IRBMED Seminar Series

Phase I Case Study

Institutional Evaluation and Regulatory Reporting

IRBMED Seminar Series

IRB Determinations

(from Mock IRB)

- Serious Adverse Event
- (Possible) Serious Noncompliance
- Unanticipated problem involving risks to subjects or others

Outcomes: Serious Adverse Event

A Serious Adverse Event (SAE) is defined by FDA and NCI as any adverse drug event (experience) occurring at any dose that in the opinion of either the investigator or sponsor results in any of the following outcomes:

1) Death

2) Life-threatening adverse drug experience

3) Inpatient hospitalization or prolongation of existing hospitalization (for > 24 hours)

4) Persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions

5) Congenital anomaly/birth defect

6) Important Medical Event (IME) that may not result in death, be life threatening, or require hospitalization may be considered a serious adverse drug experience when, based upon medical judgment, it may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition

Outcome: Serious Noncompliance

Serious Noncompliance: Noncompliance that materially increases risks or causes substantive harm to research participants or materially compromises the rights or welfare of participants, including consideration of the following:

- Harm to participants;
- Exposure of participants to a significant risk of substantive harm;
- Compromised privacy and confidentiality of participants;
- Willful or knowing misconduct on the part of the investigator;
- A violation of ethical principles; or
- Damage caused to the scientific integrity of the data collected.

Outcome: Unanticipated Problem

- Unanticipated Problems Involving Risks to Subjects or Others (UaP)

  - It is "unexpected" in either

    Nature

    Severity

    Frequency

  - It is "related" to the research; there is a reasonable possibility that the event may have been caused by the procedures involved in the research;

  - It suggests that the research places subjects or others at greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

Institutional Actions

- Address subject safety
- Conduct fact-finding
- Corrective action
- Reporting obligations

Components of the HRPP

- Convened Board (full IRB)
- UMOR *(U-M Office of Research)*
- *OoR (Medical School -Office of Research)*
- ORCR *(Office of Research Compliance Review)*
- Regulatory Affairs
- General Counsel
- Office of Clinical Safety
- Public Relations

- Critical response team developed with above representatives

Examination of the Incident

Critical / Time-sensitive

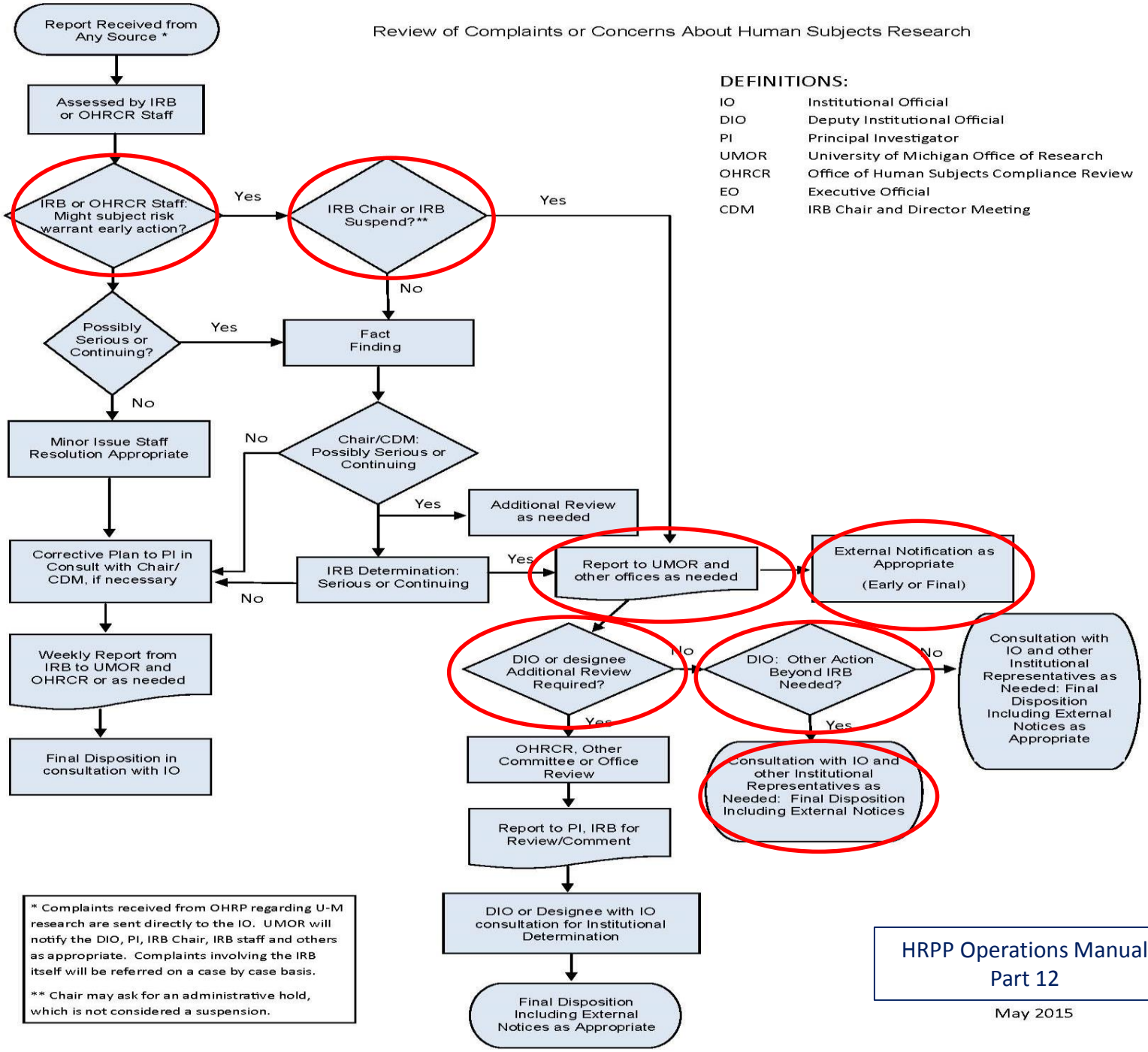
- Suspension of the research
- Assess existing circumstances
- Medical treatment of impacted individuals
- Determine other subjects at risk
- Early notifications to external agencies

