Human Research Subjects' Safety & the IRB's Role, Part II

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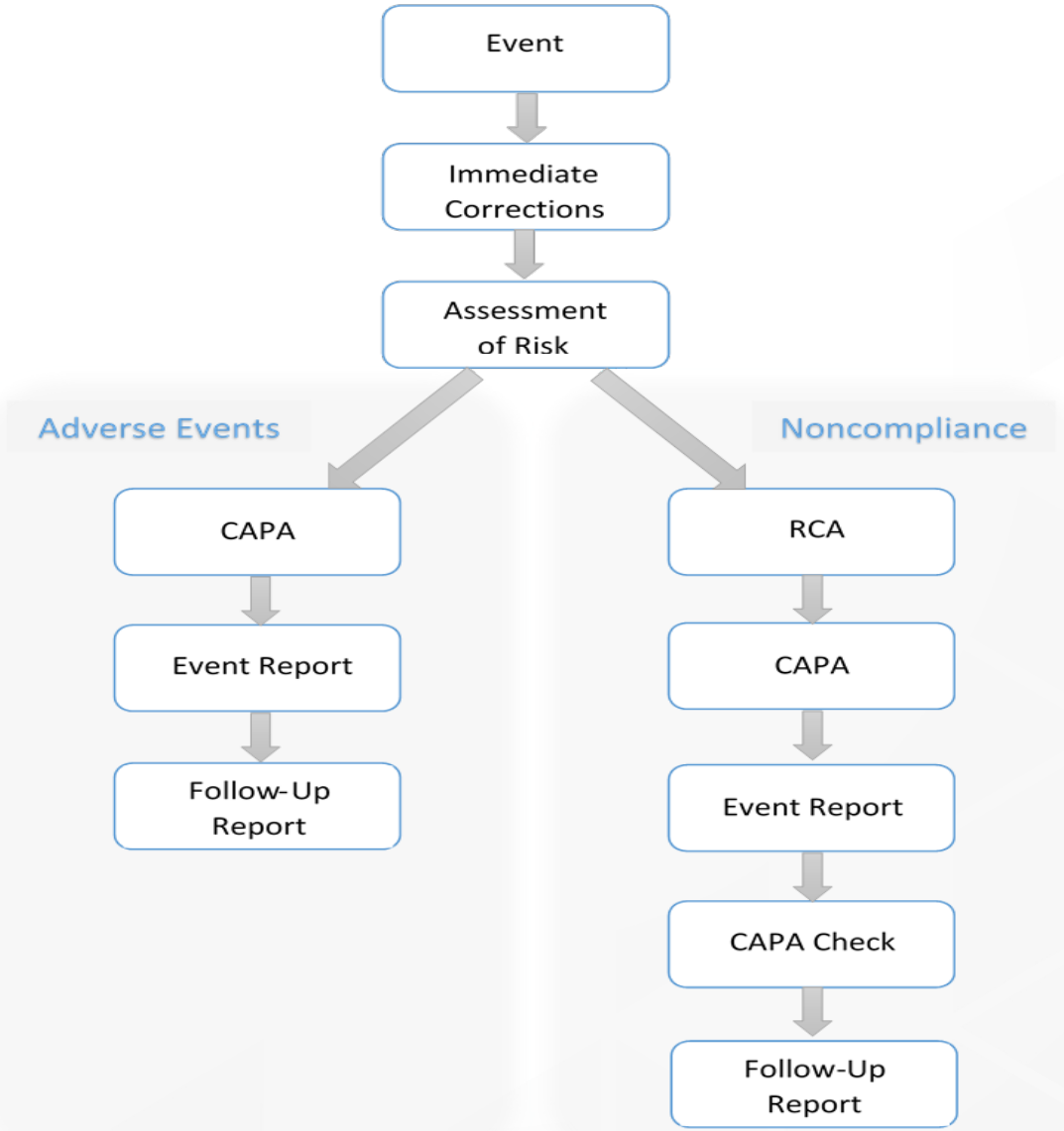
THE UNIVERSITY
of NORTH CAROLINA
at CHAPEL HILL

SOP 1401: Reporting New Safety Information, 7/3/18

Figure 1, Steps to Reporting New Safety Information



Root Cause Analysis (RCA)

Corrective & Preventive Action Plans (CAPA)

Definitions, *SOP 1401*

1. **Noncompliance**: Intentional or unintentional failure to follow applicable federal regulations, the requirements or determinations of the IRB, provisions of the IRB approved study protocol, or University policies. Can occur as a result of performing an act(s) that violate(s) requirements. Can also occur as a result of failing to act when required.

