Reportable Events

EVENT TYPE	TIMING	REQUIRED FORM
Unanticipated Problem or Adverse Event	10 days	Event Reporting Form
Death (related)	10 days	Event Reporting Form
Death (not related)	Renewal	Summary with Submission Form
Adverse Audit or Adverse DSMB/DSMC Report	10 days	Event Reporting Form
Participant Complaint	10 days	Event Reporting Form
Protocol Deviation	10 days	Event Reporting Form
Other Unanticipated Info that changes the risk benefit ratio	10 days	Event Reporting Form
Non-Compliance	10 days	Non-Compliance Reporting Form

Unanticipated Problem (UP)

- Unanticipated problems involving risk to subjects or others

- OHRP considers UPs to include an incident that meets **all** of the following criteria:
  - » Unexpected; AND
  - » Related; AND
  - » Suggests that the research places subjects or others at a greater risk of harm than was previously known.

- Unexpected: It is not a known risk of the study drug, device or procedure or subject's underlying medical condition; it's not in the protocol, consent, or Investigator's Brochure (IB); it is an anticipated event that exceeds the anticipated frequency, severity, or duration.
- Related or Possibly Related to the Research: It is possibly, probably, or definitely caused by the study drug, device or procedure; OR it is more likely than not to be related
- Greater Risk of Harm: Events that happen repeatedly, are rare in the absence of the drug/device, exceed the anticipated frequency, severity, and duration, require a change to the protocol, consent, or IB.

Unanticipated Problems

- Often require changes to the protocol, informed consent, or IB
- Often increase the risk level of the study
- May include implementation of additional monitoring of subjects
- Sometimes lead to suspensions in IRB approval or closure by DSMBs

Unanticipated Problems

- The full board must review all UPs

- The IRB must report all UPs to OHRP and FDA, as applicable, if not already reported by the sponsor or another site

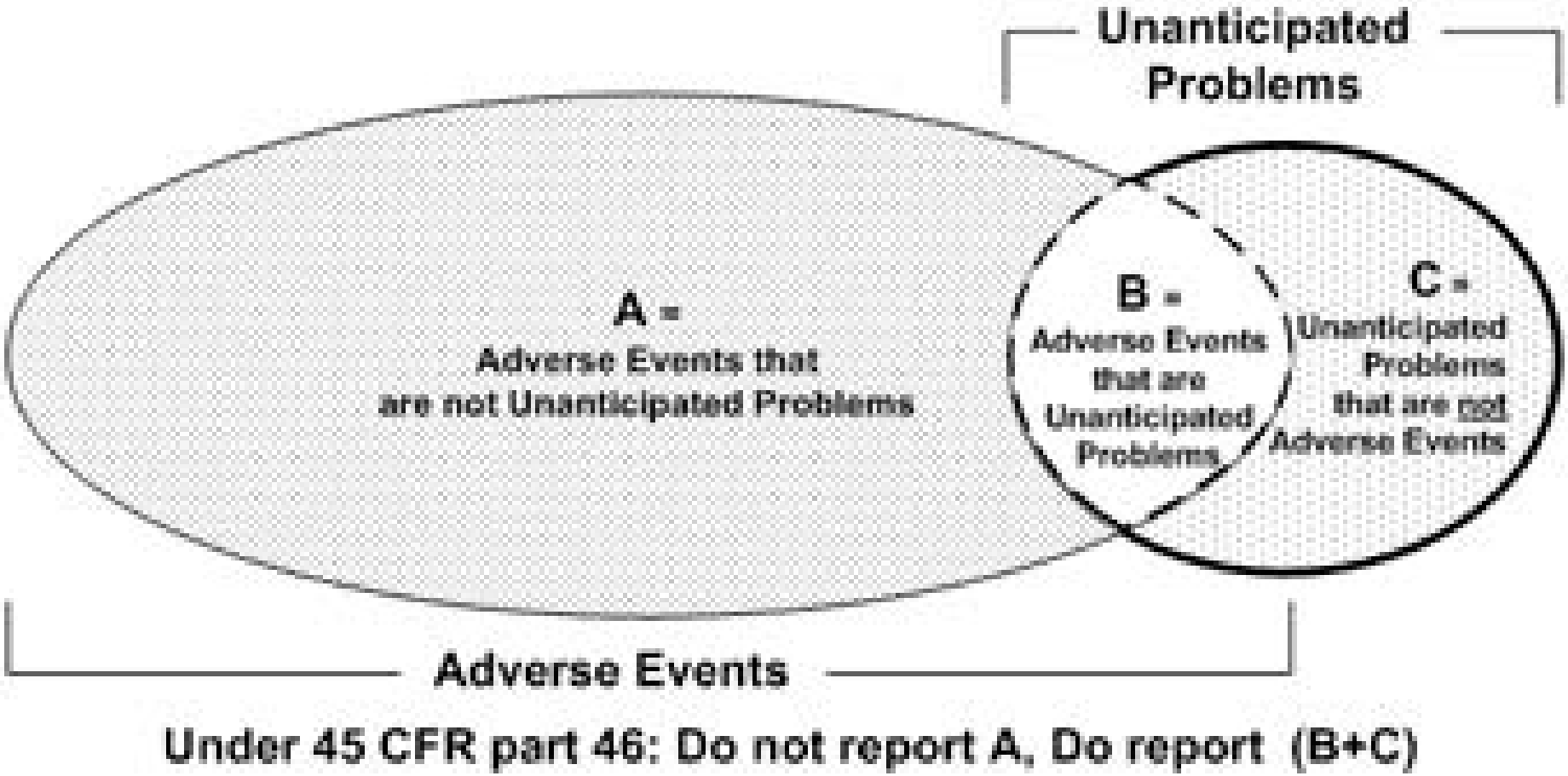
Adverse Events (AE)

