UTSW, we have a problem!

Meyad Bird, IRB Director & Erik Soliz, IRB Manager

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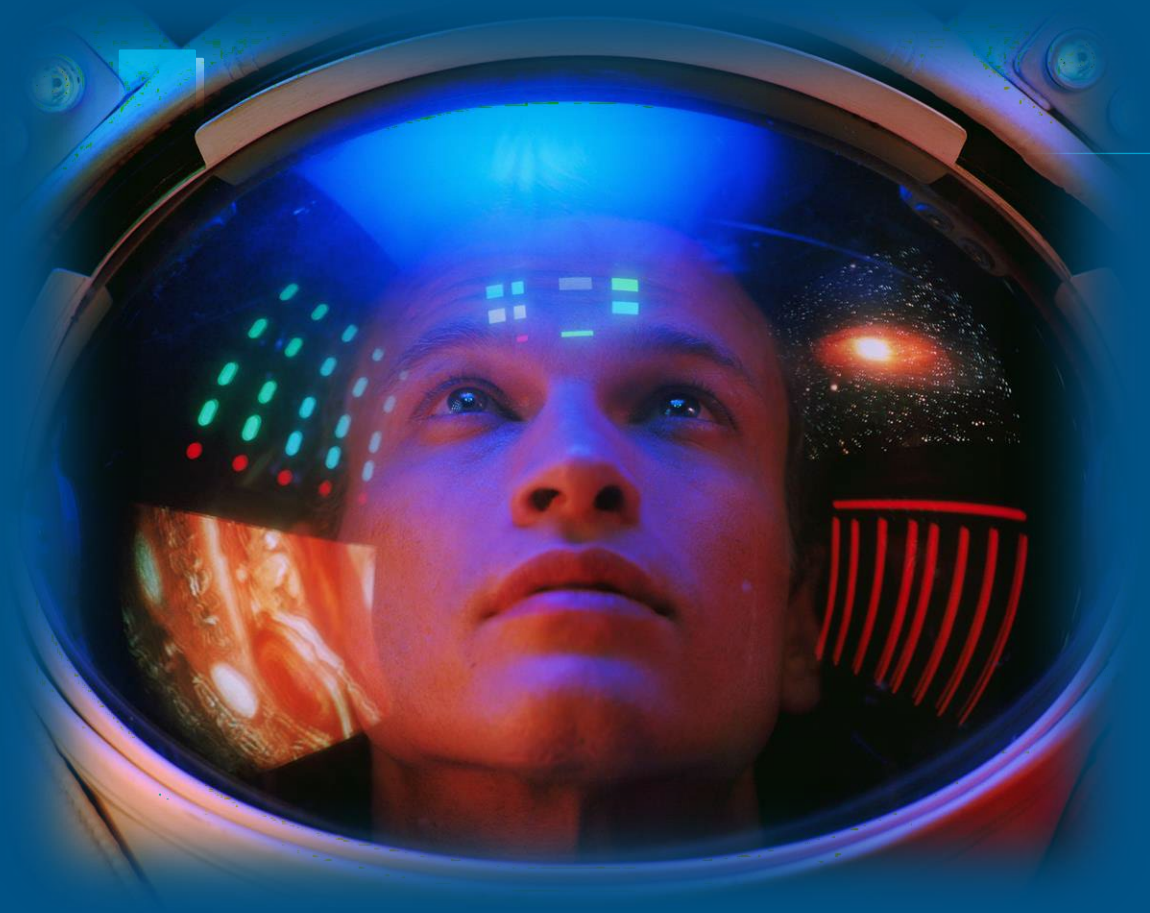
Noncompliance

Know the IRB's policy on Prompt Reporting of Noncompliance Events



Noncompliance

- Take note to what has occurred
- Important to consider so that appropriate steps be taken to:
  - protect subjects
  - Identify root cause of the event
  - Ensure that there are enough procedures in place to the noncompliance from continuing

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Corrective Actions and Preventative Actions (CAPA)

