What Investigators Need to Know About Reporting Research-Related Events to the IRB

Peg Sanders, RN, MSN, MA, CIP
Office of Human Subjects Research Protections (OHSRP)
Office of Compliance and Training

Agenda

- Review terminology related to event reporting
- Describe investigator event reporting responsibilities
- Understand the workflow for submission of reportable events to the NIH IRB and non-NIH Reviewing IRBs
- Apply the knowledge gained to case examples

Initial Assessment (Pre-session): Just give it your best guess

Event Reporting #1

35-year-old with malignant tumor

- Enrolled on study, admitted to the Clinical Center, and received unblinded study drug (under IND) over 5 days
- Subsequently, his creatine kinase (CK) increased to 3122 (normal range 39-308 U/L)
- He developed myalgia attributed to rhabdomyolysis
- Elevation in the blood CK and rhabdomyolysis are not listed as a risk of the study drug and the PI attributes this to the study drug

Which of the following best describes this event?

- An SAE that is not an unanticipated problem so no expedited reporting to the IRB is needed
- An unanticipated problem that requires expedited reporting to the IRB

Event Reporting #2

During an audit, it was discovered that a subject underwent research procedures including history and physical exam and also had research bloods drawn prior to completion of the consent process and signing the consent form.

Which of the following best describes this event?

- Unanticipated problem
- Minor deviation
- Major deviation
- New information that might affect a subject's willingness to enroll or continue on study

Event Reporting #3

A participant with renal cell carcinoma completed their last cycle of investigational chemotherapy conducted under an IND study.

- The participant was being seen monthly for follow-up visits per protocol
- Three months into follow-up, the PI heard from her family that she was admitted to the hospital over the weekend and died due to influenza
- The PI reviewed the medical records and determined that the death was unrelated to research

Which of the following best describes this event?

- An unanticipated problem that needs to be reported to the IRB within seven calendar days (expedited reporting)
- A death that is not a UP since it is not at least possibly related to the research. It does not require expedited reporting to the IRB.
- A death that is an SAE that requires expedited reporting to the IRB even though it is not related to the research

Event Reporting #4

An unencrypted email was sent to an outside physician that contained the participant's first name, diagnosis, and date of birth.

Which of the following best describes this event?

- A major protocol deviation
- An SAE
- Noncompliance that is not a protocol deviation
- A minor protocol deviation

Event Reporting #5

Participant with Parkinson disease is enrolled in an open label Phase 1 clinical trial of an investigational agent to treat severe tremor

- Protocol indicates participants receive oral study medication daily for six months
- One month after starting study drug, the participant was hospitalized with fatigue and severe anemia requiring blood transfusion
- Hematology work-up suggested immune mediated hemolytic anemia
- The known risk profile for this investigational agent does not include anemia and neither the protocol, consent nor the IB list anemia as a risk of the study drug

Event Reporting #5

Participant with Parkinson disease is enrolled in a randomized Phase 1 clinical trial of an investigational agent to treat severe tremor

- protocol indicates participants receive oral study medication daily for six months.
- one month after starting study drug, the participant was hospitalized with fatigue and severe anemia requiring blood transfusion
- hematology work-up suggested immune mediated hemolytic anemia
- the known risk profile for this investigational agent does not include anemia and neither the protocol, consent nor the IB list anemia as a risk of the study drug

Which of the following best describes this event?

- A major protocol deviation
- Not an SAE so no expedited reporting is required
- An SAE that is not a UP and that does not require expedited reporting to the IRB but that can be reported at the time of continuing review
- An SAE that is also UP that requires expedited reporting to the IRB

Policy 801 Terminology: Reportable Event*

***Reportable Event*:** An event that occurs during the conduct of human subjects research that requires **expedited** reporting to the IRB

- At NIH, reportable events requiring expedited reporting in PROTECT using a Reportable New Information Form (RNI) include:
  - **Unanticipated problems involving risks to subjects or others** (UPIRTSOs but also referred to as UPs)
  - **Non-compliance**
    - major protocol deviations

      and
    - non-compliance that is not related to a protocol deviation
  - **Deaths related or possibly related** to research activities

(continued)

*__For FDA regulated studies__, investigators are also required to report events to the study sponsor as described in the protocol.

Policy 801 Terminology: Reportable Event*

Reportable Event (continued):

- **New information** that might affect the willingness of subjects to enroll or continue participation in the study
- Any **suspension or termination of research activities**, including holds on new enrollment, placed upon the research by the study sponsor, NIH or IC leadership, or any regulatory agency
- Any **FDA Form 483** issued for NIH protocol

- All events except deaths that require expedited reporting need to be reported to the NIH IRB **within 7 calendar days** when NIH is the Reviewing IRB (also known as the IRB of Record)
- **Deaths** that are possibly, probably or definitely related to the research must be reported to the NIH IRB **within 24 hours**

***For FDA regulated studies**, investigators are also required to report events to the study sponsor as described in the protocol.

What Makes an Event an Unanticipated Problem?

Unanticipated Problems (UPs)* Must Meet *All* Three Criteria

1. **Unexpected** (in terms of nature, severity, or frequency) given
   - the research procedures described in the protocol-related documents
   - the characteristics of the population being studied
2. **Related** or possibly related to participation in the research
3. **Places subjects or others at a greater risk of harm** related to the research than was previously known or expected
   - "Harm" can include physical, psychological, economic, or social harm
   - "Others" may include research staff, family members or other individuals not directly participating in the research

*The regulations use the term "unanticipated problems involving risks to subjects or others" so these events are also referred to elsewhere as "UPIRTSOs."

Examples of Unanticipated Problems

- Subject develops bleeding requiring transfusion two days after the 3rd infusion of investigational agent and has abnormal labs (Hgb, Hct and coags) without any history of liver dz or bleeding disorder. Protocol-related documents do not list bleeding as a potential risk.
  - ➢Problem is unexpected in **nature**

- After two weeks of investigational study drug administration, a subject develops liver failure due to diffuse hepatic necrosis without any underlying liver disease. Protocol-related documents refer only to elevated hepatic enzymes as a potential adverse event related to the investigational drug.
  - ➢Problem is unexpected in **severity**

- Study of an investigational coronary stent enrolled 50 subjects by the time of the first continuing review (CR). Review of data for the CR demonstrates that 6 of the 50 subjects (12%) had acute restenosis. The risk of acute restenosis is the protocol related documents is ≤ 5%.
  - ➢Problem is unexpected in **frequency**

Events Referred to the NIH IRB

Possible unanticipated problems

and

New information that may that might affect the willingness of subjects to enroll or continue participation in the study

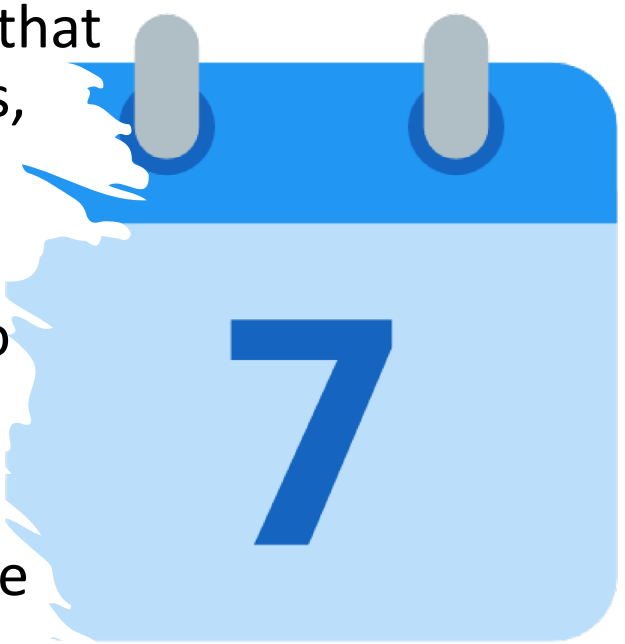
NIH IRB for determination as a UP or not and decision about any updates to the protocol and/or consent and review of any other corrective action

Policy 801 Terminology: Protocol Deviation

Protocol Deviations are a subset of non-compliance

A Protocol Deviation (PD): any change, divergence, or departure from the IRB-approved research protocol

