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1. Overview

1.1 Purpose

This policy establishes the requirements for the prompt identification, reporting, and review of unanticipated problems involving risks to subjects or others (UPIRTSO), allegations of noncompliance, serious or continuing noncompliance, and other reportable information. It defines the responsibilities of investigators to report events to the DUHS IRB. These requirements are in accordance with federal regulations, institutional policies, and accreditation standards. The overarching goal of this policy is to ensure appropriate oversight of human subjects research and to protect the rights, safety, and welfare of research participants.

This policy applies to all investigators and research personnel conducting human subjects research under the oversight of the DUHS IRB, including research conducted at DUHS, research conducted at external sites under DUHS IRB oversight through reliance agreements, and DUHS investigators conducting research under the oversight of an external IRB when DUHS internal reporting requirements apply. See Section 3. Reliance Agreements & Prompt Reporting Requirements for additional information.

2. Definitions

Complaint is defined as a concern expressed by subjects or others about the conduct of the study or a subject's participation.

Noncompliance is defined as any failure to follow:

- Applicable federal regulations, state or local laws, or institutional policies governing human subject protections, or
- The requirements or determinations of the IRB, including the requirements of the approved investigational plan (i.e., protocol deviations).

Noncompliance may result from performing an act that violates these requirements or failing to act when required. Noncompliance, including allegations of noncompliance, may be minor or sporadic, or it may be serious or continuing as defined below:

Allegations of Noncompliance describes an event that appears to constitute noncompliance, but the IRB has not yet made a formal assessment of the event.

Serious Noncompliance is defined as noncompliance that:

- increases risk of harm to subjects;
- adversely affects the rights, safety, or welfare of subjects; or
- adversely affects the integrity of the data or the research.

Continuing Noncompliance is defined as a pattern of repeated noncompliance which continues after it has been determined that noncompliance occurred, including:

- inadequate effort to take corrective actions, or
- comply with IRB requirements within a reasonable timeframe.

Unanticipated problems involving risks to subjects or others (UPIRTSO) refer to any incident, experience, outcome, or new information that:

- **Is unexpected**, meaning the incident, experience or outcome is not expected (in terms of nature, severity, or frequency) given the research procedures that are described in the study-related documents, such as the IRB-approved research protocol, electronic submission, and informed consent documents; and the characteristics of the subject population being studied; and

- **Is at least possibly related to participation in the research**, meaning there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures, interventions, products involved in the research; and
- **Indicates that subjects or others are at a greater risk of harm** (including physical, psychological, economic, legal or social harm) than was previously known or recognized

Adverse Event (AE) means any untoward or unfavorable occurrence in a human subject, including any abnormal sign (for example, abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the subject's participation in the research, whether or not considered related to the subject's participation in the research. Adverse events encompass both physical and psychological harms. They occur most commonly in the context of biomedical research, although on occasion, they can occur in the context of social and behavioral research.

Serious Unexpected Suspected Adverse Reaction (SUSAR) refers to any suspected adverse reaction to study product, including the investigational drug/s and active comparators), that is both serious and unexpected for research that is subject to the FDA's IND regulations. Sponsors, or sponsor-investigators, are responsible for determining whether an event meets all three components of this definition.

Unanticipated Adverse Device Effect (UADE) 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 related to the rights, safety, or welfare of subjects (21 CFR 812.3(s)).

3. Reliance Agreements and Prompt Reporting Requirements

For studies conducted under an IRB reliance agreement, reporting responsibilities are determined by whether the DUHS IRB serves as the IRB of record and the terms of the applicable reliance agreement.

When the DUHS IRB serves as the IRB of record, the DUHS Principal Investigator (PI) is responsible for reporting all events required under this policy in accordance with the reporting requirements and timelines described herein. This includes events occurring at DUHS and, for multisite studies in which the DUHS IRB serves as the reviewing IRB, reportable events from all relying sites, regardless of where the event occurred.

When the DUHS IRB is not the IRB of record, investigators must report to the DUHS IRB any event occurring at DUHS, involving DUHS participants, or involving DUHS personnel that the reviewing IRB has determined to be an Unanticipated Problem Involving Risks to Subjects or Others (UPIRTSO), Serious Noncompliance

(SNC), or Continuing Noncompliance (CNC), as well as any event that meets the definition of Other Reportable Information described in Section 5. These events must be reported to the DUHS IRB within 10 working days of the reviewing IRB's determination. Reports of UPIRTSOs, SNC, or CNC must include documentation of the reviewing IRB's determination, as the DUHS IRB cannot complete its review without that documentation. If the reviewing IRB has not made a determination of UPIRTSO, SNC, or CNC and the event does not otherwise meet the criteria of Other Reportable Information, reporting to the DUHS IRB is not required.

