Promptly Reportable Information

OHRE SOP 1401 Updates

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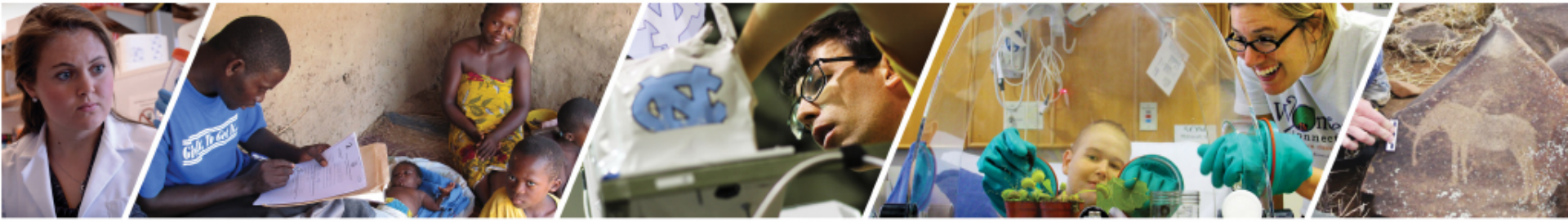

Overview

- Key changes to OHRE SOP 1401 – Promptly Reportable Information
- Overview of Definitions – revised definitions
- Updates to the NSI Form (soon to be PRI Form) in IRBIS

SOP 1401 Updates

- ✓ **New Safety Information → Promptly Reportable Information**
- ✓ Formatting changes, streamlined information
- ✓ Definitions appearing first
- ✓ Two Tables:
  - ✓ Table 1 - Promptly Reportable Information for studies for which the UNC IRB is the IRB of record and has oversight responsibilities
  - ✓ Table 2 - Promptly Reportable Information for studies being conducted by UNC Investigators under the oversight of an external IRB

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Definitions – Overview

- UPIRSO
  - Unexpected
  - Related
- Noncompliance

These definitions have not changed.

Definitions

UPIRSO - **Unanticipated problem involving risk to participants or others (UPIRSO)**

Unanticipated problems involving risks to subjects or others (also known as UPIRSO, UPIRTSO, UPs, UAPs) refer to any incident, experience, outcome, or new information that:

1. Is unexpected (in terms of nature, severity, or frequency); **and**
2. Is at least possibly related to participation in the research; **and**
3. Indicates that subjects or others are at a greater risk of harm (including physical, psychological, economic, legal or social harm) than was previously known or recognized.

Unexpected. The incident, experience or outcome is not expected (in terms of nature, severity, or frequency) given the research procedures that are described in the study-related documents, such as the IRB-approved research protocol/research plan and informed consent documents; and the characteristics of the subject population being studied.

Related. There is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research.

Definitions

Noncompliance

Noncompliance is defined as any failure to follow:

- Applicable federal regulations, state or local laws, institutional policies, or other institutional oversight governing human subject protections, or
- The requirements or determinations of the IRB, including the requirements of the approved investigational plan (i.e., the protocol).

Noncompliance can result from performing an act that violates these requirements or failing to act when required. Noncompliance may be minor or sporadic or it may be serious or continuing. Any "Noncompliance" that is not potential "Serious Noncompliance" nor "Continuing Noncompliance" is not promptly reportable as PRI but must be documented in the research record (e.g., study deviation log) with a Corrective and Preventive Action Plan, as applicable. Although in many scenarios a CAPA is appropriate, other deviations, such as out of study window visit due to subject needing to travel would not necessitate a CAPA, provided appropriate documentation is included. The documentation is subject to review by the IRB and agents of the UNC-CH HRPP.

Definitions - Overview

- Serious Noncompliance – Slight Change

- Continuing Noncompliance – Noteworthy Change

Definitions

Serious Noncompliance – NEW DEFINITION

Serious noncompliance is defined as noncompliance that increases risk of harm to subjects; adversely affects the rights, safety, or welfare of subjects; or adversely affects the integrity of the data or the research.

Previous Definition: "Noncompliance" that adversely and significantly affects the rights or welfare of participants.