Corrective Actions

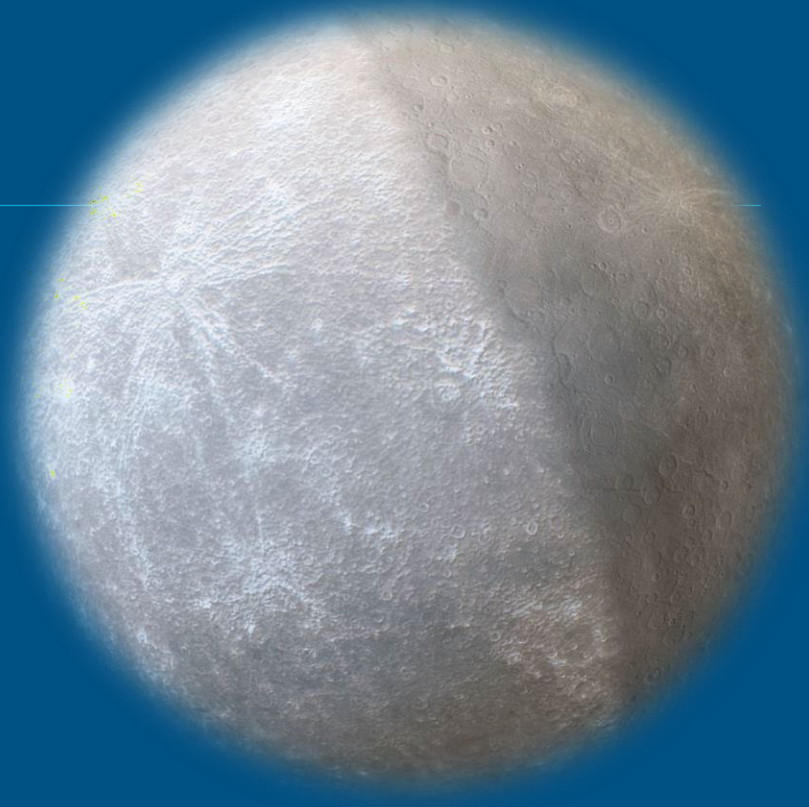
This action aims to rectify. This step usually involves taking steps to eliminate immediate hazards.

Preventative Actions

These are activities that will help prevent reoccurrence of the issue

Corrective Actions

- Care for injuries/conditions
- Verbal notification to subjects
- Additional follow-up or monitoring
- Discontinue with some or all research activities
- Notifying appropriate parties



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Preventative Actions

ROOT CAUSE ANALYSIS

DEVELOPING STANDARD OPERATING PROCEDURES

CHECKLISTS

TRAINING

MODIFYING THE STUDY

RECONSENTING SUBJECTS

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Mishap Report - Reporting the event to the External IRB

Know the IRB which provides regulatory oversight of the study at UTSW

Become acquainted with prompt reporting policies of noncompliance for the IRB of record they may be different from UTSW's IRB policies

Regardless of whether the external IRB requires prompt reporting of the event or not, you **MUST REPORT THE EVENT TO THE UTSW IRB**

If reporting to the external IRB is not required – indicate why in the Reportable Event within RE smartform

If reporting to the external IRB is required – Report the event to the reviewing IRB prior to reporting to UTSW. UTSW must be notified of the outcome of the external IRB's determination. This is required to close the event locally.

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Reporting the events – UTSW IRB

Reportable Event Type

1

Note: *Review the RE Guidance before submitting a RE: http://www.utsouthwestern.edu/research/research-administration/irb/assets/policies-combined.pdf*

* **1.0 Check ALL that apply:**

- [ ] Single-Subject Exception Request (one-time modification that is requested prior to implementation)
- [ ] Short Form Consent Request (use when non-English speaking subject presents and there is insufficient time to obtain full translation)
- [x] Noncompliance
- [ ] Unanticipated Problem Involving Risks to Subjects or Others (UPIRSO): The event is unexpected; probably or definitely related to the research; and suggests an increased risk of harm to subjects or others than was previously known or recognized
- [ ] Emergency Deviation (has already occurred and was necessary to avoid immediate apparent harm or to protect the life or physical well-being of subject(s) or others)
- [ ] Complaint (affects the rights/safety/welfare of subjects)

* **2.0 Select the special or vulnerable populations involved in the event:**

- [x] N/A - this event did or does not involve any of the following populations listed below:
- [ ] Children
- [ ] Pregnant women/fetuses
- [ ] Non-viable neonates/neonates of uncertain viability
- [ ] Prisoners
- [ ] Cognitively impaired (adult surrogate consent)
- [ ] Other

* **3.0 Date event occurred:**

9/6/2018

* **4.0 Date PI became aware of event:**

8/23/2021

The IRB uses this information to determine whether the event reporting met policy requirements

5.0 If the RE was not submitted by the PI to the IRB within 5 days, explain the reason for delay:

You must provide a reason why there was a delay in reporting to the IRB in a timely fashion. Not being aware of policy requirements is not an acceptable response.