Regardless of which IRB serves as the IRB of record, investigators and study teams must also comply with any reporting requirements specified in the applicable reliance agreement.

4. Promptly Reportable Requirements

All individuals engaged in human subjects research are responsible for promptly reporting events, concerns, and other information requiring IRB review to the Institutional Review Board (IRB) of record and, when applicable, the institution where the event occurs. Timely reporting supports IRB oversight, promotes the protection of research participants, and ensures compliance with applicable federal regulations, institutional policies, and ethical standards.

Reporting categories, timelines, and submission requirements are outlined below. Investigators and research staff are responsible for complying with these requirements. Failure to report required information in a timely and accurate manner may constitute noncompliance and may result in IRB action.

4.1 Unanticipated Problem Involving Risks to Subjects or Others (UPIRTSO)

Investigators must promptly report to the DUHS IRB any unanticipated problems involving risks to subjects or others (UPIRTSO). UPIRTSOs may also be referred to as UPs, UAPs, or UPIRSOs.

Reports of UPIRTSOs must be submitted through the electronic IRB submission system as soon as possible, but no later than:

- Within 24 hours upon learning of unanticipated study-related death or life-threatening event, the initial notification can occur via phone or email to the DUHS IRB Executive Director or Director of Compliance and Operations, by providing a brief summary of the event. Within 5 working days, study personnel must submit as a safety event in the IRB's electronic system.
- Within 10 working days for all other events after the investigator determines that an event meets the definition of a UPIRTSO. This reporting timeline begins upon recognition that the event is reportable and does not depend on the availability of complete information, final analyses, or an implemented corrective and preventive action (CAPA) plan.

Reports must include sufficient detail for the IRB to assess the nature of the event, its relationship to the research, and its impact on the safety, rights, and welfare of participants currently enrolled or

actively participating at DUHS, as well as any implications for ongoing or future study activities. Reports must also describe any known or proposed corrective or preventive actions.

If an investigator believes an event may meet the definition of a UPIRTSO, they must promptly submit an event report to the IRB for review and formal determination. Because reportability assessments are

highly study-specific, IRB staff, members, and Chairs may provide guidance but cannot make a formal determination without a submitted report. Submission enables the IRB to conduct a complete review and fulfill its regulatory and ethical responsibilities to protect research participants.

Examples of UPIRTSOs include:

- A single occurrence of a serious, unexpected event that is uncommon and strongly associated with drug exposure (such as angioedema, agranulocytosis, hepatic injury, or Stevens-Johnson syndrome);
- A single occurrence, or more often a small number of occurrences, of a serious, unexpected event that is not commonly associated with drug exposure, and is uncommon in the study population (e.g., tendon rupture, progressive multifocal leukoencephalopathy);
- Multiple occurrences of an adverse event (AE) that, based on an aggregate analysis, is determined to be an unanticipated problem. There should be a determination that the series of AEs represents a signal that the AEs were not just isolated occurrences and involve risk to human subjects (e.g., a comparison of rates across treatment groups reveals higher rate in the drug treatment arm versus a control). A summary or analyses supporting the determination should accompany the report;
- An AE that is described or addressed in the investigator's brochure, protocol, or informed consent documents, but occurs at a specificity or severity that is inconsistent with prior observations. For example, if transaminase elevation is listed in the investigator's brochure and hepatic necrosis is observed in study subjects, hepatic necrosis would be considered an unanticipated problem involving risk to human subjects. The sponsor or investigator's assessment of the divergence from the expected specificity or severity should accompany the report;
- A serious AE that is described or addressed in the investigator's brochure, protocol, or informed consent documents, but for which the rate of occurrence in the study represents a clinically significant increase in the expected rate of occurrence (ordinarily, reporting would only be triggered if there were a credible baseline rate for comparison). The sponsor or investigator's assessment of the divergence from the expected rate should accompany the report;
- AEs involving direct harm to subjects enrolled by the local investigator which in the opinion of the investigator or sponsor, may represent an UPIRTSO;
- IND Safety Reports submitted by sponsors that meet the reporting criteria under 21 CFR 312.32 for a Suspected Unexpected Serious Adverse Reaction (SUSAR). These reports must be accompanied by documentation confirming that the sponsor has submitted the IND Safety Report to the FDA. For additional information on IND safety reporting requirements, refer to Section 6, SUSAR & Adverse Event Reports.

