# To Report or Not to Report? Using the Incident Assessment Tool

May 18, 2022 - Brown Bag

Presented by: Kim Rowan, MBA, CIP
Senior Compliance Analyst

Institutional Review Board Office | Northwestern University

# Outline

- Introduction to new (optional) Guidance: Incident Assessment Tool
- To Report or Not To Report: Why ask this Question?
- Incident Assessment Tool (IAT) Steps
- When an Incident Meets IRB Reporting Criteria
- When an Incident Does Not Meet IRB Reporting Criteria
- Examples: Using the Incident Assessment Tool
- Key Takeaways
- Q&A

# Incident Assessment Tool (IAT)

During the course of a research study, unintentional mistakes in following the IRB-approved protocol or unexpected issues could happen!

The Principal Investigator is responsible for the documentation, timely reporting, investigation, and follow-up of these events.

Some of these events **meet the IRB reporting criteria**, and must be submitted to the IRB via a **Reportable New information (RNI)** Application in eIRB+.

Some of the events **do not meet the IRB reporting** criteria, and should be **documented in the research record** as a note to file or protocol deviation.

# To Report or not To Report?

## *Why ask this question*

**The IRB Office is a partner in human participant protections!**

- Sharing information with the IRB facilitates a relationship between investigators and the IRB that protects the rights and welfare of participants and the integrity of study data

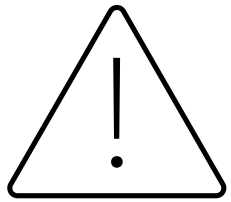
**Why an Incident Assessment Tool (AT)?**

- Adds to participant protection by facilitating the PI's formal documentation of their assessment of the event

***The PI is empowered by the regulations at 45 CFR 46.108 (a)(4)(i) to make the initial reporting determination. The PI is responsible for ensuring that all reporting obligations are met (i.e., notifying the study sponsor, lead site, etc.)***

# Challenges of Over and Under-Reporting Incidents

- Under-Reporting:
  - Safety impact –lack of adjustments to monitoring and risk mitigation to the study design, incomplete disclosure of potential new risks to participants in the informed consent form
  - Regulatory non-compliance



- Over-Reporting:
  - Impedes participant safety oversight (needle in a haystack)
  - Burdensome to the PI and to the IRB

*"The receipt of a large volume of individual AE reports without analysis of their significance to a clinical trial rarely supports an IRB's efforts to ensure human subject protection." -FDA Guidance: Adverse Event Reporting to IRBs –Improving Human Subject Protections v. Jan 2009*

# Incident Assessment Tool (IAT)

Use the Incident Assessment Tool to determine:

What to do when an incident occurs

How to document the event

How to and whom to report the issue to

# IAT Step 1: Incident Category(ies)

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 (than was previously known or recognized) because of research activities. Also, any suspected serious, continuing non-compliance with the IRB-approved protocol, or research-related injury.

# IAT Step 2: Details of the Incident

**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. If applicable, include details on how you communicated the event to the participant(s) and the participant(s) response. | | | |

# IAT Step 3: Event Assessment

**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 to the IRB. In the RNI, include a narrative of the PI's assessment of the event, and why the PI was unable to make a determination.

As outlined on the RNI Page, only events meeting the definition of serious non-compliance, continuing non-compliance, UPIRSO, or combinations of these require reporting to the IRB.

| | | |
|---|---|---|
| **1.** | Is this event possibly, or definitely **related to the research**<br>**Or**<br>Is this a protocol deviation? | ☐ **Yes** ☐ **No** |
| **2.** | Is this an **unexpected** event **or** a protocol deviation that did or **could** cause harm?<br>*Note:* Unexpected in nature, severity, or frequency than was known for the investigational agent or the population being studied. | ☐ **Yes** ☐ **No** |
| **3.** | 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.). Note: If the adverse event is serious, the answer is always yes.<br>Examples include but are not limited to:<br>• *Research conducted without IRB approval.*<br>• *Unintended disclosure of private/personal information*<br>• *Drug administration or dosing errors (regardless if an actual AE/SAE occurred)*<br>• *Study procedures performed on an ineligible participant*<br>• *Failure to obtain legally-effective informed consent or re-consent when required by the IRB* | ☐ **Yes** ☐ **No** |
| **4.** | 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<br>OR did this event occur externally with the potential to impact Northwestern participants? | ☐ **Yes** ☐ **No** |

# IAT Step 3: Event Assessment (continued)

**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 or Possibly 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. A death that is both Unanticipated and Related or Possibly Related to the research must be reported within 24 hours. 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 application.

