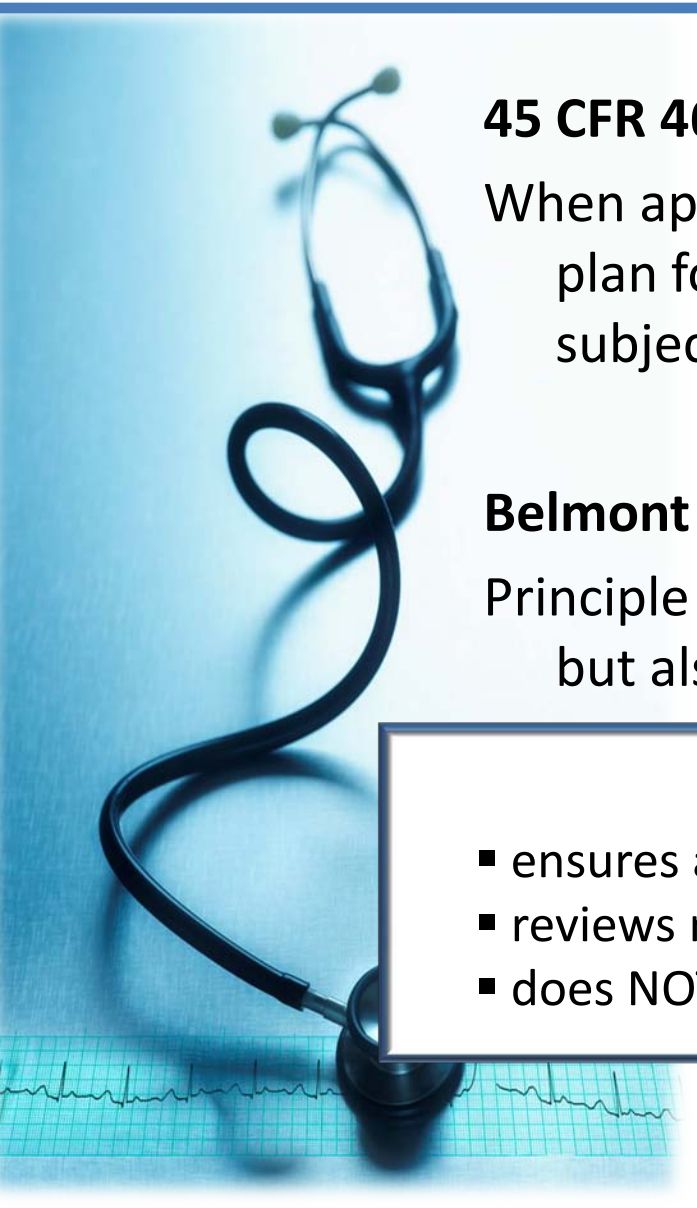
Data Safety Monitoring and the IRB

Bertha deLanda
IRB Training Specialist
Research Compliance Office
February 2011

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:

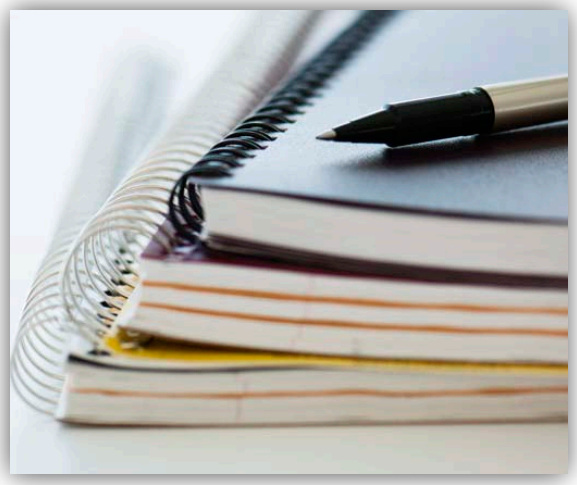
- ensures adequate monitoring plan is taking place
- reviews reports from the monitoring entity
- does NOT perform data monitoring

Data Monitoring Plan – When Is One Required?

HRPP 9.2

"The IRB requires a Data Monitoring Plan for:"

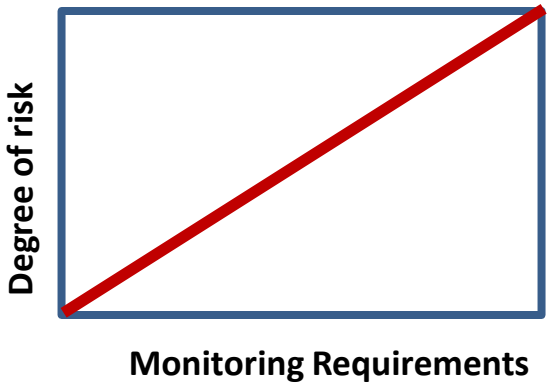
All studies considered more than low risk, including ***but not limited to***:



- 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)**

NIH Principles of Monitoring Data and Safety

- 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.

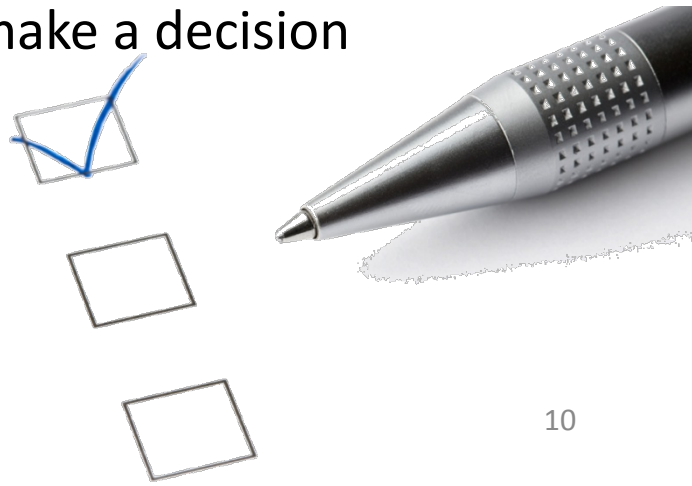
- frequency of data and event assessment
- definitions of specific triggers/stopping rules that serve as criteria for action
- as appropriate, procedures for communicating to the IRB, sponsor, and appropriate entities of the review outcomes

**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