This helps the IRB determine if additional corrective action is required centered around prompt reporting.

Exit Save Continue

* **6.0 Institution(s) where issue/event occurred:**

This helps us determine if other study sites need to be notified

- [ ] UT Southwestern Medical Center
- [x] Parkland
- [ ] Children's Health
- [ ] Texas Scottish Rite
- [ ] Texas Health Resources
- [ ] Other

2

7.0 Participant number and/or Medwatch number (if applicable):

* **8.0 How many total subjects have enrolled in this study at your site?**

427

Should the event be required to be reported to federal entities such as FDA, this information is required

* **9.0 What is the current status of the study? Check ALL that apply:**

This helps the IRB determine whether the CAPA is appropriate and whether subjects should be informed

- [ ] No subjects have yet or ever enrolled at our site
- [ ] Enrollment is ongoing at our site
- [ ] Subjects are on treatment at our site
- [ ] No subjects are on treatment at our site
- [x] Subjects are in follow-up at our site (but none are on active treatment)
- [ ] Study is complete at our site (all subjects have completed follow-up)
- [ ] Study enrollment has been temporarily suspended by the Sponsor
- [ ] Study has been terminated by the Sponsor
- [ ] Other

* **10.0 What happened?** ***Describe in detail the event or issue (e.g., if the protocol was not followed, explain what was done incorrectly):***

Provide a high-level summary of the event. Should details such as dates be needed, include in this section. Refrain from using names of individuals and instead, refer to a person by their assigned role on the study.

* **11.0 Why/how did the event occur?** ***(Describe the root cause and/or circumstances leading to the event/underlying problem/contributing factors):***

This section should be used to describe why the issue or problem occurred. You may focus on root cause findings, underlying issues or factors that contributed to the noncompliance.

This response will help the IRB identify what harms actually occurred, if any.

* **12.0 Did the event ACTUALLY affect the rights, safety, or welfare of the subject(s) (i.e., were there any AEs or other negative effects related to the event)?**

○ Yes ● No Clear

* **12.2 If no actual harm occurred, describe what risks/harms could have occurred to affect subjects' rights, safety, or welfare (i.e., were there any near-misses)?**

Describe harms. Harms can include physical harms (e.g., injury, abnormal lab values, unintended hospitalizations, etc.) and non-physical (e.g., emotional distress, breach of confidentiality, right to be informed, etc.)

* **13.0 Did the event affect the data or science of the study? (e.g.,** ***Is the data usable? Can the primary endpoint/objective be answered?)***

○ Yes ● No Clear

Consider whether the event affected the integrity or validity of the science.

* **14.0 Has the sponsor been notified?**

○ Yes ● No Clear

* **Select why the sponsor has not been notified:**

- ☑ PI is the sponsor-investigator
- ☐ Notification originated from the sponsor
- ☐ Other

*15.0 Who else has been notified? *Check ALL that apply*

- Privacy Office: ☐
- Compliance Office: ☐
- Non-UTSW IRB (i.e., Central/External/Reliance/Single IRB): ☐
- FDA: ☐
- Department Chair: ☐
- Currently enrolled subjects: ☐
- Previously enrolled subjects: ☐
- No one else has been notified: ☑
- Other: ☐

This helps the IRB understand who has been notified of the event. Failure to notify certain parties could mean that the IRB may require notification to those individuals or entities.

4

* 16.0 What has been or will be done as part of the corrective and preventive action (CAPA) plan (i.e., the PI's or sponsor's actions taken since discovery of the event and plans to prevent future occurrences)? Select all that apply.