# IAT Step 4: Root Cause Analysis and CAPA Plan

Regardless of IRB reporting, the PI should conduct and document:

## Root Cause Analysis (RCA)

- Identify and document the initiating factor and the downstream effect on the causal chain.
- How, what, where, when and why matter more than who. Focus on identifying underlying problems that contribute to the error rather than mistakes made by individuals.

## Corrective and Preventive Action (CAPA) Plans

- Address the **timeline** (actions taken and actions planned) and criteria for completion.
- Discuss the **PI's involvement**.
- Define the **personnel responsible** for overseeing implementation and evaluation.
- Include feedback mechanism to **periodically assess the effectiveness** of the CAPA.
- Provide the timeframe for **ongoing evaluation** of preventative actions.
- **Document** (and submit to the IRB when applicable) any needed adjustments.
- Define the level where changes are being made (study team or department-wide).
- Create and maintain **documentation** that demonstrates that you implemented the CAPA plan. The IRB or sponsor may request to review this documentation.
- Should be reviewed and signed by the Principal Investigator, kept on file in the research record, and submitted to the IRB for review within the RNI application (if applicable).
- Corrective and Preventive Action (CAPA) Plans

# Additional Considerations

When in doubt, contact the IRB Office at IRBCompliance@northwestern.edu

Regardless of whether your event meets IRB Reporting Criteria, additional reporting/notifications may be required.

- Contact applicable entities to notify them, develop a Corrective and Preventive Action (CAPA) Plan, and incorporate any changes they request
  - **Data Incident:** If the incident involves the unintended disclosure of private/personal information, please reach out to FSM Director of Clinical Research Operations (a-cosentino-boehm@northwestern.edu).
    - For more information, please review the IRB's guidance on evaluating reports of data incidents here.
  - **Investigational Drug Services:** If the incident involves or affects the NM Investigational Drug Services, please reach out to Investigational Drug Service (NM) nminvestigationaldrugservice@nm.org
- On all communications, please copy the IRB Office irbcompliance@northwestern.edu

# If Your Event **Meets** the IRB Reporting Criteria:

Submit an RNI to report the event to the IRB. Reporting Requirements and Timeframes.

Provide all of the information in the RNI application to allow the IRB to fully assess the event.

The PI is empowered by the regulations at 45 CFR 46.108 (a)(4)(i) to make the initial reporting determination. The PI is ultimately responsible for ensuring that all reporting obligations are met (i.e. notifying the study sponsor, lead site, etc.).

# Submitting an Exemplary RNI Application to the IRB

- You may attach the completed IAT in your RNI application (not required).
- Perform/document a **Root Cause Analysis** to determine the reason(s) that the issue arose.
- Discuss **Corrective and Preventive Actions** (CAPA) taken or planned.
  - CAPA plans should be specific, timely, and measurable, thorough, and well documented.
  - Please refer to the IRB's guidance on how to create an effective CAPA here.
- Documentation, documentation, **DOCUMENTATION**!
  - Create and maintain documentation that demonstrates that you implemented the CAPA plan. The IRB or sponsor may request to review this documentation.
- Please ensure you choose all the applicable **RNI categories** within eIRB+. More than one RNI Category may be applicable to your event.
- For Example, if your event meets both a Researcher Error and Non-Compliance then select both categories in question #3 when submitting the RNI.

# Examples of Events That **May Meet** IRB Reporting Criteria:

1. Example 1: Informed Consent Form
   - Study team consented a participant using an older version (not the currently approved version) of the ICF. The PI assessed that the version of the ICF used was missing important risk information.

2. Example 2: Protocol Deviation
   - Study team performed a study visit that was significantly out-of-window per the IRB-approved protocol. The participant was to have required safety labs performed at this visit.

3. Examples 3 & 4: Problem occurs that does meet UPIRSO criteria
   - 3. Study drug was administered to a non-study participant.
   - 4. Adverse event occurring at a rate higher than expected.

***Reminder**: RNI applications can serve multiple uses as a mechanism to provide information to the IRB. For example, the use of a Short Form for consenting a non-English speaking participant requires the submission of an RNI application in eIRB+ within 10 days of the use of the Short Form. This and other examples are on the IRB Office's Reportable New Information Page. See Additional guidance on Short Forms here.*

# If Your Event **Does Not Meet** the IRB Reporting Criteria:

Do not submit an RNI to report the event to the IRB.

Document the event within a Note To File or in the Protocol Deviation/AE Log & Maintain the completed Incident Assessment Form in your study's regulatory binder or research record.