2. **Serious Noncompliance:** "Noncompliance" that adversely and significantly affects the rights or welfare of participants.

3. **UPIRSO/Serious Adverse Event:** Unexpected, related or probably related to research and is serious or places subjects or others at greater risk of harm than previously known.

4. **Continuing Noncompliance:** Any "Noncompliance" that occurs after implementation of an IRB-approved CAPA plan that is due to the failure of the investigator and/or research team to comply with that CAPA plan OR repeated instances of noncompliance within one study or across multiple studies that has a high likelihood of resulting in Serious Noncompliance.

Definition Examples

Event	UPIRSO Or SAE	Serious Non-Compliance	Continuing Non-Compliance
Wrong dose give to subject, Arm A dose instead of Arm B		X	
Wrong dose give to subject, Arm A dose instead of Arm B for 3 months			X
Wrong dose give to subject, Arm A dose instead of Arm B & subject had a severe adverse reaction, hospitalized for a week.	X		

Events to Review

Event	UPIRSO Or SAE	Serious Non-Compliance	Continuing Non-Compliance
Begin work prior to IRB approval of study or amendment	?	?	X
Falsify data: sloppy record keeping, lost records, clinic date & times missing or unclear, values unclear (0.5 or 5?)	?	X	?
Don't consent subjects properly or at all, i.e., give consent on way to surgery	?	X	?
Wrong dose or placebo given to subject	?	X	?
Repeated non-adherence to protocol: -dose administration out of window; -consent witness signatures done days after consent signed by subject;	?	X	X
Continue to use wrong consent form after IRB required re-consenting of subjects with new consent and information.	?	?	X

Events to Review

Event	UPIRSO Or SAE	Serious Non-Compliance	Continuing Non-Compliance
Subject death	X	?	?
Subject received dose triple strength and is hospitalized	X	X	?
Disregard an exclusion criteria when enrolling subjects at UNC.	X	X	?
Dosing subjects prior to checking labs	?	X	?
Childhood experience survey that elicits transient psychological reaction, not included in consent.	X	?	?
Childhood survey, but elicits very strong reactions, subject hospitalized	X	X	?
Childhood survey, PI continues the study after above events, does not report to the IRB or modify the consent or amend the study.	X	X	X
Do not follow through on CAPA plan.	?	?	X

Evaluation of Event by the IRB

- Is the event consistent with the risk information previously reviewed and approved by the IRB?
- Is the event related to the research?
- If the study is industry sponsored, in the judgment of the sponsor, what is the likelihood that the event was related to the research?
- In the judgment of the PI, should the consent form be revised?

Possible Actions by the IRB

- The IRB can require new information be provided to subjects & some or all (current, future, past) subjects re-consented.
- Require modifications.
- Revise the continuing review schedule, for example 3-or 6-month reviews.
- Require monitoring of the informed consent process.
- Require monitoring by an outside source.
- Suspend or terminate the research if subjects are at undue risk.

46.113 Suspension or Termination of IRB Approval of Research

An IRB shall have ***authority to suspend or terminate*** approval of research that is ***not being conducted*** in accordance ***with the IRB's requirements or*** that has been ***associated with unexpected serious harm to subjects***. Any suspension or termination of approval shall include a statement of the reasons for the IRB's action and shall be ***reported promptly to the investigator, appropriate institutional officials, and the department or agency head.***

Case Study

Study: Interventional drug trial

Events:

1. Missed safety labs 5 times on various studies overseen by PI
2. CAPA not followed
3. Subject became septic and died

IRB Evaluation & Decision?

1. **Is it a UPIRSO/SAE?**
2. **Is it non-compliance?**
3. **Is it continuing non-compliance?**