- **Major Deviations:** Deviations from the IRB approved protocol that have, or may have the potential to negatively impact, the rights, welfare or safety of the subject, or to substantially negatively impact the scientific integrity or validity of the study
- **Minor Deviations:** Deviations that do not have the potential to negatively impact the rights, safety, or welfare of subjects or others, or the scientific integrity or validity of the study



➢ When NIH is the Reviewing IRB, **major PDs** must be reported to the IRB using the electronic IRB event form **within 7 calendar days**

Protocol Deviations: Major vs. Minor

Major Deviations

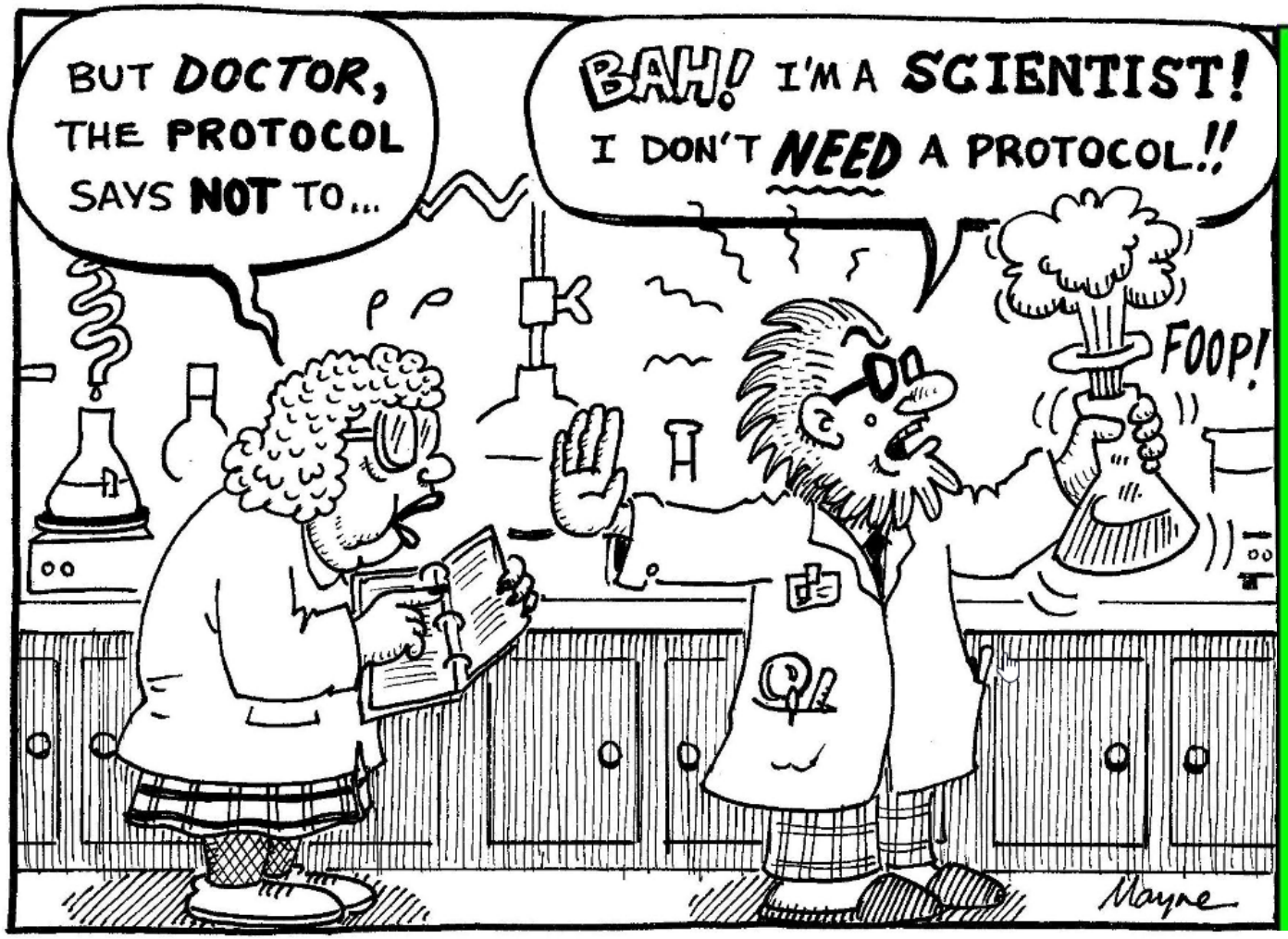
- Failing to obtain legally effective consent prior to initiating research procedures (including failure to obtained signed consent when required)
- Informed consent obtained by someone other than individuals authorized by IRB
- Enrollment of a participant who did not meet all inclusion/exclusion criteria
- Medication errors, such as administering the wrong study drug to a participant or the wrong dose of the right study drug
- Failing to conduct a study procedure or administer a study assessment that was meant to assess the safety of the individual's continuation in the study
- Study visit conducted outside the required timeframe that, in the opinion of the investigator, may impact the safety of the participant
- Performing a research procedure that has not been approved by the IRB
- Failure to report an Unanticipated Problem to the IRB and/or sponsor of the study
- Failure to follow the IRB-approved safety monitoring plan