- ☑ Departed from the protocol without prior IRB approval to eliminate apparent immediate harm or to protect the subject's life or physical well-being (describe below)
- ☐ Modify protocol or study procedures (describe below)
- ☐ Modify informed consent form or process (describe below)
- ☑ The research will be voluntarily placed on hold, pending more information or resolution of problem
- ☐ The research will be voluntarily closed
- ☐ Additional training of study staff will be provided (describe below)
- ☐ No action is planned (describe below)
- ☐ Other (specify) (describe below)

This is where you inform the IRB of the procedures you have done or plan to do to resolve and prevent the event from happening again. Noncompliance will typically always involve additional training.

* 16.1 Provide details for the CAPA plan:

This area is for you to detail items selected above. Remember to include specifics such as what will be changed in the consent form whether some or all subjects will be reconsented, etc.

If you provided training - include what topic was discussed and provide evidence of the individuals who underwent the training by uploading a sign-in sheet.

Exit Save Continue

sIRB Reporting

- It is important for the lead PI and research team to understand UTSW's reporting requirements.
- Relying sites are subject to UTSW's IRB policies regarding prompt reporting of noncompliance

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Documenting in Regulatory File

- Record the event on deviation tracking log
- Evaluate whether the event should be promptly reported
- Should events rise to the level of a Reportable Event, record the planned preventative actions in your research records. Including **who** will complete them and **when** they will be completed
- Evidence of completion of actions plans should be maintained with the CAPA Plan
- Record who is responsible for implementing, assessing, and closing the CAPA Plan
- Should it be necessary, reassess whether the CAPA plan needs to be updated

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Mission: Report and Resolve

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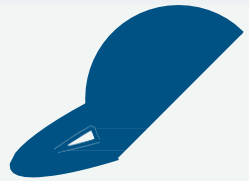
UPIRSO & UADE



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Know the IRB's policy on Prompt Reporting of Unanticipated Events

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UPIRSO/UADE Observatory: Take note to what has occurred

Internal events

- Will typically be an adverse event but can be new information based on literature
- PI responsible for:
  - Providing appropriate participant care and eliminate hazards to the participant
  - Evaluating and taking steps to ensure that harm does not continue for others

External Events/Information

- PI responsible for:
  - Reviewing all incidents, experiences, and outcomes [information] that may represent UPIRSO or UADE
  - Determining whether any reviewed incidents, experiences, and outcomes represent a possible UPIRSO or UADE
- Important to consider so that appropriate steps be taken to
  - Protect subjects
  - Ensure harm does not continue for the single subject or others

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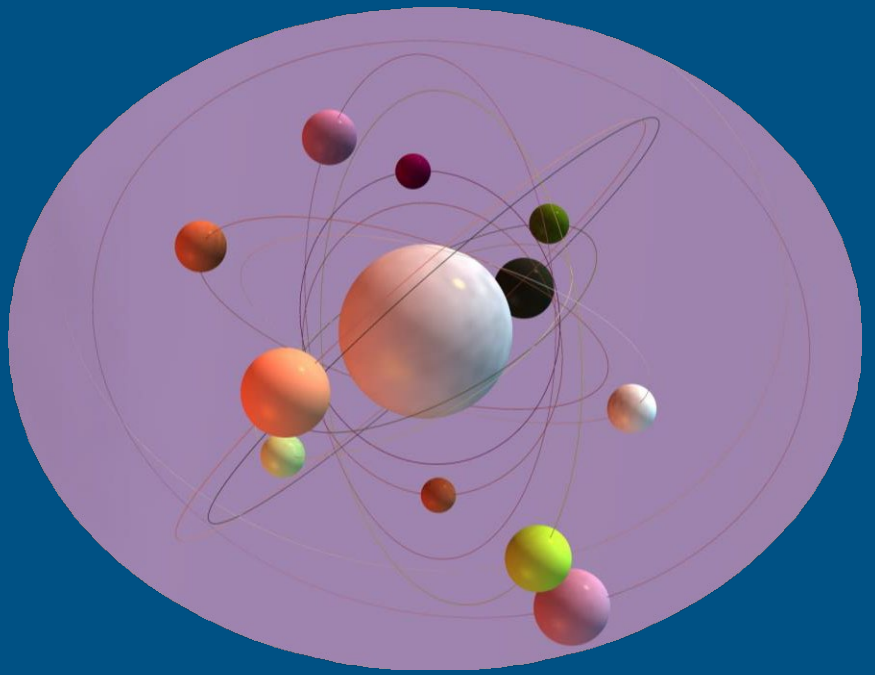
Corrective Actions – Eliminating immediate hazards