The PI is empowered by the regulations at 45 CFR 46.108 (a)(4)(i) to make the initial reporting determination. The PI is ultimately responsible for ensuring that all reporting obligations are met (i.e. notifying the study sponsor, lead site, etc.).

# How to Document an Event that Does Not Meet IRB Reporting Criteria

**Document** events **in real time** to ensure completeness and accuracy of the data.

## Note to File

- Gives context; clarify an error, omission or discrepancy, or document a problem or corrective action.
- File within the research record or participant file (as applicable).

## Protocol Deviation (PD) Log

## Adverse Events (AE) Log

- The PI should periodically assess for patterns across the lifetime of the study.

## Root Cause Analysis and CAPA Pan

## IRB Office Study Support Tools:

- Protocol Deviation Log
- Note to File Template
- Regulatory Binder Checklist
- Research Record Components

# Examples of Events That **May Not Meet** IRB Reporting Criteria:

1. Example 1: Informed Consent Form
   - Study team consented a single participant using the correct version of the ICF but with an IRB stamp that was no longer the current eIRB+ stamped version. There were no changes between the version that was used to consent the participant and the currently approved version. The PI added a signed and dated note to file to document that the correct version of the ICF was used and documented a CAPA Plan to prevent recurrence.

2. Example 2: Protocol Deviation
   - A participant failed to complete and turn in their study diary on time and submitted the study diary a week late. The PI assessed that the event did not cause or have the potential to cause harm nor did it undermine the integrity of the study data. The PI recorded the event in their protocol deviation log.

3. Example 3: Adverse Event – does not meet UPISRO criteria
   - During a research procedure that involves walking on a treadmill for 20 minutes, a participant fell and bruised their knee. The informed consent form contains the potential risk of injury from a fall. The PI recorded the event in their Adverse Event log.

***Reminder**: The PI is responsible for ensuring all applicable notifications and reporting obligations are met (i.e., Investigational Drug Services, sponsor, lead site, etc.).*

# Examples
# -
# Using the Incident Assessment Tool

# Using the IAT: Example 1

*Single use of a non-IRB-stamped ICF to consent a participant*

- **Step 1: Type of Event**:
  - ☑ Other Unexpected Events
- **Step 2: Study Information and Details of the Event(s)**:
  - The event occurred for a single participant at a Northwestern site.
  - Study team consented one participant using a version of the ICF without the IRB approval stamp.
  - The PI reviewed the ICF and assessed that there were no changes between the version that was used to consent the participant and the currently approved version (same version but with an older IRB approval stamp and not the current IRB approval stamp).
  - The PI notified the participant about the error at their next study visit.

# Using the IAT: Example 1

*Singles use of a non-IRB-stamped ICF to consent a participant*

- **Step 3: Event Assessment:**
  - ☑ Related to the Research
  - ☑ Unexpected
  - ☐ Did/could cause harm, adversely affect the rights or welfare of participants or undermine the scientific integrity of the data
  - ☑ Occurred at NU and/or has potential to impact NU participants

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

*RNI not required. Document in the PD log.*

# Using the IAT: Example 1

*Single use of a non-IRB-stamped ICF to consent a participant*

- **<u>Step 4: Root Cause Analysis & Corrective and Preventative Action (CAPA) Plan</u>**
  - RCA: The error occurred because there was no SOP or checklist for study personnel obtaining consent.
  - Immediate corrective actions include the PI adding a signed and dated NTF within the participant file to document the error.
  - Preventive actions include implementation and training on a new documentation of consent checklist.
  - Achievable deadline for the new checklist to be trained on and implemented provided.
  - Feedback/evaluation loop: the PI designated the lead coordinator to review executed consent forms weekly to assess if the checklist has been successful in preventing further recurrence.
  - Should the same error occur again in the future, it may meet the IRB reporting criteria and the PI should submit an RNI.

# Using the IAT: Example 2

*Adverse Event*

- **Step 1: Type of Event**:
  - ☑ Adverse Event/Serious Adverse Event

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

- The event occurred for a single participant and during a study visit at Shirley Ryan Ability Lab.
- During a research procedure that involves walking on a treadmill for 20 minutes, a participant fell and bruised their knee.
- The informed consent form contains the potential risk of injury from a fall, including the possibility of bruising or injuring your knee.
- Immediate actions taken were to ensure the participant was okay and that they received the care required for their injury.