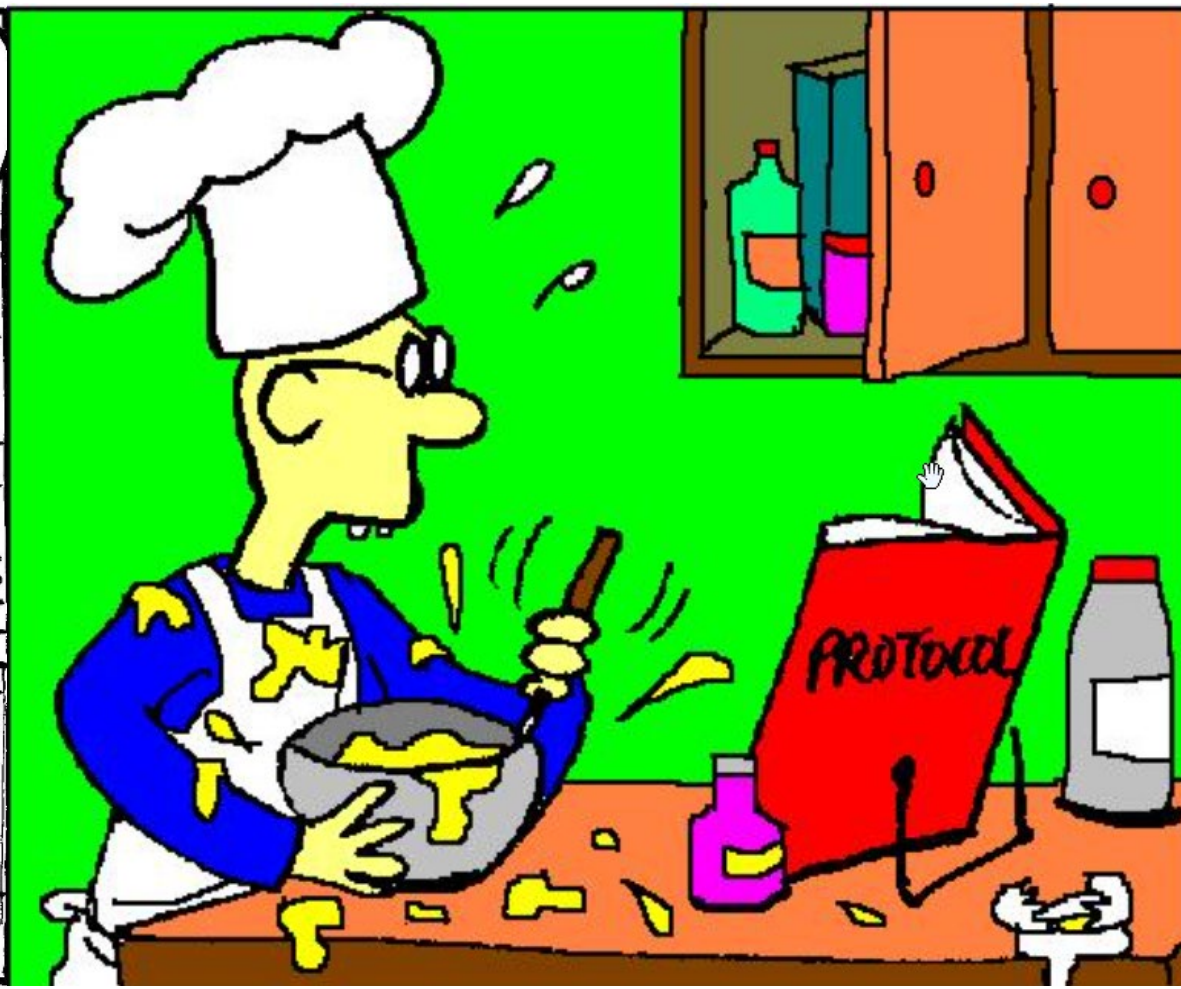
Protocol Deviations: Major vs. Minor

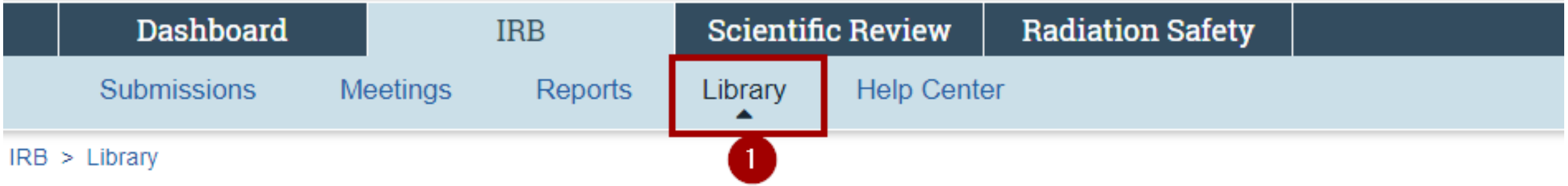
Minor Deviations

- Completing a study visit outside of the required timeframe when, in the opinion of the investigator, there are no safety implications
- Receiving completed questionnaires back from participants where items are missing but not to the extent that scientific endpoints will be affected
- Use of an expired consent form in which the information contained is not substantively different than the currently approved consent, unless the deviation occurs repeatedly
- Minimal over-enrollment
- A signed copy of the consent form was not given to the participant
- Documentation deficiencies in the consent form such as:
  - The participant signs the consent form but does not print their name in the signature block. *Note: A participant who does not sign and date the consent form prior to the initiation of research is considered a **major** deviation*

Investigators must follow the IRB approved protocol, "except when necessary to eliminate apparent immediate hazards to the subject." (§46.108(a)(3)(III) and § 56.108(a)(4))







IRB > Library

Library

Name	Document
Not Human Subjects Research Application	Not_Human_Subjects_Resea
Single Patient Modification Request	Single_Patient_Planned_Mod
Single Patient Use Expanded Access Form	Single_Patient_Use_Expande

3

3 items

page 1 of 1

Single Patient Use Modification

Note, all fields must be completed.

Protocol Title:

Do you have sponsor approval for this modification?

Note: If yes, attach sponsor approval to your modification form.

Select

Describe planned deviation and include justification for why this deviation is needed:

Please describe how the modification will/will not impact the safety of the subject or the scientific integrity of your protocol:

Location of Event:

- ◯ NIH CC
- ◯ Other NIH site
- ◯ Other

Other NIH site location, please specify:

Other location, please specify:

Describe how you will inform the subject of this change?

Describe how this modification is only affecting one individual and why your protocol should not be modified to make this change?

Provide any additional information that the IRB should know in order to make this determination:

Policy 802 Terminology: Non-compliance

Non-Compliance (NC): Failure of investigator(s) to follow the applicable laws, regulations, or institutional policies governing the protection of human subjects in research or the requirements or determinations of the IRB, whether intentional or not

- When NIH is the Reviewing IRB, **non-compliance** (*including major protocol deviations and NC not related to protocol deviations)* needs to be reported to the IRB using the electronic IRB event form within **7 calendar days**
- If OHSRP leadership determines the event is noncompliance that is neither serious nor continuing, an outcome letter with this information is sent to the PI PI proxy and the person submitting the RNI

If a major deviation or NC that is unrelated to a protocol deviation is determined by OHSRP leadership to constitute possible serious and/or continuing non-compliance, the event is referred to the NIH IRP Research Compliance and Review Committee (RCRC)

Events Referred to the NIH RCRC

Major Deviations and non-compliance (NC) unrelated to protocol deviations that OHSRP leadership believes may constitute possible serious and/or continuing noncompliance

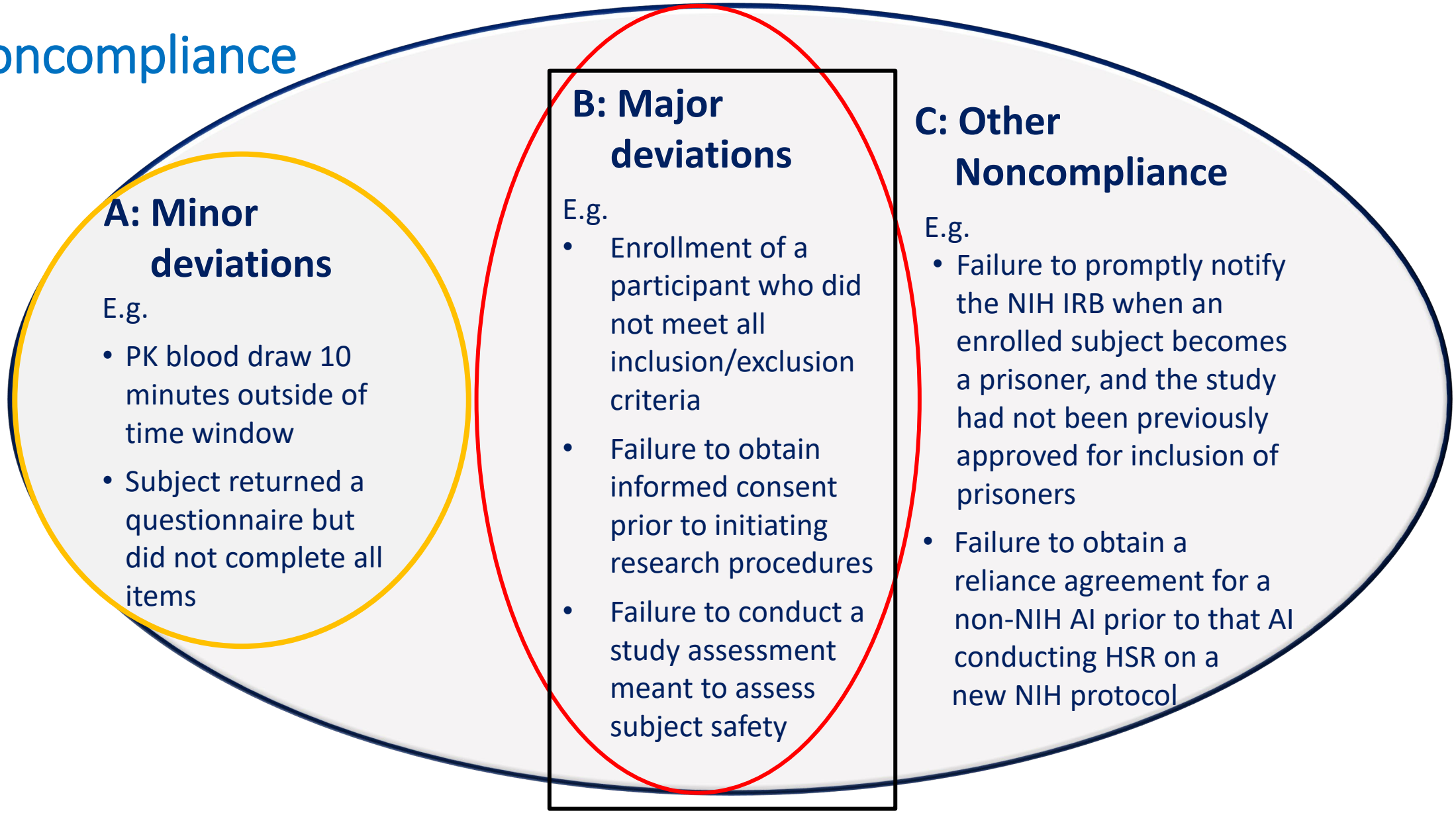
NIH RCRC for determination as to whether the NC is serious or continuing and decision about adequacy of the proposed other corrective action