- Care for injuries/conditions
- Verbal notification to subjects
- Additional follow-up or monitoring
- Discontinue with some or all research activities
- Notifying appropriate parties



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Preventative Actions

- Halting the entire study
- Halting a component of the study (e.g., enrollment)
- Submitting follow-up reports as applicable

- Contacting institutions involved with the event for recommendations or additional requirements
- Notification of currently enrolled or completed subjects
  - Immediately via phone call
  - Reconsenting at next scheduled visit

- Modifying the protocol and consent form and other pertinent documents
- Modify the consent process/plan to re-consent enrolled participants
- Increase monitoring by updating procedures,
- Change the DSMP

Situation Report: Reporting the event to the External IRB

Know the IRB which provides regulatory oversight of the study at UTSW

Become acquainted with prompt reporting UPIRSO and UADE policies of that IRB as they may be different from UTSW's IRB policies

Regardless of whether the external IRB requires prompt reporting of the event or not, you **MUST REPORT THE EVENT TO THE UTSW IRB**

If reporting to the external IRB is not required – indicate why in the Reportable Event within RE smartform

If reporting to the external IRB is required – Report the event to the reviewing IRB prior to reporting to UTSW. UTSW must be notified of the outcome of the external IRB's determination. This is required to close the event locally.

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Reportable Event Type

Note: *Review the RE Guidance before submitting a RE: http://www.utsouthwestern.edu/research/research-administration/i*

* **1.0 Check ALL that apply:**

- [ ] Single-Subject Exception Request (one-time modification that is requested prior to implementation)
- [ ] Short Form Consent Request (use when non-English speaking subject presents and there is insufficient time to obtair
- [ ] Noncompliance
- [x] Unanticipated Problem Involving Risks to Subjects or Others (UPIRSO): The event is unexpected; probably or definite
- [ ] Emergency Deviation (has already occurred and was necessary to avoid immediate apparent harm or to protect the li
- [ ] Complaint (affects the rights/safety/welfare of subjects)

* **2.0 Select the special or vulnerable populations involved in the event:**

- [x] N/A - this event did or does not involve any of the following populations listed below:
- [ ] Children
- [ ] Pregnant women/fetuses
- [ ] Non-viable neonates/neonates of uncertain viability
- [ ] Prisoners
- [ ] Cognitively impaired (adult surrogate consent)
- [ ] Other

* **3.0 Date event occurred:**

12/28/2020

* **4.0 Date PI became aware of event:**

5/1/2023

5.0 If the RE was not submitted by the PI to the IRB within 5 days, explain the reason for delay:

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* **6.0 Institution(s) where issue/event occurred:**

- [ ] UT Southwestern Medical Center
- [ ] Parkland
- [ ] Children's Health
- [ ] Texas Scottish Rite
- [ ] Texas Health Resources
- [x] Other

Select where the event occurred. If other, list the site name if known, if not known, indicate "non-UTSW or affiliate site". This assists the IRB in meeting our reporting requirements consistent with any established MOU or IAA with our affiliates or when we serve as the IRB of record. For sIRB studies you need to list the site where the event occurred.

* **Other institution name:**

site 19

7.0 Participant number and/or Medwatch number (if applicable):

* **8.0 How many total subjects have enrolled in this study at your site?**

34

Indicate total # of subjects enrolled which is reported to the FDA. For sIRB studies you would need to include the total number enrolled at the site where the event occurred.

* **9.0 What is the current status of the study? Check ALL that apply:**

- [ ] No subjects have yet or ever enrolled at our site
- [ ] Enrollment is ongoing at our site
- [ ] Subjects are on treatment at our site
- [x] No subjects are on treatment at our site
- [ ] Subjects are in follow-up at our site (but none are on active treatment)
- [ ] Study is complete at our site (all subjects have completed follow-up)
- [x] Study enrollment has been temporarily suspended by the Sponsor
- [ ] Study has been terminated by the Sponsor
- [ ] Other

Item 10.0 – Describe the unanticipated event in detail in a manner that is concise that identifies the actual event.

