Northwestern | OFFICE FOR RESEARCH

What To Do When Something Does Not Go As Planned

Incident Assessment,
Root Cause Analysis,
& Corrective and Preventive Action Plans

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Today's Agenda

- What To Do When Something Does Not Go As Planned
- Do I Need to Report to the IRB Office?
  - Incident Assessment Tool
  - Next steps
- Identify the Root Cause
- Crafting a **Specific**, **Timely**, and **Measurable** Corrective and Preventive Action (**CAPA**) Plan
  - Document & Assess the Effectiveness of the CAPA
  - Revising the CAPA or closing/completing the CAPA plan

What To Do When Something Does Not Go As Planned

- Unintentional mistakes in following the IRB-approved protocol or unexpected issues may occur during the conduct of a study.
  - i.e., Noncompliance (with protocol/regulations/IRB policies); Unanticipated problems (such as a serious adverse event deemed possibly related to the research)
- **Immediate corrective actions** are those necessary to protect the rights, welfare, or safety of participants.
- The reporting and review of these events must occur in a timely, meaningful way so that research participants can be protected from avoidable harms.
- The PI is responsible for documentation, (if applicable) timely reporting, investigation, and follow-up.

Do I Need to Report to the IRB Office?

(new!) Incident Assessment Tool:

1. Type of Event
2. Study Information, Event Details
3. Event Assessment
4. Root Cause Analysis & Corrective and Preventative Action (CAPA) Plan

1: Type of Event

Select **all** that apply to this Event(s).

☐ **Adverse Event/Serious Adverse Event**

An Adverse Event (AE) is any unfavorable or unintended event, including abnormal laboratory findings, symptom of disease, or death, associated with the participant's participation in the research or the use of an investigational test article. An AE in research may occur even in the absence of any error or protocol deviation and does not necessarily have to be caused by any identifiable aspect of the research.

Serious Adverse Events (SAE) include those that result in death, life-threatening injury, hospitalization (or prolongation of existing hospitalization), results in a persistent or significant disability/incapacity, or a congenital anomaly or birth defect. An event that requires intervention to prevent one of these outcomes is considered a serious adverse event.

"Life-threatening" includes any adverse experience that places the participant, in the view of the investigator, at immediate risk of death from the reaction as it occurred.

☐ **Protocol Deviation/Violation**

A protocol deviation is any alteration or deviation (whether accidental, unintentional, or intentional) from the IRB-approved research plan as defined in the IRB-approved protocol. Please note, breaches of confidentiality are to be considered unexpected even if they are described in the Informed Consent Form (ICF).

☐ **Unanticipated Problem (must meet all):**

Any information, including any incident, experience, or outcome that meets ALL of the following conditions:

1. is unexpected (in terms of nature, severity, or frequency) given the procedures described in the research protocol documents (e.g., the IRB-approved research protocol and informed consent document) and the characteristics of the human subject population being studied;
2. is related or possibly related to participation in the research ("possibly related" means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and
3. and suggests that the research places human subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized, even if no harm has actually occurred.

☐ **Other Unexpected Events**

Any event that exposes a research participant or others to an increased risk of harm because of research activities. Also, any suspected serious, continuing non-compliance with the IRB-approved protocol, or research-related injury.

2: Study Information and Details of the Event(s)

Complete each section in sufficient detail.

Principal Investigator (PI):			Name of the person filling out the form:
STU#:			Study Title:
Participant IDs: *(please do not include identifiable data in this form, such as participant name. If there are multiple participants with different outcomes, please detail these outcomes in the sections below).*		Date(s) of Event:	Date the PI became aware of the Event: Please see the required reporting timeframe

DESCRIBE EVENT: Provide a detailed summary of the event, including: the circumstances under which the event occurred, how many participants were impacted by the event, the progress of these participants on the timeline of the study, the status/outcome of the event for participants, the site location(s) affected, the frequency of the event, actions taken by the PI or members of the study team, corresponding dates, etc.

3: Event Assessment

Answer the four questions below to determine whether you must report the event to the IRB. Please submit a Reportable New Information (RNI) item via eIRB+ if the event meets the reporting criteria. If the PI is unable to make a determination, please submit an RNI to report the event. In the RNI, include a narrative of the PI's assessment of the event, and why the PI was unable to make a determination.