Research Compliance and Review Committee (RCRC)

For protocols under review by the NIH Intramural IRB, the RCRC:

- Is a duly convened NIH IRB
- Has stable membership including IRB members who are experienced clinical researchers
- Reviews events submitted via RNI form referred by OHSRP leadership to determine if they constitute serious and/or continuing non-compliance
- Provides consistency in determinations
- Focuses on adequacy of the proposed corrective action

Noncompliance



- Events in A + B + C represent noncompliance
- Only B and C need to be reported to the NIH IRB within 7 calendar days
- Events in A can be reported at Continuing Review (as part of a high-level summary of all deviations)

Determinations Reported to Federal Agencies

- NIH IRB Determinations of UP

OR

- RCRC Determinations of serious and/or continuing NC

OR

- IRB or RCRC suspension or termination of NIH protocol

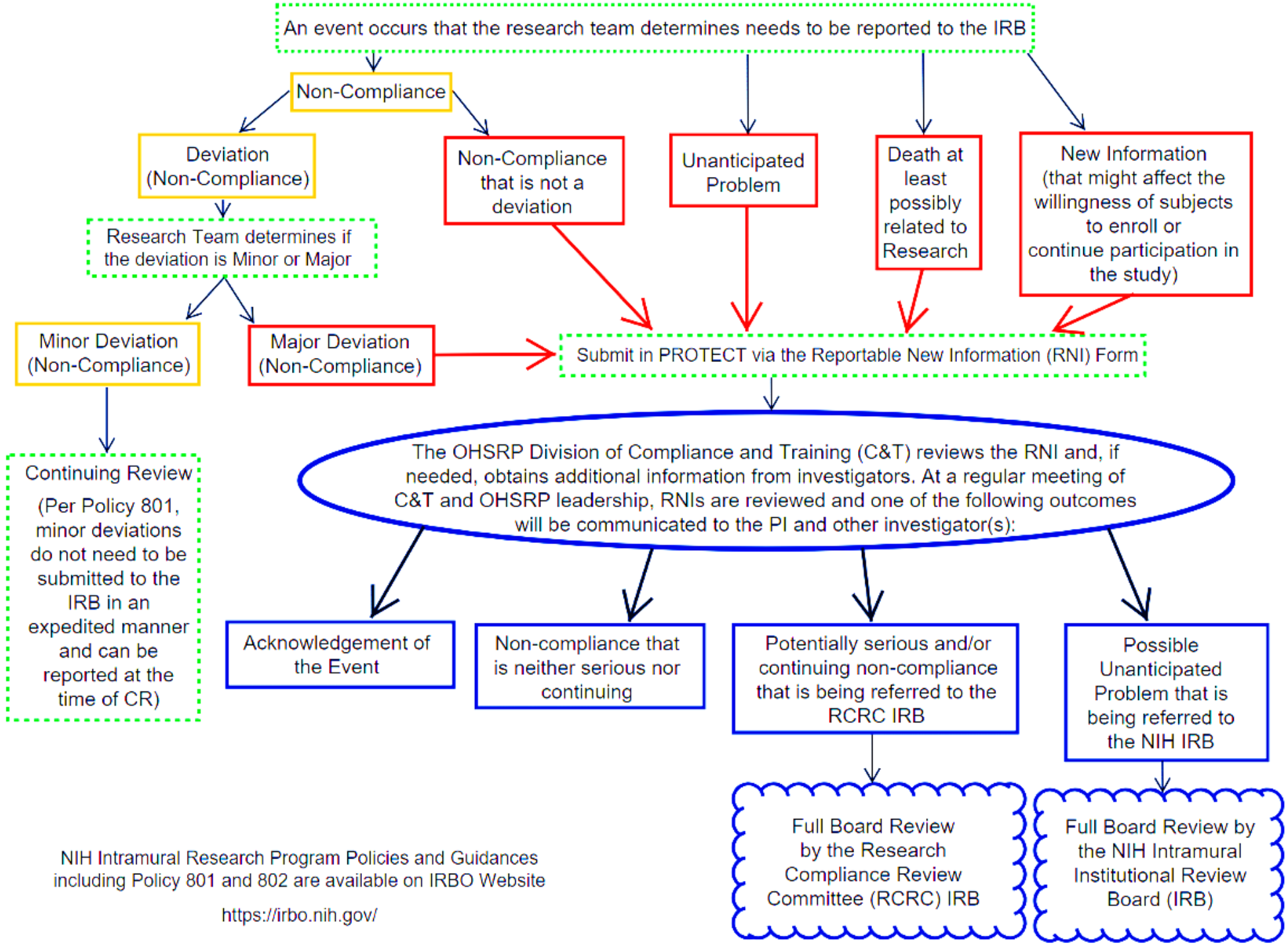
OHRP

HHS Office for Human Research Protections

and, if applicable,

U.S. Food & Drug Administration

FDA



NIH Intramural Research Program Policies and Guidances including Policy 801 and 802 are available on IRBO Website

https://irbo.nih.gov/

Timeframe for Submitting Reportable New Events in PROTECT

Within 24 hours

- Deaths that are possibly, probably or definitely related to the research

Within 7 calendar days

- Possible unanticipated problems
- Major protocol deviations
- Non-compliance that is not related to a protocol deviation
- New information that might affect the willingness of subjects to enroll or continue participation in the study
- Any suspension or termination of research activities, including holds on new enrollment, placed upon the research by the study sponsor, NIH or IC leadership, or any regulatory agency
- Any FDA Form 483 issued for NIH protocol

Adverse Events (AEs)

- Any untoward medical occurrence in a human subject, including any abnormal sign, symptom, or disease, temporally associated with the subject's participation in research, whether or not considered related to the subject's participation in the research