* **10.0 What happened? *Describe in detail the event or issue (e.g., if the protocol was not followed, explain what was done incorrectly):***

A participant at an external non-UTSW site experienced an event of anaphylactic shock, which was determined to be probably (or definitely) related to the research.

Item 11.0 – This is where you describe the root cause of the event and note the causality of the event to the approved research and who (PI or sponsor) made this determination.

* **11.0 Why/how did the event occur? *(Describe the root cause and/or circumstances leading to the event/underlying problem/contributing factors):***

* 12.0 Did the event ACTUALLY affect the rights, safety, or welfare of the subject(s) (i.e., were there any AEs or other negative effects related to the event)?
● Yes ○ No Clear

* 12.1 How did the event ACTUALLY affect the rights, safety, or welfare of the subject(s)? (Include any AEs and other negative effects related to the event):

Explain how the UPRISO or UADE impacted the welfare and safety of the subject(s) by describing how the event increased risk and/or harm to subjects.

* 13.0 Did the event affect the data or science of the study? (e.g., *Is the data usable? Can the primary endpoint/objective be answered?)*
○ Yes ● No Clear

Item 13.0 It is important for the IRB to know whether the UPIRSO or UADE impacted the data or the science of the study. (i.e. device malfunction)

* 14.0 Has the sponsor been notified?
● Yes ○ No Clear

* 14.1 Describe the sponsor's determinations and actions. Include the date of initial sponsor notification:

Sponsor's determination and actions will assist and dictate the CAPA Plan.

Item 15.0 Knowing who was notified assists the IRB in ensuring the appropriate entities have been made aware and the response to Item 15.1 assists in knowing what actions have been or will be made. (i.e. FDA halting study for further analysis)

*15.0 Who else has been notified? *Check ALL that apply*

Privacy Office:	☐
Compliance Office:	☐
Non-UTSW IRB (i.e., Central/External/Reliance/Single IRB):	☐
FDA:	☐
Department Chair:	☑
* Date notified:	5/1/2023
Currently enrolled subjects:	☐
Previously enrolled subjects:	☐
Other:	☐

* 15.1 For those notified in 15.0, describe their determinations, responses, and/or actions of each below.

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* **16.0 What has been or will be done as part of the corrective and preventive action (CAPA) plan (i.e., the PI's or sponsor's actions taken since discovery of the event and plans to prevent future occurrences)? Select all that apply.**

- [ ] Departed from the protocol without prior IRB approval to eliminate apparent immediate harm or to protect the subject's life or physical well-being (describe below)
- [ ] Modify protocol or study procedures (describe below)
- [ ] Modify informed consent form or process (describe below)
- [ ] The research will be voluntarily placed on hold, pending more information or resolution of problem
- [ ] The research will be voluntarily closed
- [ ] Additional training of study staff will be provided (describe below)
- [x] No action is planned (describe below)
- [ ] Other (specify) (describe below)

* **16.1 Provide details for the CAPA plan:**

This section is used to describe in detail what has been done as part of the CAPA.

You will need to be specific, especially when training is planned. You will need to include what information was disseminated, who received training, and the date training was complete.

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sIRB Reporting

Know which sites that are relying on the UTSW IRB

Ensure you have detailed information on the event that occurred at external sites to provide the level of detail required in the RE Smartform submission.

Ensure your external sites are aware of their responsibility to notify the Lead PI/Research Team of events that require prompt reporting according to the UTSW HRPP Reporting Policy

You **MUST REPORT APPLICABLE EVENTS TO THE UTSW IRB** that occur at other sites relying on the UTSW IRB