- Any untoward or unfavorable medical occurrence in a human subject, including any abnormal sign symptom, or disease, temporally associated with the subject's participation in the research, whether or not related to the research

- Encompass both physical and psychological harms

- Most commonly occur in the context of biomedical research

AE or UP



Under 45 CFR part 46: Do not report A, Do report (B+C)

Protocol Deviation or Violation

- A protocol deviation occurs when the study departs from the IRB-approved protocol in <u>any</u> way **without the investigator first obtaining IRB approval**.

- Promptly reportable when there is a substantive change to the protocol or procedures involving risks (or with the potential to recur) that adversely affect the rights, welfare, or safety of subjects; the integrity of the research data; OR the subject's willingness to continue

Protocol Deviation / Violation

- Subject refused blood draw
- Subject did not complete drug diary
- Power was lost and drug was not kept at appropriate temperature
- Subject seen outside of window because he/she cancelled appointment
- Use of prohibited medications *
- Enrolling subjects who did not meet the inclusion/exclusion criteria*
- Unauthorized (i.e. not IRB Approved) persons (faculty, staff, students, residents, etc.) participating in the conduct of a research study *
- Loss or corruption of samples and/or data*
- Changing the protocol without prior IRB approval *

Non-Compliance (NC)

- Any action (or inaction) of the study team associated with the conduct or oversight of the study that fails to comply with federal or state regulations or institutional policies

Serious Non-Compliance

- Any action or activity associated with the conduct or oversight of research involving human subjects that fails to comply with federal regulations or institutional policies governing such research that increases the risks to participants, decreases the potential benefits or compromises the integrity of the human subject program
- Individual instances of non-compliance that are deemed not serious may constitute serious noncompliance when considered collectively

Examples of Serious NC

- Human subjects research conducted without IRB approval
- Subjects enrolled without consent
- Subjects enrolled without meeting inclusion/exclusion criteria (always serious NC per OHRP)
- Substantive change to the research implemented without IRB approval (unless implemented to avoid harm and always serious NC per OHRP)

Continuing Non-Compliance

- A pattern of non-compliance that suggests a likelihood the non-compliance will continue without intervention
- OHRP considers non-compliance is continuing if it persists after the investigator knew or should have known about it

Examples of Continuing NC

- Repeated informed consent discrepancies
- Repeatedly late submissions of reportable events
- Repeated lapses of IRB approval during which human subjects research occurs

Resources

- Guidance on Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events (HHS)

- OHRP Reviewing and Reporting Unanticipated Problems (OHRP, HHS, Video)

- Guidance for Clinical Investigators, Sponsors, and IRBs – Adverse Event Reporting to IRBs (FDA)