- Any SAE that occurs in a Bioavailability (BA) or Bioequivalence (BE) study;
- Unanticipated Adverse Device Effects (UADEs);
- Any other AE or safety finding (e.g., based on animal or epidemiologic data) that indicates subjects or others might be at risk of serious, unanticipated harms that are reasonably related to the research. These would cause the sponsor to modify the investigator's brochure, study protocol, or informed consent documents, or would prompt other action by the IRB to ensure the protection of human subjects. An explanation of the conclusion should accompany the report.
- Reports (including reports from DSMBs, DMCs, internal post-approval monitoring groups) that indicate that risks are greater than previously known, or that indicate that the research should be modified, suspended, or halted.
- Sponsor, institutional office, or lead investigator/coordinating center-imposed suspension or termination of some or all research activities due to an increase risk of harm to participants,
- An unanticipated event related to the research that exposes subjects or others to potential risk but that does not involve direct harm;
- A breach of confidentiality or loss of research data (e.g., a laptop or thumb drive is lost or stolen);
- A failure to obtain informed consent as approved by the DUHS IRB.
- An unanticipated event related to the research that results in actual harm or exposes individuals other than the research subjects (e.g., investigators, research assistants, students, the public, etc.) to potential risk;

4.2 Noncompliance, Serious Noncompliance, & Continuing Noncompliance

Investigators and study staff are responsible for assessing protocol deviations and other potential instances of noncompliance against the definitions of serious noncompliance and continuing noncompliance. This assessment, including the rationale, must be documented in study records, regardless of whether the event meets the reporting threshold for submission to the IRB.

Documentation of these assessments must be maintained and may be used to identify trends and inform corrective or preventive actions. These records may be reviewed during audits, continuing review, or upon request by the IRB or other components of the DUHS Human Research Protection Program (HRPP).

Investigators are responsible for promptly reporting possible serious or continuing noncompliance to the DUHS IRB as reportable information in the electronic IRB system within 10 working days.

Noncompliance may result from a variety of causes, including unintentional error, misunderstanding, inadequate training, negligent oversight, or willful disregard. Regardless of intent, any noncompliance that may affect participant safety, rights, welfare, or the integrity of the research must be reported.

Continuing noncompliance is not limited to issues previously identified by the IRB and may also include failure to implement required corrective actions or failure to comply with directives issued by the IRB,

DUHS compliance offices, sponsors, funding agencies, regulatory authorities, or other institutional entities.

Examples of Events that may be Serious or Continuing Noncompliance that must be reported:

- A protocol deviation that harmed subject(s) or others or placed subject(s) or others at increased risk of harm, including those that may be found by auditors, internal or external, DSMB reports, or
- Coordinating Center Reports. Please also refer to Section 7, Sponsor Coordinating Center Reports, DSMB Reports, Internal & External Audit Reports.
- Conducting human subjects research without IRB approval or exemption determination or otherwise obtaining institutional permission prior to proceeding.
- Starting research prior to meeting the conditions required by the IRB and receiving an IRB notification of approval or conducting research during a lapse in approval without IRB Chair consultation.
- Failure to obtain informed consent, reconsent, or provide participants with new information about study risks as required by the IRB.
- Receiving a written report from a federal agency (e.g., FDA Form 483) indicative of noncompliance
- Initiating changes to the study without IRB approval, including using unapproved materials (such as fact or information sheets, recruitment materials, questionnaires, focus group guides, scripts, or other materials provided to participants). Please also refer to "Other Reportable Information".
- Failure to complete institutionally required human subjects' protection training prior to engaging in human subjects research.
- Failure to complete the IRB application or other forms related to human subjects research in a true and accurate manner.
- Failure to adhere to directions, requirements, or procedures from any component of the DUHS Human Research Protection Program (HRPP)
- Failure of any organization or office with a defined responsibility for oversight of any part of the HRPP to fulfill its obligations.

If an individual, whether an investigator, study staff member, or other party, is uncertain whether an event constitutes reportable noncompliance, they may contact the IRB Executive Director, IRB Compliance or Operations Director, or IRB Chair to discuss the situation informally. This consultation does not replace the responsibility to document their assessment and report events that meet the definition of serious or continuing noncompliance or reportable protocol deviations.