Adverse Events (AEs)-FDA

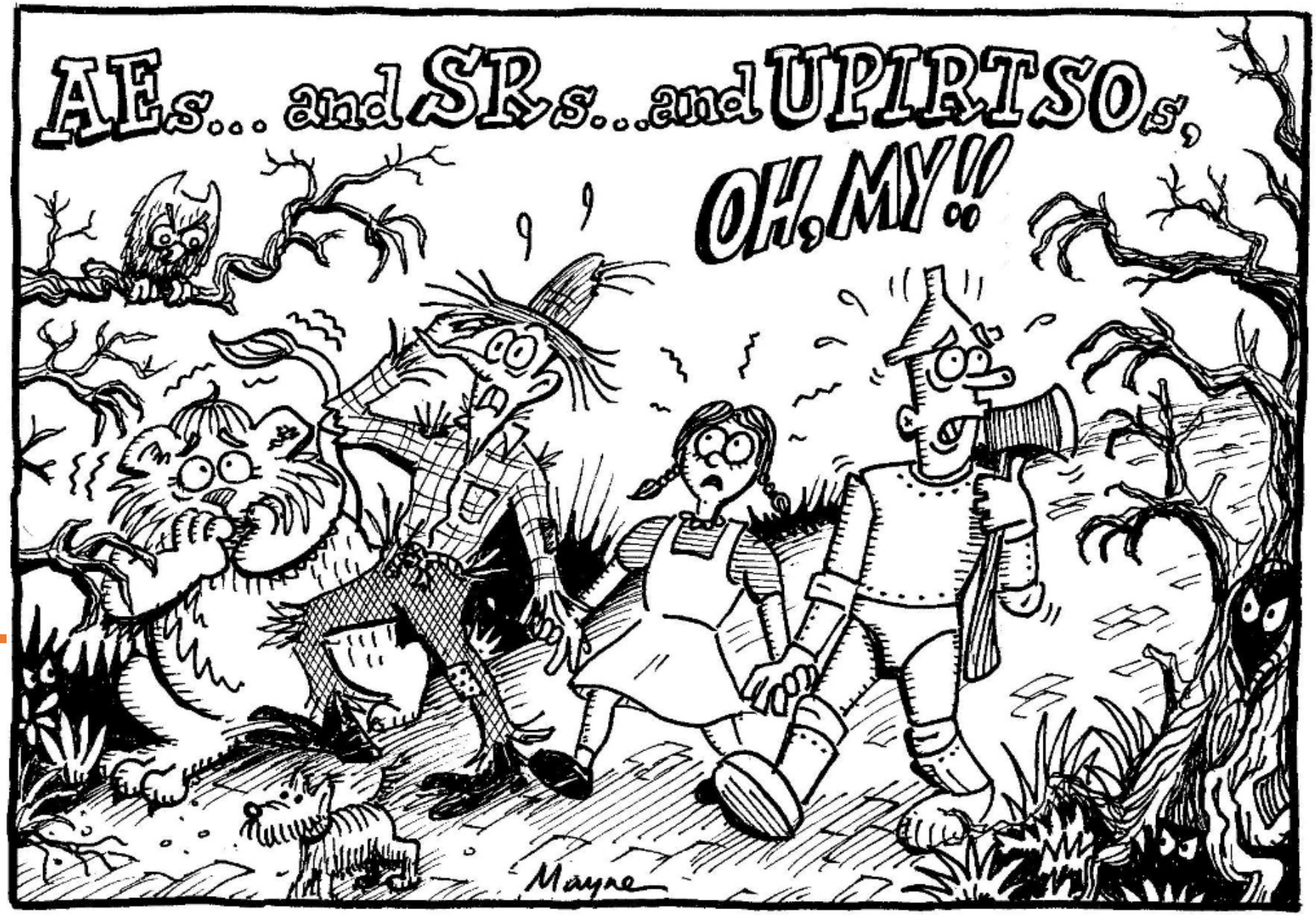
- In the context of FDA-required reporting for **drugs** being studied, an AE means any untoward medical occurrence associated with the use of a drug in humans, whether or not considered drug related
- Regarding research with FDA regulated **devices**, we refer to ***unanticipated adverse device effect*** [UADE] which means any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects

Characterization of an Adverse Event as Serious

Serious Adverse Event (SAE): is any event that:

1. Results in death OR
2. Is life-threatening OR
3. Results in patient hospitalization or prolongation of existing hospitalization OR
4. Results in a persistent or significant disability/incapacity or substantial disruption of the ability to conduct normal life functions OR
5. Results in a congenital anomaly/birth defect OR
6. Based on appropriate medical judgment, may jeopardize subject's health and may require medical or surgical intervention to prevent one of the other outcomes above

Serious Adverse Events (SAEs) vs. Unanticipated Problems



Unanticipated Problems must meet *all* three criteria

1. **Unexpected** (in terms of nature, severity, or frequency) given
   a) the research procedures described in the protocol-related documents; and
   b) the characteristics of the population being studied
2. **Related** or possibly related to participation in the research
3. **Places subjects or others at a greater risk of harm** related to the research than was previously known or expected
   - "Others" may include research staff, family members or other individuals not directly participating in the research
   - "Harm" can include physical, psychological, economic, or social harm

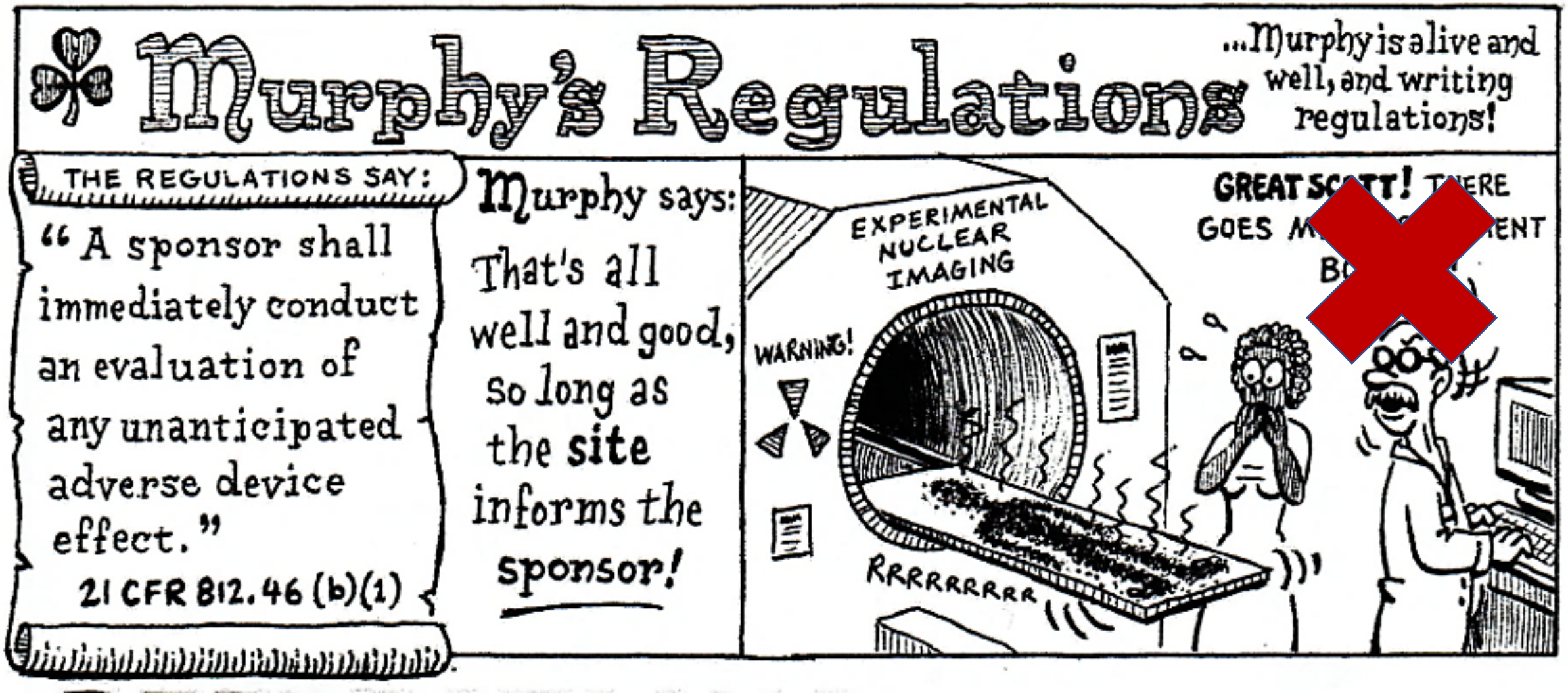
Reporting AEs and SAEs

AEs and SAEs (other than death) **only** need to be reported to the IRB in an expedited manner if they meet criteria for one of the other event categories requiring expedited reporting*

- For example: If an event is considered an SAE because it resulted in hospitalization of the participant, unless it also meets the three UP criteria or represents new information that might affect a subject's willingness to enroll or continue on study, it would not need to be reported in PROTECT within 7 days
- If an event is an SAE because the participant died, it only needs to be reported within 24 hours if it meets the criterion of being at least possibly related to research

*As per the earlier slide, in IND and IDE studies requirements for reporting these events to the sponsor may be different (and expedited reporting may be needed). Investigators need to comply with those reporting requirements.