# Using the IAT: Example 2

*Adverse Event*

- **Step 3: Event Assessment:**
  - ☑ Related to the Research
  - ☐ Unexpected
  - ☑ Did/could cause harm, adversely affect the rights or welfare of participants or undermine the scientific integrity of the data
  - ☑ Occurred at NU and/or has potential to impact NU participants

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

*RNI not required. Document in the AE log.*

# Using the IAT: Example 2

*Adverse Event*

- **<u>Step 4: Root Cause Analysis & Corrective and Preventative Action (CAPA) Plan</u>**
  - Immediate actions included ensuring the participant was okay.
  - The PI recorded the event in their AE log.
  - An RCA and CAPA plan is not required for all Adverse Events that occur.
  - The PI should document this event in the Adverse Event log, and periodically assess the AE log throughout the lifetime of the study for any trends.

# Using the IAT: Example 3

*Administration of study drug to non-study participant.*

**Additional Notifications: Investigational Drug Services (IDS):** When an incident involves or affects the NM IDS, notify them at nminvestigationaldrugservice@nm.org to develop a Corrective and Preventive Action (CAPA) Plan and incorporate any changes they request.

- **Step 1: Type of Event**:
  - ☑ Protocol Deviation/Violation
  - ☑ Unanticipated Problem
- **Step 2: Study Information and Details of the Event(s)**:
  - This event occurred at a study visit at NMHC and involved one individual.
  - Study drug inadvertently administered to a non-study participant that had surgery the same day as the study participant.
  - Error was discovered at the end of the surgery when the nurse asked for confirmation of the MRN. The name listed was for the study participant, and not the individual.
  - The patient was informed of the occurrence and is being monitored with no adverse effects noted to date.
  - PI assessed that, although no harm occurred to the patient, there was potential for harm.

# Using the IAT: Example 3

*Administration of study drug to non-study participant.*

- **Step 3: Event Assessment:**
  - ☑ Related to the Research
  - ☑ Unexpected
  - ☑ Did/could cause harm, adversely affect the rights or welfare of participants or **undermine the scientific integrity of the data**
  - ☑ Occurred at NU and/or has potential to impact NU participants

**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 Possibly Related to the research must be reported within 24 hours of PI knowledge.

*Submit an RNI in eIRB+ to report the event to the IRB*

# Using the IAT: Example 3

*Administration of study drug to non-study participant.*

- **Step 4: Root Cause Analysis & Corrective and Preventative Action (CAPA) Plan**
  - RCA: There was no standard practice or workflow established.
  - Immediate corrective actions included notifying the patient affected, following their progress, and updating the IRB as required.
  - Preventive actions include the re-training of study personnel (achievable deadline, roles & dates of training, sign-in sheet provided).
  - New SOP: Individual responsible for overseeing new process: The study coordinator and/or researcher will confirm and document secondary checks utilizing a newly created SOP checklist.
  - The PI also documented the event in the PD log, and will review participant records in real-time to assess whether preventive measures have been successful in preventing recurrence and will update the IRB with any adjustments made.

# Incident Assessment Tool – Feedback Survey

- Survey as a tool to obtain researcher feedback on the utilization of the IAT
  - *Are the instructions clear? Is the IAT useful for study teams? Does the IAT improve the RNI process (facilitate ancillary review if needed, minimize additional clarification requests from the IRB, etc.)?*
- Survey link will be embedded on the RNI Webpage next month (June 2022)
- Take the survey at any time, through the link on the RNI Page
  - Positive and Constructive feedback is encouraged!

*Reach out to Kim Rowan (kim.rowan@northwestern.edu) with any questions/comments on the IAT or survey*

*Your feedback is valued*

# Key Takeaways

The Incident Assessment Tool can be used to help the PI assess whether:

- The incident meets the IRB reporting criteria and must be submitted to the IRB via an RNI application; or
- The incident does not meet IRB reporting criteria and may be documented within the research record.

The PI is empowered by the regulations to make the initial assessment.

The PI is responsible for ensuring that all other reporting obligations are met (i.e., study sponsor, lead site, etc.).

The IRB Office has several support tools and templates to help you maintain compliant records.

Your constructive feedback helps strengthen our Human Research Protections Program!

# Resources

- Reportable New Information (RNI)
- Corrective and Preventive Action Plans
- IRB Office Study Support Tools And Templates:
  - Protocol Deviation Log
  - Note to File Template
  - Documentation of Consent Process Form
- Human Research Policies & Guidance
  - Guidance on Evaluating Reports of Data Incidents

Additional Federal Guidance on what must be reported to the IRB:

- Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events: OHRP Guidance.
- Adverse Event Reporting to IRBs - Improving Human Subject Protection, Guidance Clinical Investigators, Sponsors, and IRBs (fda.gov)
- Attachment C: Recommendation on Protocol Deviations | HHS.gov

Thank you!

Questions/Feedback on the Incident Assessment Tool?