Prompt Reporting to UTHSA IRB or an External IRB

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Objectives

• Describe federal and institutional requirements for Prompt Reporting
• Identify how and where to report unanticipated problems and noncompliance
• Provide examples of events or issues which are sensitive to the institution
• Discuss the importance of Prompt Report tracking
Federal Requirements

The IRB must establish and follow written procedures for ensuring prompt reporting to the IRB, appropriate institutional officials, OHRP, and the appropriate federal department or agency of:

(1) Any unanticipated problems involving risks to human subjects or others;

(2) any instance of serious or continuing noncompliance with the regulations or the requirements or determinations of the IRB

DHHS - 45 CFR § 46.108(a)(4)(i)
FDA - 21 CFR § 56.108(a)(3), (4) & (b)
Regulatory Issues

Are issues which may affect regulatory criteria for IRB approval and include

• UPIRSO
• UADE
• Violations
Unanticipated Problems Involving Risks to Subjects or Others (UPIRISO)

- **Unexpected**
  - In terms of nature, severity, or frequency

- **Related or Probably Related**
  - To the participation in the research (more sure than unsure)

- **Increased Risk of Harm**
  - Suggests a greater risk of harm than was previously known or recognized
Unanticipated Adverse Device Effects

Serious adverse effect on health or safety, any life-threatening problem, or death

Caused by or associated with a device

That was not previously identified in nature, severity, or degree of incidence in the investigational plan
# Protocol Departures

## Deviations
- Unintentional departure from the approved protocol without prior IRB approval that **does not** have the potential to affect subject safety or integrity of the science
  - *Usually outside the control of the investigator*

## Violations
- Intentional departure from the approved protocol without prior IRB approval that has the potential to **cause harm/increase risk of harm, affect scientific integrity, or impacts subject rights, welfare, or safety** = potentially serious and continuing noncompliance
  - *Usually deliberate departures*

## Emergency Violations
- Intentional departure from the approved protocol **without prior IRB approval** that occurs in an emergency situation such that the departure is required to **eliminate an immediate hazard** = internal UPIRSO
  - *Usually departures made for safety reasons*

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Prompt Reporting Required for Noncompliance and UPIRSO
What to report?
- UPIRSO/UADE
  - Adverse Event
  - Non-Adverse Event
- Noncompliance
  - Serious and/or Continuing

When to report?
- Based on external information – 14 days
- Based on internal information – 7 days
- Shortened reporting for life-threatening or events of death – 48 hours
Reporting to the External IRB

• What to report?
  • Report according to external IRB policy and procedures
  • Copy or forward copy to OCR

• When to report?
  • Report within the time frame indicated in the external IRB policy and procedures
Importance of Reporting and Tracking Noncompliance

• Tracking **all** noncompliance occurring at an institution allows for the Reviewing IRB (UTHSA or External) to make appropriate determinations regarding **continuing** noncompliance.

• External IRB policies may require consultation with the local IRB/institution for input prior to a determination.
Institutional Requirements

• Events or issues which are **sensitive to the institution** must be promptly reported to the Office of Clinical Research (OCR).
  • Any events or issues which may indicate there is a deficiency in the investigators research program that may negatively impact the institution.
  • May require reporting to AAHRPP
  • For events reported to the UTHSA IRB, the IRB works with the institution to complete regulatory review
  • External IRB relies upon UTHSA OCR to obtain institutional feedback on issues
  • Some institutional issues are not regulatory issues
Examples of Issues Sensitive to the Institution

• Failure to follow institutional requirements (examples):
  • Personnel engaging in research activities without prior approval
  • Data incidents involving private identifiable information
  • Any issues involving a HIPAA waiver/authorization
  • Any issues involving a conflict of interest (COI)
  • Any issues involving local safety committee approvals
• Suspension or termination of site by Sponsor
• Compliance actions from sources other than UTHSA
• OHRP Determination Letter†
• FDA Warning Letter, 483 Inspection Reports or Restrictions placed on an IRB or Investigator†
• Arbitrations or settlements initiated related to human subject protections†
• Press coverage of a negative nature involving the institution†

†AAHRPP Element I.5.D – reporting required within 48hrs of notification
Reporting to the Institution Only

• What to report?
  • Issues that are sensitive to the institution when reporting to the IRB is not required

• When to report?
  • Within 7-14 days or sooner if applicable
# Examples of Regulatory and Institutional Issues

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<th>Institutional</th>
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| HIPAA Incidents or Breaches of Confidentiality | Failure to adequately protect the confidentiality of the data  
45 CFR 46. 111(a)(7) | Compliance Office  
HOP 11.2.1 Use and disclosure of Protected Health Information without Authorization |
| Issues with scans involving radiation exposure | Failure to ensure risk to subjects are minimized  
45 CFR 46. 111(a)(1) | Radiation Safety Committee approvals  
HOP 8.5.2 Radiation Safety |
| Personnel engaging in research activities where subject safety is compromised | Failure to ensure risk to subjects are minimized  
45 CFR 46. 111(a)(1) | Institutional Scope of Practice  
OCR Policy: Research Team Training, Qualifications, and Delegation of Authority |
| An undisclosed conflict of interest where the conflicted individual monitors subject safety | Failure to ensure adequate provisions the monitoring for subject safety  
45 CFR 46. 111(a)(6) | Conflict of Interest Committee  
HOP 10.1.6 Conflicts of Interest in Research and Disclosure |
How to submit Prompt Reports

New Website
How to Report - UTHSA IRB Prompt Reports

Is prompt reporting to the Reviewing IRB required?