FDA Required Reporting to the Sponsor

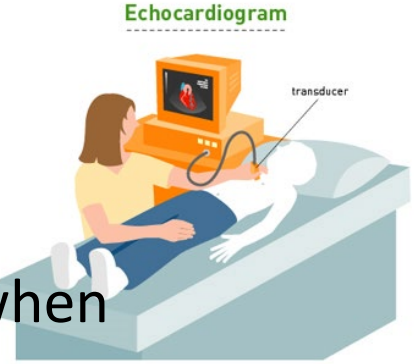


When NIH Relies on External (non-NIH) Reviewing IRB

- External IRB policies for event reporting apply
  - PI must report to external IRB in compliance with *their* policies
  - External IRB makes determinations of serious/continuing NC, and UPs and can also suspend or terminate the study
- If the event occurred at an NIH site, or directly impacts the NIH site, duplicate reporting to NIH within the same NIH IRB timeframe is required
- If the Reviewing IRB makes a determination of serious and/or continuing non-compliance regarding an NIH investigator, then, even if the determination has already been provided to OHSRP either directly or via the NIH Institutional Official (IO)/designee, the NIH PI /designee must report this in PROTECT **within 7 calendar days** of any member of the research team being notified of the determination by the Reviewing IRB
- Additional reporting may also be required as specified by an NIH Institute/Center (IC) or other NIH policy

Examples

General Examples



The one-month echocardiogram was missed. A major toxicity of the IND product is cardiotoxicity. The next NIH timepoint was not until two-months when the missed test was noted.

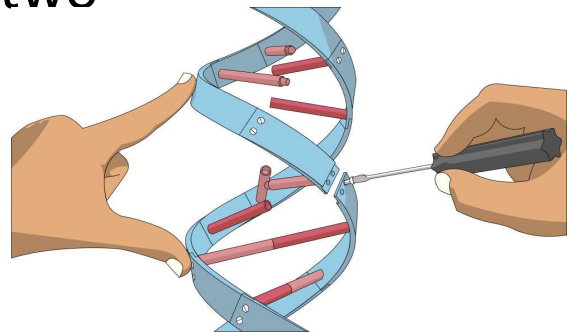
Major Deviation

Phlebotomist forgot to draw extra tube of blood for an exploratory endpoint and the participant has already left NIH. The PI indicates that the lab was not a safety test and would not substantially negatively impact the scientific integrity or validity of the study.

Minor Deviation

The participant missed his one-month post gene therapy visit during which important safety testing was required. He did not return to NIH until his two-month visit.

Major Deviation



General Examples

A subject on a Phase I study for breast and ovarian cancer developed therapy-related Myelodysplastic Syndrome/Acute Myeloid Leukemia which is not listed in the Investigator Brochure, protocol or ICF.

Possible Unanticipated Problem

- ✓ Unexpected as it was not listed in the protocol, IB or ICF
- ✓ Related to the research
- ✓ Resulted in harm

Reminder: Letters and scripts informing participants of new risks or information need to be approved by the IRB and should be included in the protocol modification submitted to the IRB to update the protocol and the ICF.

Note: This event is likely to be forwarded to the NIH Intramural Research IRB for Full Board review

The Reportable New Information Form (RNI)

Reportable New Information

1. **RNI short title:** (uniquely identify this new information report)

2. * **Date any member of the study team became aware of the information:**

3. **Date event occurred:**

Provide brief descriptive title. This also helps you locate events for auditing purposes. For example:

- Possible PII breach
- Missed safety labs
- Procedures performed before consent
- Death

(You do not need to enter the protocol # here.)

4. **Identify the categories that represent the new information:** (check all that apply)

- ☐ **Non-compliance:** Failure of an investigator to follow the applicable laws, regulations, or institutional policies governing the protection of human subjects in research, or the requirements or determinations of the Institutional Review Board (IRB), whether the failure is intentional or not.
- ☐ **Major Protocol Deviation**: Deviation from the IRB-approved protocol that has, or may have the potential to negatively impact, the rights, welfare or safety of the subject, or to substantially negatively impact the scientific integrity or validity of the study.
- ☐ **New information** that might affect the willingness of a subject to enroll or remain in the study. Examples include, but are not limited to:
  - An interim analysis that indicates a new risk or decreased effectiveness of the study intervention such that acceptability of risk is impacted
  - Withdrawal, restriction or modification of marketing approval of a drug, device or biologic used in the research
  - Publication in the literature or new marketing approval of a drug or device shown to be effective for the condition under study
- ☐ **Complaint:** Complaint of a subject that cannot be resolved by the research team.
- ☐ **Death of a subject** that is deemed to be at least possibly due to the research.

Unanticipated Problem involving risks to subjects or others (UP). To be an UP, the event must be deemed by the researcher to meet the following 3 criteria:

- Unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied; and

- 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

- Suggests that the research places subjects, or others (which may include research staff, family members or other individuals not directly participating in the research) at a greater risk of harm (including physical, psychological, economic, or social harm) related to the research than was previously known or expected

☐ **Audit:** Audit, inspection, or inquiry by a federal agency.

☐ **Confidentiality:** Breach of confidentiality.

☐ **Unreviewed change:** Change to the protocol taken without prior IRB review to eliminate an apparent immediate hazard to a subject.

☐ **Incarceration:** Incarceration of a subject in a study not approved by the IRB to involve prisoners.

☐ **Suspension:** Premature suspension or termination of the research by the sponsor, investigator, or institution.

5. * **Briefly describe the new event:**

- Describe the sequence of events in sufficient detail so that it is clear
- Indicate whether or not the event potentially impacts the rights, safety or welfare of the participant or the scientific validity or data integrity
- If there is a dose error, delay or change, indicate which day/cycle was affected and, if applicable, the study arm
- If the RNI is being submitted outside the required window, explain why
- If procedures were conducted prior to obtaining consent, list what labs/procedures were done and if they were for research

6. * **Describe corrective actions that have already been taken and any additional measures planned:**

- Provide details of steps taken to correct the problem and address any immediate safety concerns or subject rights
- Explain specific steps to be taken to prevent recurrence of the problem in the future
- The corrective action should address the specific **cause** of the event.
- If relevant, indicate if a STARS report was submitted

7. **In the submitter's opinion:**

a. * **Does this information indicate a new or increased risk, or a safety issue?**
○ Yes ○ No Clear

b. * **Does the study need revision?**
○ Yes ○ No Clear

c. * **Does the consent document need revision?**
○ Yes ○ No Clear

If revisions are required, describe them in the text box above for question regarding corrective actions and additional measures.

8. **Related studies and modifications:**

ID	Short Title	Investigator	State	IRB Office
There are no items to display				

9. **Attach files containing supporting information:**

+ Add

Name
There are no items to display

6. * **Describe corrective actions that have already been taken and any additional measures planned:**

7. **In the submitter's opinion:**

a. * **Does this information indicate a new or increased risk, or a safety issue?**
○ Yes ○ No Clear

b. * **Does the study need revision?**
○ Yes ○ No Clear

c. * **Does the consent document need revision?**
○ Yes ○ No Clear

If revisions are required, describe them in the text box above for question regarding corrective actions and additional measures.

Add the protocol(s) on which the event occurred here. If the same event affected multiple protocols, list all that were affected.

8. **Related studies and modifications:**

ID	Short Title	Investigator	State	IRB Office
There are no items to display				

9. **Attach files containing supporting information:**

+ Add

Name
There are no items to display

How well did you do with the earlier case examples?

Event Reporting #1

35-year-old with malignant tumor

- Enrolled on study, admitted to the Clinical Center, and received unblinded study drug (under IND) over 5 days
- Subsequently, his creatine kinase (CK) increased to 3122 (normal range 39-308 U/L)
- He developed myalgia attributed to rhabdomyolysis
- Elevation in the blood CK and rhabdomyolysis are not listed as a risk of the study drug and the PI attributes this to the study drug

Which of the following best describes this event?

- An SAE that is not an unanticipated problem so no expedited reporting to the IRB is needed
- An unanticipated problem that requires expedited reporting to the IRB

Event Reporting #1

35-year-old with malignant tumor

- Enrolled on study and received unblinded study drug (under IND) over 5 days
- Subsequently, his creatine kinase (CK) increased to 3122 (normal range 39-308 U/L)
- He developed myalgia attributed to rhabdomyolysis
- Elevation in the blood CK and rhabdomyolysis are not listed as a risk of the study drug and the PI attributes this to the study drug

Unanticipated Problem

- ✓ Unexpected event
- ✓ Possibly related to research
- ✓ Increased risk to the subject

Likely also requires expedited reporting to the sponsor. Make sure that it is reported within the time frame required by the sponsor.