Fact-finding related to the incident

- Critical response team
  - Contributing circumstances still exist
  - Begin more detailed assessments
- IRB
- University offices
- Ad hoc faculty committee
- Sponsor / CRO

Examination of the Circumstances

- How did the event unfold?
- Was the protocol followed?
  - Possibility of an error
  - Was there an intentional protocol deviation
- Did the protocol design address all subject safety issues?
- Did the protocol have appropriate safety checks built in?



HRPP Operations Manual
Part 12

May 2015

IRBMED Seminar Series

Elements of Evaluation

IRB

The IRB determinations of the event:

- Serious Adverse Event
- Unanticipated Problem
- Serious and/or continuing Non-Compliance

Suspension of the Study (others also have ability to suspend research)

Assure all institutional HRPP components are aware of circumstances

Elements of Evaluation

UMOR

Vice President for Research = Institutional Official for HRPP

- Responsible party under the FWA

Imposes any institutional sanctions or remediation requirements

Makes external reports

Receives internal reports as to progress of ongoing corrective actions

Elements of Evaluation

OoR

Works closely with UMOR and IRBMED to assure appropriate and timely response to the circumstances

May participate in assuring that ongoing corrective actions are met

Elements of Evaluation

ORCR – Office of Research Compliance Review

Conducts an independent audit of the research study

- Provide details of the event
- Interview individuals involved in the event

Provides ongoing monitoring of the study (if the suspension is lifted)

Audits/Monitors other studies under the oversight of the PI

Elements of Evaluation

Regulatory Affairs

Participates in the fact-finding and resolution of the incident

Close partner with UMOR and the IRBMED in evaluation, response, and any necessary ongoing oversight

Elements of Evaluation

Office of Clinical Safety

- Close partner with other offices to evaluate the *clinical* safety issues involved and indicated corrective actions

Elements of Evaluation

Public Relations

Provides accurate and timely information to the media and the general public

- External media sources
- U-M sources

Reporting Obligations

- Federalwide Assurance of Compliance (FWA)
  - Appropriate institutional officials
  - Head of any federal department or agency conducting or supporting the research
    - NIH
    - Department of Defense
    - Etc.
  - Applicable regulatory bodies
    - OHRP (Office for Human Research Protections)
    - FDA (for research subject to FDA oversight)

Regulatory Reporting

Written reports

- Detail of the incident
- Name of UM PI
- Any applicable federal funding
- Participant outcomes
- Root cause analysis
- Corrective actions
- Subject follow-up and notification as indicated

Agency response (Pat Ward will discuss further)

- Request additional information
- Site visit to U-M
- Institutional sanctions
- Individual (PI/study team) sanctions

Questions ?