1.	Did this event occur at Northwestern University, NMHC, SRALab, NM Affiliates, or a site for which Northwestern is the IRB of record **or** involve a Northwestern University, NMHC, SRALab, and/or NM Affiliated study participant or employee? For additional sites, refer to this page: Northwestern Affiliates & Chicagoland Partners: Institutional Review Board (IRB) Office - Northwestern University	☐ **Yes** ☐ **No**
2.	Is this event possibly, or definitely **related to the research** **Or** is this a protocol deviation?	☐ **Yes** ☐ **No**
3.	Is this an **unexpected** event **or** a protocol deviation? *Note:* Unexpected in nature, severity, or frequency than was known for the investigational agent or the population being studied.	☐ **Yes** ☐ **No**
4.	Did , or could, this event cause harm, increase the risk of harm, adversely affect the rights or welfare of participants or undermine the scientific integrity of the data, or is the event an allegation of such non-compliance? (Harm includes physical, psychological, economic, or social harm.) Examples include but are not limited to: • *Research conducted without IRB approval.* • *Unintended disclosure of private/personal information* • *Missed safety laboratory assessments* • *Drug administration or dosing errors (regardless if an actual AE/SAE occurred)* • *Study procedures performed on an ineligible participant* • *Failure to obtain legally-effective informed consent or re-consent when required by the IRB*	☐ **Yes** ☐ **No**

If all answers to the above questions (#1-4) are "YES," submit an RNI in eIRB+ within 5 business days of the date the PI became aware of the Event.

Death of an NU participant or a participant at a site where Northwestern is the IRB of Record that is both Unanticipated and Related to the research must be reported within 24 hours of knowledge or notification.

If ANY answers to the above questions (#1-4) are "NO," Do not report the event to the IRB via an RNI. Complete this form to document the event and the PI's determination that the event did not meet the IRB reporting criteria. Save this completed form in your study-specific regulatory binder or research record.

If the answers to the above questions (#1-4) are "YES," and the Northwestern University IRB is not the IRB of record, if the event involves Northwestern University, NMHC or NM affiliated sites, or SRAlab participants or their identifiable data, please submit a Reportable New Information application in eIRB+ within 5 business days of the date the PI became aware of the Event. Please review your External IRB's timeframe for submitting reportable events. The event should be concurrently reported to the IRB of record if it meets their reporting criteria and the determination letter from the External IRB should be submitted to NU IRB via the RNI form.

Additional Notifications. Please reach out to the applicable entities below to notify them of the incident, develop a Corrective and Preventive Action (CAPA) Plan, and incorporate all changes they request into the RNI application that you submit to the IRB.

- **Data Incident:** If the incident involves the unintended disclosure of private/personal information, please reference the Guidance on Evaluating Reports of Data Incidents on the Guidance Page for the appropriate steps and notifications.

Next Steps: If the event **does not meet the reporting criteria**

- File documentation of the event and the PI's assessment in your regulatory binder or research record.
  - To document the event, PIs may use:
    - Protocol Deviation Log
    - Incident Assessment Tool
- Do not submit an RNI in eIRB+.

Next Steps: If the event **does meet the reporting criteria**

- Submit an RNI in eIRB+
  - Ensure you provide sufficient detail to accurately describe the event. Include:
    - Dates of when events occurred or when you took actions
    - Roles of those individuals involved (no names)
    - Participant ID numbers, if consented, or the number of potential participants if the event involves individuals who have not consented to participate in the study.
  - You may attach or copy the information from the Incident Assessment Tool within the RNI application in eIRB+.

Other Reporting Obligations

- The PI must meet all other reporting obligations (i.e., study sponsor, lead site, etc.).
- The PI must notify the appropriate institutional stakeholders of the event, who may have input on the CAPA plan.
  - Data Incidents: contact FSM Director of Clinical Research Operations a-cosentino-boehm@northwestern.edu
  - Events that involve IDS Pharmacy: contact Investigational Drug Service (NM) nminvestigationaldrugservice@nm.org
  - On all communications, please include the IRB Compliance Unit irbcompliance@northwestern.edu

Identify the Root Cause

- A root cause analysis is not intended to lay blame on an individual
- The preventive actions in the CAPA plan cannot be formulated without identifying the cause of the error or deviation.

Root Cause Review

- On March 28, 2019 the new project manager for the study was reviewing the records and identified that the records for participants 0278 and 0270 did not include documentation of payment for their first study visit. Those visits occurred on November 12, 2018 and October 15, 2018, respectively. The project manager notified the principal investigator the same day and contacted ASRSP to find out whether checks had been sent to those participants. The project manager received the response from ASRSP on April 2, 2019 that the participants were not paid. The project manager requested that ASRSP process the payments to the participants the same day.
- **Root Cause: The research associate didn't process the payments for the participants.**
- Corrective Actions: ASRSP confirmed the participants were sent payment via check on April 7, 2019.
- **Preventive Actions: The research associate who made the error is no longer at Northwestern.**

Root Cause Review

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- **Root Cause: There wasn't a process in place to review participant records on an ongoing basis to ensure that all procedures were followed, as required.**
- Corrective Actions: ASRSP confirmed the participants were sent payment via check on April 7, 2019
- Preventive Actions: Beginning immediately, when participants complete study visits that require payment **processing, the research associate will place a request for payment with ASRSP and document the request in the participant record using a newly developed record sheet. The project manager will review the participant records monthly to ensure that all study procedures, including participant payments, are completed and recorded appropriately and document the review on the record sheet.**