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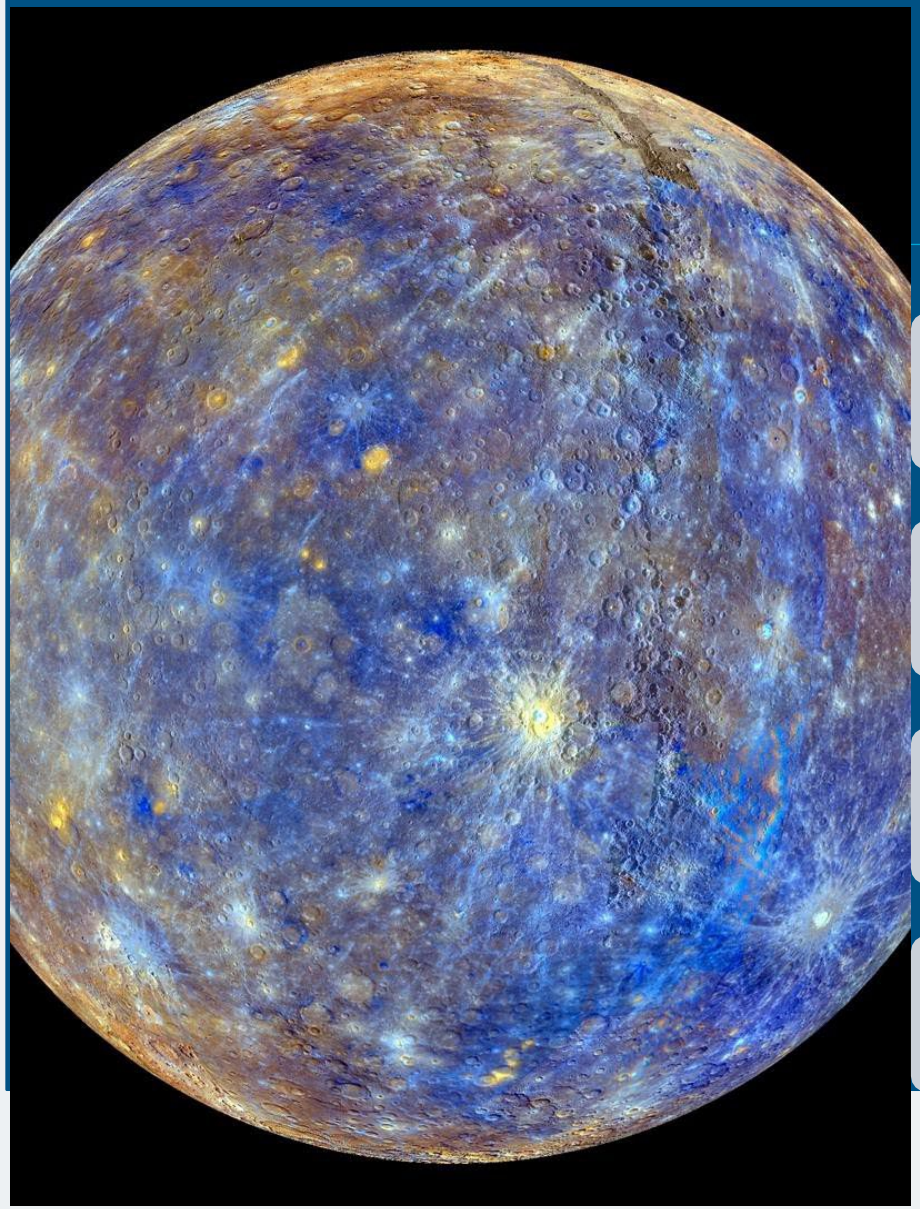

Documentation in Research Regulatory File

- Record the event on AE & UPIRSO tracking log. This includes events that may be considered UADE events
- Evaluate whether the event meets criteria as a reportable event, record actions taken to eliminate immediate hazards and other actions that are planned as preventative actions in your research records.
- Evidence of completion of actions should be maintained with the CAPA Plan as well as any participant research record as applicable
- It may be necessary to update the CAPA plan if the IRB requires additional actions to the proposed CAPA Plan

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Mission: Report and Resolve

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Post-Mission Brief

- Be aware of the reporting policies regarding noncompliance and UPIRSO/UADEs
- Take note to what has occurred
- Eliminate immediate hazards
- Develop a plan in place to help prevent the issue from reoccurring
- Report events according to the review IRB's policies
- Always report your events to UTSW when UTSW IRB is not the IRB of record
- Ensure that reports are thorough and provide enough information so that the IRB does not need to ask for additional CAPA items
- Document the event, including CAPA, in research records

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Thank You!

- **We'd love to hear your feedback.** We invite you to provide your evaluation of Research Matters and of the Human Research Protection Program.

- Visit: https://ais.swmed.edu/redcap/surveys/?s=3PRJFCFJJW

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