YES and UTHSA IRB

Submit a local UT Health San Antonio Prompt Report Form

Pre-Review

• A designated member reviewer (DMR) of the IRB will review the report to ensure there is enough information for the IRB to make a determination.

Issues sensitive to the Institution

• The DMR will work with OCR and other components of the institution (e.g., Compliance or CTO).

IRB Review

• An IRB determination is made and the IRB notifies PI and appropriate entities (e.g., OHRP, FDA, etc.)

May be returned to OCR for follow-up on institutional requirements
How to Report - External IRB Prompt Reports

Is prompt reporting to the Reviewing IRB required?

YES
and external IRB

Submit to the IRB of Record using their process; provide copy to OCR

Reporting for External IRB Studies
Submit to the IRB of record using their policies/procedures and process.

Copy OCRmail@uthscsa.edu on the submission.

OCR will process the submission in REDCap for the study team and send the study team an OCR review letter when complete.

An OCR letter will be issued when complete

Only after IRB review (if applicable)
How to Report - Institutional Only Reporting

Is prompt reporting to the Reviewing IRB required?

NO
but institutional issue

Submit a local UT Health San Antonio Prompt Report Form for issues sensitive to the Institution

Institutional Only Reporting

For UTHSA or External IRB (not requiring IRB reporting):
Submit the local UT Health San Antonio Prompt Report form for OCR Review.

Submit UT Health San Antonio Prompt Report form (REDCap Survey)

Need help deciding what to report?

• Quick guide on sensitive issues which require prompt reporting to the institution
• Institutional Review Policy and Procedure

An OCR letter will be issued when complete
Scenarios
Scenario 1

There is a multi-center study where UTHSA is the reviewing IRB for UHS, STVHCS, and University of Carolina - Chapel Hill (UNC). The study coordinator at UNC has not required subjects, enrolled at UNC, to complete the post-intervention blood draw to monitor for adverse drug effects. UNC enrolled 5 subjects and none have undergone this monitoring procedure. The PI at UNC notes that there is a problem with conducting the blood draw at the commercially used lab and has placed a hold on further enrollment of subjects until the issue is resolved.

• Does this event require prompt reporting? - Yes
• Which institution does the event get reported to? – UTHSA
Scenario 2

A research study coordinator conducted non-clinical research activities for a UTHSA IRB study and an External IRB study without approval from the Office of Clinical Research.

• Does this event require prompt reporting to the IRB or institutional only reporting? – to the institution

• If applicable, how would you proceed with reporting? - Access and report on the UTHSA Prompt Report form
Scenario 3

The FDA conducted a local audit for Dr. Smith which encompassed multiple studies. As a result of the audit, the FDA issued a 483 inspection report which included studies for which an External IRB has oversight. The inspection report noted that the drug was not being stored at the protocol dictated temperature. The drug had been administered to several subjects.

- Does this event require prompt reporting? - Yes
- Who does the report get sent to? - All reviewing IRBs and if the study is reviewed by an external IRB, the event would also be copied to UTHSA OCR
- If applicable, how would you proceed with reporting? - Access and report using the local Prompt Report form or review and follow External IRB reporting policy/procedures and copy UTHSA OCR
Scenario 4

A study conducted in the Department of X, for which UTHSA is the reviewing IRB requires that the study drug be prepared using a special technique and therefore must be prepared by a licensed physician. A study coordinator was notified that a subject was ready to be treated with the study drug, followed the study drug manual for preparation of the drug, and administered the study drug to the subject. Per the protocol, this was outside of the study coordinator’s scope of practice. There was not a way to determine if the study drug was prepared correctly; however, the subject has not reported any adverse events.

• Does this event require prompt reporting? - Yes
• Which institution does the event get reported to? – UTHSA IRB
• What would the flow of the review look like? – The event would be reported using the UTHSA Prompt Report form. The IRB would work with the institution/OCR for input on the drug preparation procedure. The IRB would make a determination and request follow-up by the institution, if necessary.
Summary

• Prompt Reporting of unanticipated problems and serious and/or continuing noncompliance has both federal and institutional requirements

• It is important to know which IRB is the Reviewing IRB for your research study

• Policies and procedures for prompt reporting of regulatory issues is based on the Reviewing IRB

• Contact the appropriate IRB or UTHSA OCR office with questions on prompt reporting
Questions about research & regulations? Our experts are here for you.

The VPR Research Concierge Service offers walk-in regulatory guidance and assistance at no charge!

Briscoe Library – 2nd Floor Computer Classroom – Room 2.011

- **CTO**
  Clinical Trials, Budget & Subject Payment

- **OCR**
  External IRB Human Studies, Personnel & Training

- **IRB**
  UTHSA IRB Human Studies

- **IACUC**
  Animal Studies & ORCA

- **OIRB**
  Site feasibility assessment,/FDA guidance
  Clinical trials, enrollment, adverse events
  IRB review, grandfathering, waivers

- **ORCA**
  Animal studies, institutional animal care
  IRB review, grandfathering, protocols

- **Wednesday, January 29th**
  9 am-12pm

- **Tuesday, February 4th**
  1pm-4pm

- **Wednesday, February 12th**
  9am-12pm