Corrective and Preventive Action (CAPA) Plan

- Corrective Actions: Taken to address the immediate cause of the RNI report.
  - Ex. The Principal Investigator notified participant 0326 that the study team incorrectly administered double the intended dose of study drug. Participant 0326 acknowledged the error, has not reported any adverse reactions, and continues to actively participate in the study.
- Preventive Actions: Taken to ensure no recurrence of the cause of the RNI report.
  - Ex. On May 23, 2019, all members of the study team underwent training on the study drug dosing and implemented a new process to document dispensation of study drug. The study team member obtaining the study drug from the research pharmacy will take the participant specific study drug form to the pharmacy. The research pharmacist and the study team member will inspect the study drug bottle and study drug pills, confirm the dosage, and document their review on the study drug form.

Corrective and Preventive Action (CAPA) Plan

- When creating a CAPA plan you should consider the following:
  - The plan should be:
    - Specific
    - Timely
    - Measurable

Ex. All members of the study team responsible for obtaining informed consent will undergo retraining by the principal investigator and project manager on how to obtain and document consent. The training will occur by October 23, 2018, with attendance recorded. The documentation of the training will be kept in the study records.

Corrective and Preventive Action (CAPA) Plan

- When creating a CAPA plan you should consider the following:
  - The plan should include:
    - A feedback mechanism to assess the effectiveness of the CAPA;
    - Criteria for completing the CAPA

Ex. The research project manager will review all informed consent forms to determine whether the research team correctly documented consent. If the research project manager does not identify any errors after 6 months or 10 newly consented participants, the research project manager will transition to conducting quarterly reviews on 10% of newly consented participants' consent forms. If the research project manager does not identify any errors, then the research project manager will move to as-needed reviews.

Corrective and Preventive Action (CAPA) Plan

- When creating a CAPA plan you should consider the following:
  - Is this event or deviation a recurrence, for which you already have a CA**PA** plan in place?
    - If yes, rather than writing a new preventive action plan:
      - Detail the actions that you'll take to determine why the plan failed,
      - The changes to the plan that you'll make, and
      - The ongoing assessment of the preventive action plan to determine if it is still working

Reporting Timeframes

- Death of an NU/NU Affiliate* Participant that is Unanticipated, Related:
  - **Within 24 hours of knowledge or notification**
- Reportable New Information: Information pertaining to an NU/NU affiliate* that meets the criteria:
  - **Within 5 business days of knowledge or notification**

External IRB Studies

When the Northwestern University IRB has ceded review to an external IRB and an event occurs…

- Review the External IRB's definitions and timeframe for submitting external events.
- Definitions for what is reportable and the timelines for reporting differ at every IRB.
  - If the event meets the external IRB reporting criteria, the PI must report the event to the external IRB.
  - If the event also meets the NU IRB reporting criteria, the PI must concurrently report the event to the NU IRB.

External IRB Studies

- If the event **does not** meet the external IRB reporting criteria, but **does** meet the NU IRB reporting criteria:
  - Submit the RNI to the NU IRB in eIRB+
  - Include a statement in the RNI application that the PI did not report the event to the external IRB because the PI determined that the event did not meet the external IRB's reporting criteria.

Multi-Site IRB Studies

- When the Northwestern University IRB takes on the responsibility of serving as the IRB of record for external sites, you have a new role…
- Study Coordinating Center
  - Your responsibility is to ensure that the other study teams are evaluating events according to the Northwestern IRB reporting criteria; and
  - Facilitating the RNI submission in the eIRB+ system and communication between the site and the NU IRB

Reportable Events

- IRB Determinations that require reporting to federal oversight/funding agencies and/or university and affiliate HRPP stakeholder:
  - Serious Non-Compliance
  - Continuing Non-Compliance
  - Unanticipated Problems Involving Risk to Subjects Others
  - Suspension of the Research
  - Termination of the Research

From the date that the IRB Panel makes a reportable determination, the IRB Office Compliance Team has **30 business days** to send the report. (HRP-094 – External Reporting Process)

Reportable Events

- External reports: Those sent to the federal funding agencies and/or federal oversight agencies. (NIH, FDA, DOJ, VA, etc.)
- All external reports are also reported to university and affiliate HRPP stakeholders
  - Investigator's supervisor, Department Chair, IRB Executive Director, Associate Vice President for Research, Vice President for Research, etc.
- University reports: When a study is not federally funded or under the oversight of a federal agency, the event(s) are reported to university and affiliate HRPP stakeholders.

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**Please reach out to Kim with feedback or questions on the Incident Assessment Tool!*

General Compliance Questions or Concerns:
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