Definitions

Continuing Noncompliance – NEW DEFINITION

Continuing Noncompliance is defined as a pattern of repeated noncompliance which constitutes after it has been identified that noncompliance occurred, including inadequate effort to take corrective actions or comply with IRB requirements within a reasonable timeframe.

The identification of noncompliance is not restricted to the IRB, and may include, but is not limited to: auditors, monitors, UNC-CH's CTQA Program, principal investigator, other IRBs, and the study team.

Previous definition: 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.

Why?

- SNC definition revision is an informative change and does not affect how/when information is reviewed by the IRB.

- CNC definition revision is in an effort to harmonize definitions across institutions and is in line with the SMART IRB platform (a platform/agreement for initiating multi-site research, in which UNC participates)

Table 1. Promptly Reportable Information for studies for which the UNC IRB is the IRB of record and has oversight responsibilities*		
UPIRSO	**Any incident, experience, outcome, or new information that are (1) unexpected, (2) related or at least possible related to participation in the research, and (3) indicates that subjects or others are at a greater risk of harm (including physical, psychological, economic, legal, or social harm)**	**Submit a PRI form in IRBIS within 7 days of the event****
A single occurrence of a serious, unexpected event that is uncommon and strongly associated with drug exposure (such as angioedema, agranulocytosis, hepatic injury, or Stevens-Johnson syndrome).		
Unanticipated Adverse Device Effects (UADEs)		
Serious and Continuing Noncompliance	**Any failure to follow (1) Applicable federal regulations, state or local laws, institutional policies, or other institutional oversight governing human subject protections, or (2) The requirements or determinations of the IRB, including the requirements of the approved investigational plan (i.e., protocol deviations) that is serious or continuing.**	**Submit a PRI form in IRBIS within 7 days of the event****
Conducting human subjects research without an IRB-approved protocol or exemption		
Failure to obtain informed consent or reconsent as required by the IRB.		
Other Promptly Reportable Information	**Any other incident, experience, outcome, or new information that is required to be reported in a timely matter to the OHRE but does not meet the criteria of UPIRSO, Serious or Continuing Noncompliance**	**Submit a PRI form in IRBIS within 7 days of the event or receipt of information****
Protocol deviation that is made to eliminate an immediate hazard to a subject without IRB approval.		
Audit, inspection, or inquiry by a federal agency		

Please refer to SOP 1401 for full list of Promptly Reportable Information

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Table 2. Promptly Reportable Information for studies being conducted by UNC Investigators under the oversight of an external IRB (e.g., reliance agreement with institution, commercial IRB, or NCI-IRB).	
UPIRSO Determination by External IRB	Submit a PRI form in IRBIS within 7 days of the external IRB's UPIRSO determination. Include the external IRB's determination letter and any additional applicable documentation or information. The UNC-Chapel Hill OHRE Compliance Manager should be contacted prior to any determination being sent to a regulatory agency.
Serious and Continuing Noncompliance	Submit a PRI form in IRBIS within 7 days of the external IRB's Serious and Continuing Noncompliance determination. Include the external IRB's determination letter and any additional applicable documentation or information. The UNC-Chapel Hill OHRE Compliance Manager should be contacted prior to any determination being sent to a regulatory agency.

Table 2. Promptly Reportable Information for studies being conducted by UNC Investigators under the oversight of an external IRB (e.g., reliance agreement with institution, commercial IRB, or NCI-IRB).		
Other Promptly Reportable Information	**Any other incident, experience, outcome, or new information that is required to be reported in a timely matter to the OHRE but does not meet the criteria of UPIRSO, Serious or Continuing Noncompliance**	**Submit a PRI form in IRBIS within 7 days of the event or receipt of information****
A complaint or concern expressed by subjects or others about the conduct of the study or a subject's participation.		
Audit, inspection, or inquiry by a federal agency		
Written report from a federal agency (e.g., FDA Form 483)		
State board action that (1) will affect the ability to conduct or complete the research as approved by the IRB or (2) increases risk to subjects or others (e.g., suspension of professional license)		
Any event, incident or situation that has generated adverse media attention or congressional interest.		
An event that involves a potential (1) inappropriate sharing or disclosure of a participant's personal identifiers and/or protected health information, (2) privacy incident (3) security incident, or (4) breach of privacy or confidentiality.		