Event Reporting #2

During an audit, it was discovered that a subject underwent research procedures including history and physical exam and also had research bloods drawn prior to completion of the consent process and signing the consent form.

Which of the following best describes this event?

- Unanticipated problem
- Minor deviation
- Major deviation
- New information that might affect a subject's willingness to enroll or continue on study

Event Reporting #2

During an audit, it was discovered that a subject underwent research procedures including history and physical exam and also had research bloods drawn prior to completion of the consent process and signing the consent form.

Major Deviation

- Information to consider and include in RNI:
  - ✓ Was there sufficient documentation of the consent process in the medical record?
  - ✓ What tests or procedures has the participant completed?
  - ✓ Was the participant's data entered into the research database?
  - ✓ What is the status of the samples and data if there is no documentation of consent?

Event Reporting #3

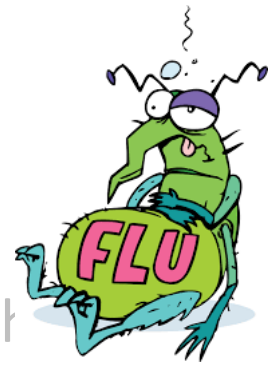
A participant with renal cell carcinoma completed last cycle of investigational chemotherapy conducted under an IND study.

- The participant was being seen monthly for follow-up visits per protocol
- Three months into follow-up, the PI heard from her family that she was admitted to the hospital over the weekend and died due to influenza
- The PI reviewed the medical records and determined that the death was unrelated to research

Which of the following best describes this event?

- An unanticipated problem that needs to be reported to the IRB within seven calendar days (expedited reporting)
- A death that is not a UP since it is not at least possibly related to the research. It does not require expedited reporting to the IRB.
- A death that is an SAE that requires expedited reporting to the IRB even though it is not related to the research

Event Reporting #3



A participant with renal cell carcinoma completed last cycle of investigational chemotherapy that is part of an IND study. The participant was being seen monthl for follow-up visits. Three months into the follow-up phase, the research team received an email from her family that she was admitted to the hospital over the weekend and died. The family said that they were told that the participant died from an influenza infection. The PI reviewed the medical records and determined that the death was unrelated to research

X Possibly related to research **(NO)**

Event (death) is an SAE that is not a UP

- Does not require expedited reporting to the IRB
- Can be reported at the time of CR
- May require expedited reporting to the sponsor (check the protocol)

Event Reporting #4

An unencrypted email was sent to an outside physician that contained the participant's first name, diagnosis, and date of birth.

Which of the following best describes this event?

- A major protocol deviation
- An SAE
- Noncompliance that is not a protocol deviation
- A minor protocol deviation

Event Reporting #4

An unencrypted email was sent to an outside physician that contair participant's first name, diagnosis, and date of birth.

Non-compliance that is not a protocol deviation

Information to consider and include in RNI:

- All potential or actual PII breaches must be reported to the NIH Privacy Office through the Incident Response Team (IRT).
- Report to the IRT by emailing IRT@nih.gov or calling the Incident Response Team Hotline at 301-881-9726. Also notify the IC Privacy Coordinators.
- The IRT will do an evaluation and notify you of their risk assessment. This assessment must be provided at the time the investigator responds to the stipulation issued by OHSRP Compliance and Training.

Note: The IRT report is used by OHSRP leadership in determining level of NC.

Event Reporting #5

Participant with Parkinson disease is enrolled in an open label Phase 1 clinical trial of an investigational agent to treat severe tremor

- Protocol indicates participants receive oral study medication daily for six months
- One month after starting study drug, the participant was hospitalized with fatigue and severe anemia requiring blood transfusion
- Hematology work-up suggested immune mediated hemolytic anemia
- The known risk profile for this investigational agent does not include anemia and neither the protocol, consent nor the IB list anemia as a risk of the study drug

Event Reporting #5

Participant with Parkinson disease is enrolled in an open label Phase 1 clinical trial of an investigational agent to treat severe tremor

- protocol indicates participants receive oral study medication daily for six months.
- one month after starting study drug, the participant was hospitalized with fatigue and severe anemia requiring blood transfusion
- hematology work-up suggested immune mediated hemolytic anemia
- the known risk profile for this investigational agent does not include anemia and neither the protocol, consent nor the IB list anemia as a risk of the study drug

Which of the following best describes this event?

- A major protocol deviation
- Not an SAE so no expedited reporting is required
- An SAE that is not a UP and that does not require expedited reporting to the IRB but that can be reported at the time of continuing review
- An SAE that is also UP that requires expedited reporting to the IRB

Event Reporting #5

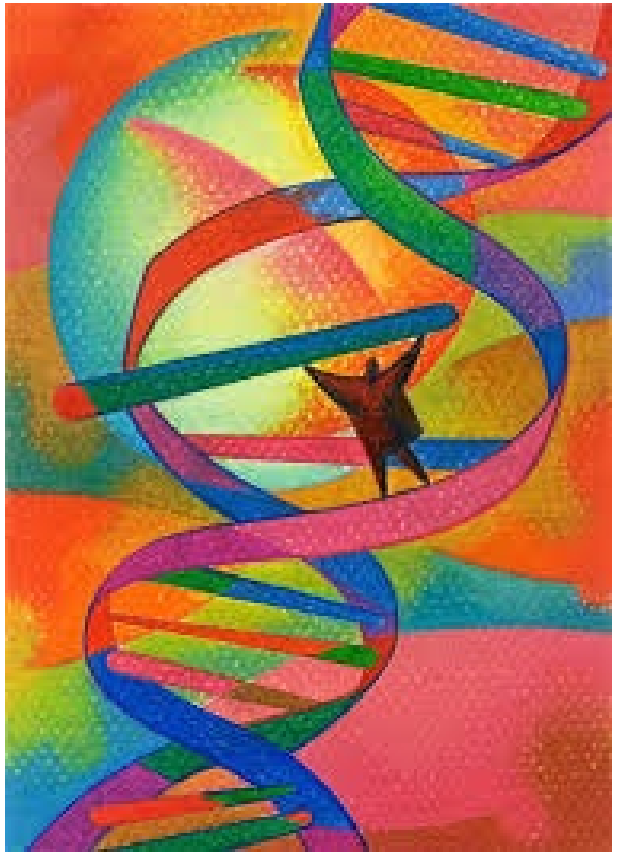
Event: Subject developed unexpected severe anemia possibly related to research

Unanticipated Problem

- ✓ Unexpected event
- ✓ Possibly related to research
- ✓ Increased risk to the subject

Likely also requires expedited reporting to the sponsor. Make sure that it is reported within the time frame required by the sponsor.

Event Reporting #6



During an IC audit, it was discovered that one of the enrolled participants did not have the correct genetic mutations required by the study inclusion criteria. Study treatment is based on the presence of specific mutations.

Which of the following best describes this event?

- Minor deviation
- Major deviation
- Noncompliance that is not a protocol deviation
- Unanticipated problem

Event Reporting #6

During an IC audit, it was discovered that one of the enrolled participants did not have the correct genetic mutations required by the study inclusion criteria. Study treatment is based on the presence of specific mutations.

Major Deviation

- Information to consider and include in RNI:
  - Where is participant in the course of the study and do changes need to be made? (e.g., Withdraw them if still pre-treatment since they are not eligible?)
  - How does this event affect the participant's safety and treatment outcome?
  - How does this impact the scientific integrity or validity of the study?

Event Reporting #7

The protocol specifies that a follow-up survey be performed at the 6-month follow-up visit. Some of the questions were not answered by several of the participants, but the scientific integrity of the study was not affected, and the survey is not being used to assess safety.

Which of the following best describes this event?

- Minor deviation
- Major deviation
- Noncompliance that is not a protocol deviation
- Unanticipated problem

Event Reporting #7

The protocol specifies that a follow-up survey be performed at the 6-month follow-up visit. Some of the questions were not answered by several of the participants, but the scientific integrity of the study was not affected because an adequate number of questions were completed to allow for full analysis.

Minor Deviation

The deviation did not impact the rights, safety or welfare of the participants and did not impact the scientific integrity of the study.

Thank You!

