Reportable Events

- UNANTICIPATED PROBLEMS (UPs)
- PROTOCOL DEVIATIONS
- PROTOCOL VIOLATIONS
- GENERAL NONCOMPLIANCE
- SERIOUS NONCOMPLIANCE
- CONTINUING NONCOMPLIANCE

Unanticipated Problems (UPs)

- *Unanticipated Problem (UP):* An unanticipated problem involving risk to participants or others is defined by meeting ALL 3 of the following criteria:
  - Was not anticipated or foreseen;
  - Involves risk or harm to participants or others; AND
  - Was probably or definitely related to, or caused by, the research activity in the judgment of the investigator
    - *NOTE: UPs are "unanticipated" and therefore are not generally identified in the consent document. Anticipated problems that occur at a greater severity or frequency than previously expected may qualify as UPs reportable to the IRB*

IRB Process for Review of UPs

- When reports are received, the ORSP Director, IRB Chair and/or designated reviewer of the protocol make an initial evaluation about whether it is a UP
- If the IRB Chair/reviewer determines that it is NOT a UP involving risk to participants or others, no further action is taken
- If report IS a UP, it must be referred for review to the next IRB panel meeting
  - NOTE: The Chairperson (and/or designated reviewer) may act independently in order to ensure the immediate safety of the research participants.

Convened IRB Determinations for UPs

- The Panel is to make the following determinations:
  - confirm that the designation of UP applies,
  - evaluate the adequacy of immediate actions taken by the investigator to protect the subject or others from further risk,
  - determine the status of actions taken by the Chair/designee,
  - determine whether other actions are indicated, including changes to the research and consent form
- For UPs that are accompanied by, or are the result of, a protocol deviation or violation, the IRB is also to determine whether the protocol deviation/violations describes Serious or Continuing Noncompliance.

Protocol Deviations and Violations

- *Protocol Deviation:* Any change to the IRB-approved protocol taken without prior IRB review to eliminate an apparent immediate hazard to a research participant(s)

- *Protocol Violation:* An accidental or unintentional change to the IRB approved protocol that harmed participants or others or that indicates participants or others may be at increased risk of harm.

  - NOTE: Protocol deviations and violations (that caused harm or increased risk) are considered Unanticipated Problems

Outcomes of IRB UP Review

- Possible actions after Reportable Event review:
  - Modification of the research protocol
  - Modification of the consent form
  - Additional information provided to past subjects
  - Notification to current subjects
  - Requirement to re-consent subjects
  - Monitoring of research
  - Monitoring of consent process
  - Suspension of research
  - Termination of research
  - Request emergency panel to discuss
  - Request more information
  - Referral to other organizational entities
  - No action (if appropriate)

Noncompliance (General)

- **Noncompliance:** failure on the part of the PI or any member of the research team to:
  - adhere to the terms of the VCU IRB approval and/or
  - abide by applicable laws, regulations, or VCU policies.
    - Some examples of noncompliance: Failure to obtain IRB approval prior to initiating research activities, continuing research after study expiration without obtaining continuing review approval, failure to adhere to the approved protocol

- General noncompliance may vary in severity based upon the overall risk potential of the noncompliance and its frequency. Noncompliance determined to be general in nature and not serious and/or continuing is not reportable to regulatory authorities or sponsors.

Serious Noncompliance

- **Serious Noncompliance:** failure to adhere to the terms of the VCU IRB approval and/or abide by applicable laws, regulation, or VCU policies when that failure increases risk to participants or adversely affects the rights and welfare of the participants.
  - Some examples of serious noncompliance include conducting a research protocol without oversight of a functional investigator, conducting a study without informed consent
  - NOTE: Serious noncompliance is a finding that is determined by the convened IRB Panel. The finding of serious noncompliance must be reported to regulatory authorities and the sponsor.

Continuing Noncompliance

- **Continuing Noncompliance:** repeated noncompliance by an individual investigator either on a single protocol or across multiple protocols, or a pattern of ongoing activities that indicate a lack of understanding of human subjects protection requirements that may affect research subjects or the validity of the research.
  - NOTE: Continuing noncompliance is a finding that is determined by the convened IRB Panel. The finding of continuing noncompliance must be reported to regulatory authorities and the sponsor.

IRB Process for Review of Noncompliance

- When reports are received, the ORSP Director (with the IRB Chair/designee as needed) evaluates the severity of the allegation or report
- The ORSP initiates fact-finding activities, which may include reviewing study documentation and corresponding with the PI
  - Possible outcomes of fact finding:
    - Dismissal of an unsubstantiated allegation;
  - Referral to other appropriate university processes (e.g., misconduct investigation);
  - No further action required (i.e., for minor violations);
  - Corrective actions required (i.e., for minor violations);
  - Further investigation required;
  - Refer to convened IRB if based on an unanticipated problem involving risk to subjects or others or may involve serious and/or continuing noncompliance.

Convened IRB Determinations for Noncompliance

- The IRB will review all documentation, including any results of fact-finding by ORSP
- The IRB will determine whether the noncompliance is serious and/or continuing based on the definitions provided
- The IRB will determine whether the investigator satisfactorily resolved the noncompliance and whether corrective actions are needed

Outcomes of IRB Noncompliance Review

- Possible actions imposed by the IRB in response to a determination of serious or continuing noncompliance may include, but are not limited to:
  - Research study specific corrective action
  - Education of the investigator(s) and research team
  - Modification to the protocol or other study documents
  - Require that subjects be re-contacted and provided with updated information or re-consent subjects
  - Notification of current subjects when such information may relate to subjects' willingness to continuing participating in the research
  - Providing additional information to past subjects
  - Limit or prohibit publication of data
  - Discarding data or samples associated with the noncompliance
  - Suspension or termination of the research
  - Letter of reprimand to the investigator, which may be copied to the department chair
  - Disqualify the investigator(s) from conducting research involving human subjects at VCU
  - Require periodic monitoring or auditing
  - Enforce more frequent continuing review

Reporting Requirements After IRB Review

- The VCU IRB will report, within 30 days of identifying a reportable event, the following to relevant regulatory and oversight agencies for non-exempt research, regardless of funding:
  - unanticipated problems involving risks to subjects or others;
  - serious and/or continuing noncompliance with the requirements or determinations of the IRB; and
  - suspension or termination of previously approved research.

Reportable Events: Helpful Hints

- Look for commentary from the IRB staff or chair, including suggestions/requested edits upon initial review
- Consider the enrollment status and ongoing active status of participants with the information provided
- Look for a proposed “plan of action” to address the reportable event by the study team
- Corrective actions are to correct the problem, not punish the researcher
- Remember: A reportable event is not always an unanticipated problem
  - A formal determination of an unanticipated problem must be made, if applicable.

VCU IRB Written Policies and Procedures (WPPs)

- WPP VII-6: Required Reporting of UPs Involving Risk or Harm to Subjects or Others: http://www.research.vcu.edu/human_research/irb_wpp/VII-6.htm
- WPP VIII-9: Investigations of General, Serious or Continuing Noncompliance: http://www.research.vcu.edu/human_research/irb_wpp/VIII-9.htm
- WPP VII-4: Reporting to Regulatory Agencies: http://www.research.vcu.edu/human_research/irb_wpp/VII-4.htm
- WPP VIII-8: Suspensions and Terminations of Previously Approved Research: http://www.research.vcu.edu/human_research/irb_wpp/VIII-8.htm