



**University of Michigan  
Medical School**

# **IRB Regulations 203**

**Writing a Study Specific Adverse Event (AE)  
Reporting Plan and  
Data & Safety Monitoring Plan (DSMP)**

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# Objectives

- To provide information about federal regulations and NIH expectations regarding plans for monitoring data and safety of human subjects
- To provide information on construction of data and safety monitoring plan appropriate to minimal to moderate risk studies
- To provide information on how to develop an adverse event reporting plan

# Definitions/Concepts

## Data and Safety Monitoring Plan (DSMP)

- Plan to reduce risks & minimize harms
- Planned monitoring of adverse events
- Measures to assure the integrity of all study data
- It may be part of a protocol or a stand-alone document

# Definitions/Concepts

## Study Specific AE Reporting Plan

- Which AEs will be reported
- Timeframes for reporting
- To whom AEs will be reported
- It may be part of a DSMP or a stand-alone document.

# DSMP

## Why go to the trouble?

- Protection of subjects
- Data integrity = sound research
- Improves NIH review scores
- Speeds IRB review

# Study Specific AE Reporting Plan

## Why go to the trouble?

- Minimize reporting burden
- Less reporting saves money
- Demonstrates understanding of IRB policies
- IRB appreciation



*Thank You*

# DSMP

## Why it speeds IRB review

**21 CFR §56.111 and 45CFR §46.111:  
Criteria for IRB approval of research.**

In order to approve research the IRB shall determine:

- risks to subjects are minimized
- the research plan makes adequate provision for monitoring data collected to ensure the safety of subjects
- there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

# FDA Concerns

Inadequate data monitoring:

- results in a 'critical destruction' of study outcomes
- results in poor quality data
- results in random errors (sloppiness)
- biases the data
- obscures differences between treatments
- undermines determinations of effectiveness.

# National Institutes of Health Concerns

NIH and Investigators must:

- provide appropriate oversight
- ensure the safety of participants
- ensure validity and integrity of the data

# NIH continued

- Monitoring should be commensurate with risks.
- Risk associated with participation in research must be minimized to the extent practical.
- Monitoring should be commensurate with size and complexity of the study.

## NIH continued

- Oversight can range from monitoring by the principal investigator to the establishment of an independent data and safety monitoring board for a large clinical trials, high risk studies or studies involving vulnerable populations.

# Elements of a DSMP

- Explain who will monitor the trial and/or receive AE reports.
  - PI
  - Multiple members of the study team
  - Sponsor monitor or CRO
  - Data and Safety Monitoring Board (DSMB)
- Describe how often and how data is examined in the course of trial conduct
- What do the monitors look for?

# Elements of a DSMP

- Estimated risk level for each cohort of the study
- How risks will be minimized
  - Consider physical, emotional, social, and financial risks
- How subjects' privacy will be protected
- How data confidentiality will be achieved
- Stopping rules for terminating the study
- Qualifications of the PI and study team
- Required study team education

# Elements of a DSMP

- How conflicts of interest will be handled
  - Inherent bias of a principal investigator (or a direct report of the PI)
  - Physicians recruiting their own patients
  - Financial conflicts of interest

# Elements of a DSMP

- Quality-control procedures to assure data accuracy and completeness
  - Validate eligibility of patients accrued to the study
  - Check for the presence of a signed informed consent
  - Determine compliance with protocol.
  - Determine whether AEs are being reported to oversight entities as required
  - Compare veracity of data in the research record with the primary source documents

# Elements of a DSMP

- Plans for reporting of adverse events
  - In grant applications, describe the processes and oversight UM has in place
  - Specify standard reporting or study specific plan
    - IND and IDE studies, moderately high risk to high risk studies, use the UM Standard AE Timetable
    - Sponsored multi-site trials, use the sponsor's AE reporting plan IF AND ONLY IF it includes the appropriate level of detail

# Elements of a Study Specific AE Reporting Plan

- Describe type of AEs to be reported
  - Begin with the UM Standard Timetable as a guide. What does it require that would NOT provide protection for the subjects?
- AEs may be described:
  - in a very specific list
  - in a general way.

# Elements of a Study Specific AE Reporting Plan

- Examples of AEs described in a “general way” for minimal/moderate risk studies not under an IND or IDE:
  - Only those AEs with a *causal* relation to the research will be reported.
  - Only those AEs with a *causal* relation to the research or to the subjects’ disease progression will be reported. AEs attributable to other maladies common in this population will not be reported.