PRI Form Changes – New Questions

Is this submission regarding an Investigator's Brochure (IB) update?

1. Did the IB update change the risk assessment from what was previously approved?

2. Have any current or past subjects that are under the purview of UNC's IRB experienced these risks?

3. Please provide a reconsent or verbal notification plan that includes current and past participation and onset of the risk in regard to the study-specific timeline, or explain why reconsent or verbal notification is not applicable.

PRI Form Changes – New Questions

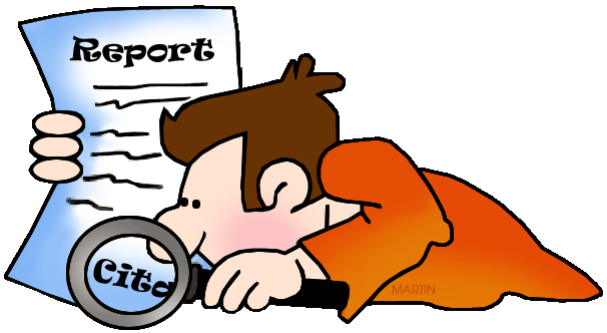
Does the event involve a potential (1) inappropriate sharing or disclosure of a participant's personal identifiers and/or protected health information, (2) privacy incident, (3) security incident, or (4) breach of privacy or confidentiality?

- UNC Institutional Privacy Office is notified (for both UNC and External IRBs)
- UNC IRB – Complete the remainder of the PRI form
- External IRB – Report any final determinations of the reviewing IRB

PRI Form Changes – New Questions

Has this event or issue been identified as noncompliance previously for either this study or other studies that the PI has oversight of (e.g., deviation log, monitor or auditor report, CTQA findings, external IRB)?

In review of the study's deviation log, are there any similar issues or events?



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PRI Form Changes – New Questions

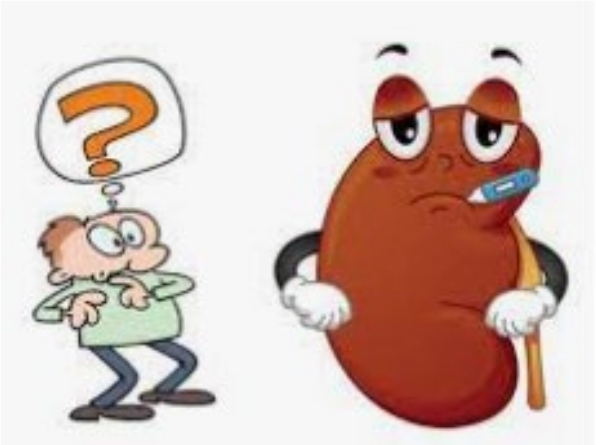
Is this submission regarding other Promptly Reportable Information as outlined in Table 1 and Table 2 of SOP 1401?

1. Please describe what is being reported and ensure all attachments are included.
2. Does this Promptly Reportable Information require a modification or changes to study documents or the protocol?
3. Is this an IND Safety Report from the Sponsor that meets the criteria for reporting to the FDA?
    - Please confirm that the Sponsor has submitted the report to the FDA.

Scenario 1

A UNC research participant experiences acute kidney injury.

- Who is the reviewing IRB?
- Is it related?
- Is it unexpected?



Scenario 2

A change in the protocol was implemented prior to the change being submitted to and approved by the IRB.

- Who is the reviewing IRB?
- Was the change made to eliminate immediate risk or hazard?
  - If yes → Other reportable information

Scenario 3

Five research participants signed the incorrect version of the informed consent form.

- Monitoring report from 5/1/2021 identified that 3 participants signed the incorrect version of the informed consent form.
    - Monitoring report from 9/1/2021 identified that 2 participants signed the incorrect version of the informed consent form.

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Questions