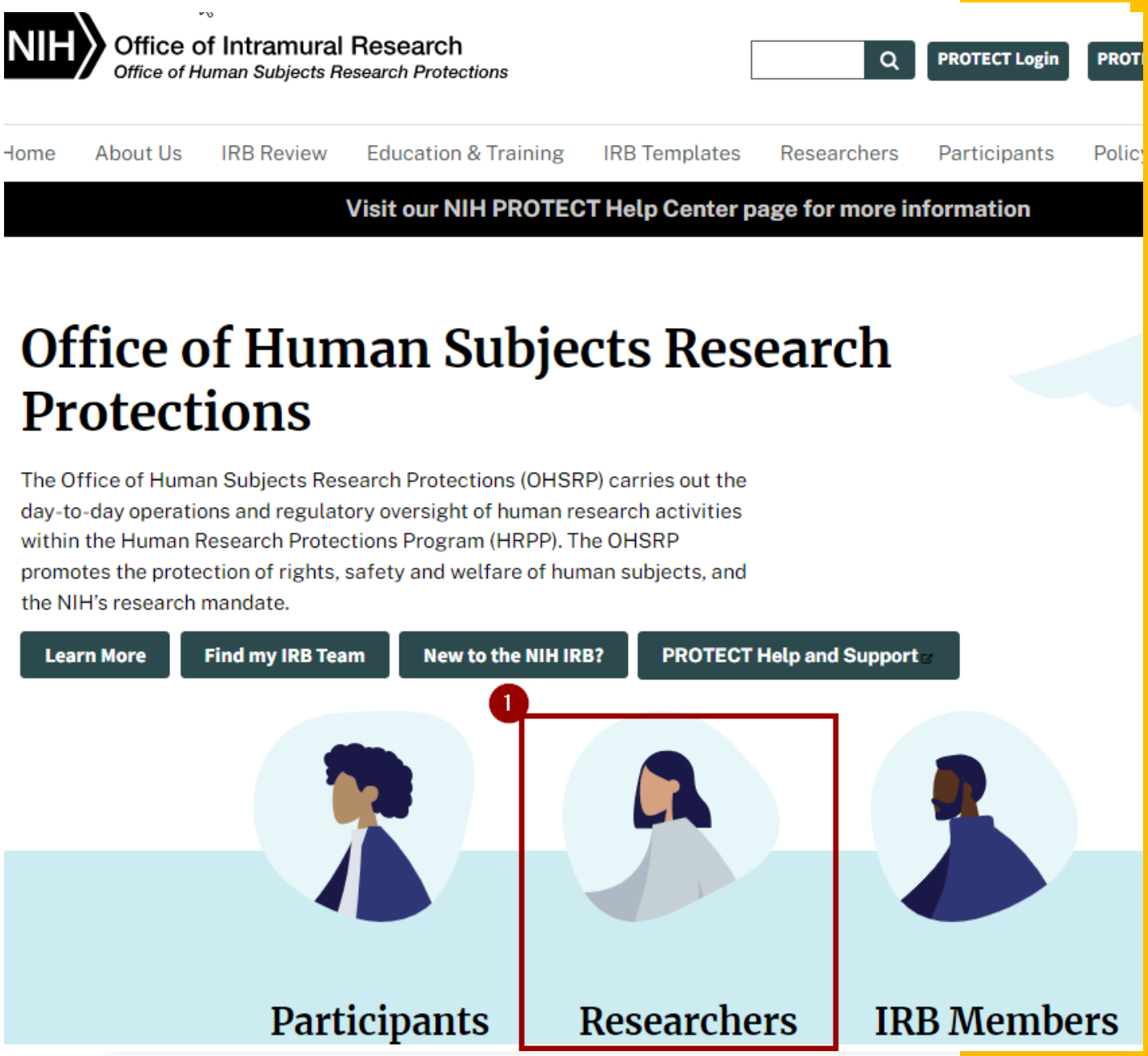
OHSRPCompliance@od.nih.gov

OHSRP website: https://irbo.nih.gov/confluence/display/ohsrp/

Posted Resources

- **Policy 801,** *Reporting Research Events:* https://policymanual.nih.gov/3014-801
- *Guidance for Reporting Research Events and Noncompliance*: https://irbo.nih.gov/confluence/download/attachments/36241835/801.%20Guidance%20-%20Reporting%20Research%20Events%20and%20Non-compliance%20v.6-09-2023.pdf?version=1&modificationDate=1688676741882&api=v2 (Click here to download the pdf.)
- OHRP: *Guidance on Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events*
- **Other Presentations:** https://irbo.nih.gov/confluence/display/ohsrp/Presentation+Archive+Static
  - OHSRP Education Series Presentation May 2019: *NIH Intramural Research Program New Policies: Reporting Research Events and Non-compliance in Human Subjects Research)* Video and Slides
  - *OHSRP Education Series May 2021: Two Years Since Release of the "NEW" OHSRP Research Related Event Reporting Policies: How is the IRP Doing?* Video and Slides
- **FAQs: General and Short Form Consent Processes** https://irbo.nih.gov/confluence/display/ohsrp/Frequently+Asked+Questions#FrequentlyAskedQuestions-FAQConsent
- **Compliance FAQs** https://irbo.nih.gov/confluence/display/ohsrp/Frequently+Asked+Questions#FrequentlyAskedQuestions-FAQCompliance

https://irbo.nih.gov/confluence/display/ohsrp/



NIH Office of Intramural Research
Office of Human Subjects Research Protections

PROTECT Login | PROTRAK/PQS Login | iRIS Login

Home | About Us | IRB Review | Education & Training | IRB Templates | Researchers | Participants | Policy & Guidelines

Visit our NIH PROTECT Help Center page for more information

Researchers

NIH Investigator Manual for Human Subjects Research

2

NIH Investigator Seminar Series

NIH Investigator Seminar Series information

Topic	Session date/time/link	Slides	Recorded Video
Determining Whether Your Project Might Require an Exemption or IRB Review, Including Submission of a Secondary Research Protocol	Monday, February 13, 2023 3:00 - 4:00 PM	Download	Recorded Video
IRB role, function & authority	Monday, March 13, 2023 3:00 - 4:00 PM	Download	Recorded Video
Planning your protocol	Monday, April 17, 2023 3:00 - 4:00 PM	Download	Recorded Video
Consent Forms and Processes: What Investigators Need to Know	Monday, May 8, 2023 3:00 - 4:00 PM	Download	Recorded Video
Investigator Responsibilities	Monday, June 12, 2023 3:00 - 4:00 PM	Download	Recorded Video
What Investigators Need to Know About Scientific Review of New and Ongoing Protocols	Monday, July 10, 2023 3:00-4:00 PM	Download	Recorded Video
Implementing the NIH Genomic Data Sharing Policy: What Intramural Investigators Need to Know	Monday, August 7, 2023 3:00-4:00 PM	Download	Recorded Video
Privacy and Confidentiality Requirements in Human Subjects Research - The Common Rule and Beyond	Monday, September 11, 2023 3:00-4:00 PM	Download	Recorded Video

Documentation and Document Management in Clinical Research	Monday, November 13, 2023 3:00-4:00 PM	Download	Recorded Video
What Investigators Need to Know About Reporting Research Related Events	Monday, December 11, 2023 3:00-4:00 PM https://nih.zoomgov.com/j/1608710077		
Quality Management in Clinical Research	Monday, January 22, 2024 3:00-4:00 PM https://nih.zoomgov.com/j/1610365339		
FDA-Regulated Studies: What Investigators Need to Know	Monday, February 12, 2024 3:00-4:00 PM https://nih.zoomgov.com/j/1603893783		
NIH Investigators and Multi-Site Research	Monday, March 11, 2024 3:00-4:00 PM https://nih.zoomgov.com/j/1605665931		
Know Before You Go-International Research	Monday, April 08, 2024 3:00-4:00 PM https://nih.zoomgov.com/j/1615507559		
Research Enrolling "Vulnerable" Individuals- What Investigators Need to Know	Monday, May 13, 2024 3:00-4:00 PM https://nih.zoomgov.com/j/1605643080