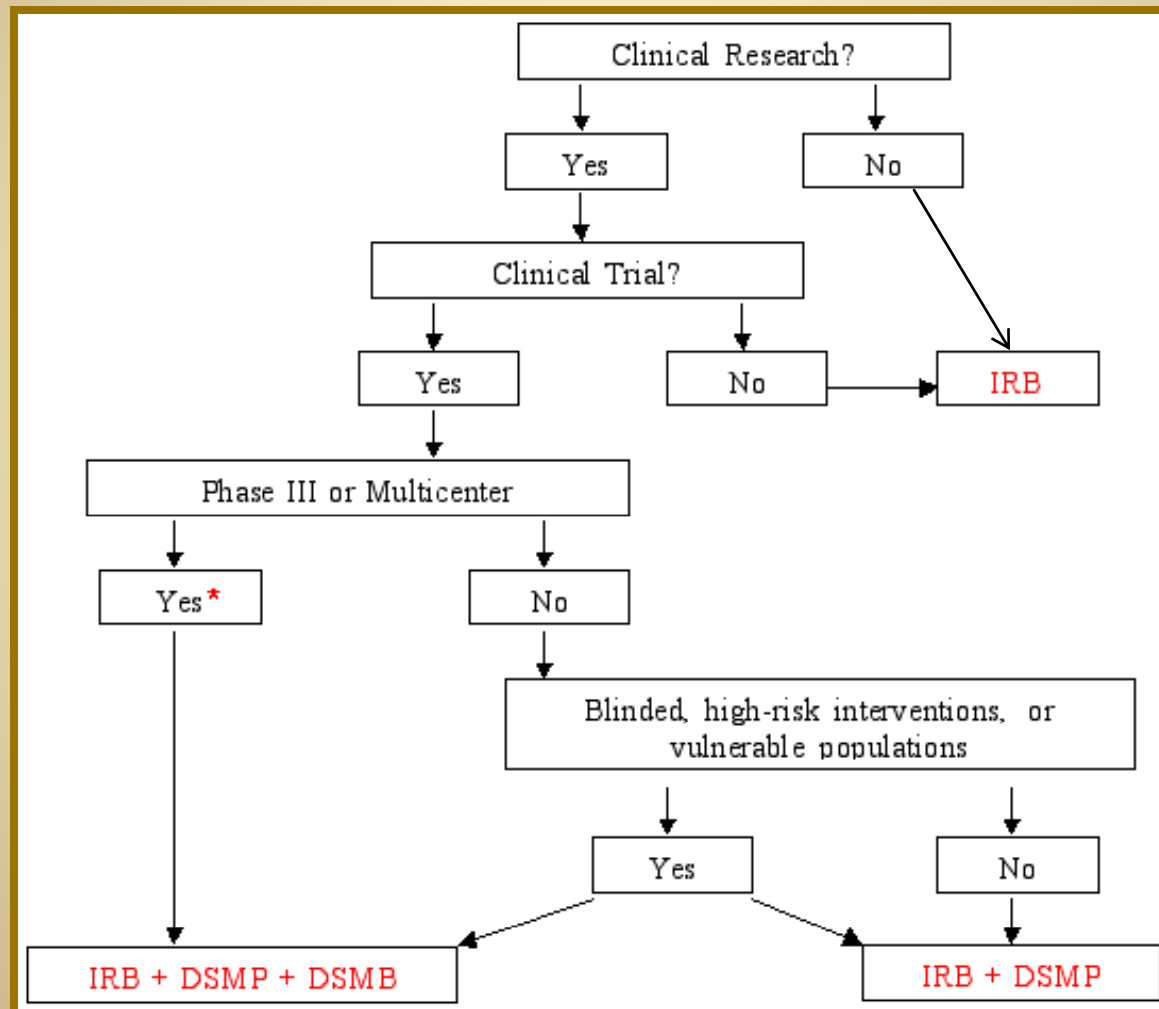
# Elements of a Study Specific AE Reporting Plan

- Examples of “common maladies”:
  - Death in a elderly population with a history of stroke and diabetes in a quality of life study
  - Drug overdose in a hepatitis study of drug abusers
  - Routine childhood diseases in a study of how school lunches affect obesity in 6 to 10 year olds.

# Elements of a Study Specific AE Reporting Plan

- When cohorts of a study vary significantly and/or the risks differ between cohorts, make a different plan for each cohort.
  - Provide rationale for having different plans if the justification will not be obvious to those not involved in the research
  - Use tables, headings, or other graphic elements that add to clarity of the plan

# Sample Decision Chart for Determining Oversight and DSMP



# Studies Not Greater than Minimal Risk and DSMPs



DSMP for a chart review? Is she crazy?



# Chart Review DSMP

## Foreseeable Risks & Likelihood

- Inappropriate invasion of privacy (rare)
- Data loss or breach of confidentiality (rare)
- If the nature of the disease or treatment is such that there are additional risks include these (e.g. additional risk of stigmatization if there was a confidentiality breach on an HIV related study)

# Chart Review DSMP *continued*

## Steps to Reduce and Monitor Risks

- Study team will be trained in privacy, confidentiality, and security and complete the PEERRS Human Subject Module and UMHS HIPAA training
- Computers and all storage devices will be password protected
- Data will not be stored outside of the locked laboratory OR Data transferred to PDAs, laptops, CDs, flash drives, etc. will be encrypted and password protected.

## Adverse event Reporting

[http://www.med.umich.edu/irbmed/ae\\_orio/#retro](http://www.med.umich.edu/irbmed/ae_orio/#retro).

# Handouts