4.3 Allegations of Noncompliance

Anyone may report concerns or allegations of noncompliance to the Institutional Official, IRB Executive Director, IRB Compliance Director, or the confidential institutional phone or website for reporting compliance concerns. These concerns can be made verbally, by email, or by other means. Individuals making such reports are expected to do so in good faith, maintain confidentiality, and, unless reporting anonymously, cooperate with any subsequent fact-finding related to the report. Any allegation of non-

compliance will be referred to the IRB Executive Director or designee. In most instances, the Executive Director or designee will submit a written inquiry to the related Principal Investigator (PI) for the research study in question. However, in cases where the identity of the complainant must be protected or based on the severity of the allegation, the Executive Director or designee may submit a written request to the Duke University Office of Audit, Risk and Compliance to conduct a directed audit in response to the allegation.

Once either the response from the PI or the audit report has been received, the Executive Director or Delegate, in conjunction with the Lead IRB Chair, may conclude that the allegations have a basis in fact. In such cases, the processes under the IRB Review and DUHS Reporting of Promptly Reportable Information will be followed. Otherwise, no further action is taken, and the PI is informed that the IRB considers the issue to be resolved. The matter may be referred to other institutional entities for evaluation and management as applicable.

If an individual, whether an investigator, study staff member, or other party, is uncertain whether an event constitutes reportable noncompliance, they may contact the IRB Executive Director, IRB Compliance or Operations Director, or IRB Chair to discuss the situation informally. This consultation does not replace the responsibility to document their assessment and report events that meet the definition of serious or continuing noncompliance or reportable protocol deviations.

5. Other Reportable Information

Other Reportable Information includes any incident, experience, outcome, or new information that must be reported to the DUHS IRB in accordance with this policy, regardless of whether it meets the criteria for an Unanticipated Problem Involving Risks to Subjects or Others (UPIRTSO), Serious Noncompliance (SNC), or Continuing Noncompliance (CNC). Investigators are responsible for promptly reporting Other Reportable Information to the DUHS IRB as reportable information in the electronic IRB system within 10 working days, unless otherwise specified below.

The categories of Other Reportable Information are organized below based on whether the DUHS IRB serves as the IRB of record. If DUHS IRB is not the IRB of record the following events should be submitted regardless of the reviewing IRB's processes or timelines.

Information or Event	DUHS is the IRB of Record	Non-DUHS IRB is the IRB of Record
Any information that may impact the rights, safety, or welfare of subjects or inform the IRB's oversight of the research	Report	Report to IRB of record as required, do not report to DUHS IRB unless otherwise reportable.
Written report or action of a government agency, regarding the research, the PI, or the research staff, including: • Conviction of a crime	Report	Report to DUHS IRB, and IRB of record as applicable.

• FDA Warning Letter • NIDPOE (Noticed of Initiation of Disqualification Proceedings and Opportunity to Explain) • Suspension, termination, or restriction of an IRB's authority to oversee research • Suspension, termination, restriction, or expiration of an institution's FWA. • Suspension by a federal or governmental agency (e.g., FDA, HHS). • OHRP Determination Letter, or similar. • Allegation of Noncompliance or Finding of Noncompliance • Unauthorized disclosure of confidential information.		
Information or Event	DUHS is the IRB of Record	Non-DUHS IRB is the IRB of Record
Changes made to the research without prior IRB approval to eliminate apparent immediate hazards to the subject(s); • For device studies subject to FDA's IDE regulations, any deviation from the investigational plan to protect the life or physical well-being of a subject in an emergency must be reported to the sponsor and the IRB of record no later than 5 working days after the emergency occurred.	Report	Report to IRB of record as required, do not report to DUHS IRB unless otherwise reportable.
Notice of: • Any negative actions by a government oversight office, including, but not limited to, OHRP Determination Letters, FDA Warning Letters, FDA 483 Inspection Reports with official action indicated (classification as "OAI" is typically made after FDA has had the opportunity to review the responses to a 483), FDA Restrictions Placed on IRBs or Investigators, and any corresponding compliance actions taken under non-US authorities related to human research protections. • Any litigation, arbitration, or settlements initiated related to human research protections. • Any press coverage (including but not limited to radio, TV, newspaper, online publications) of a negative nature regarding human subjects research conducted at or by DUHS or DUHS program for the protection of human research participants. NOTE: The above events must be reported to the HRPP/IRB Office by email as soon as the investigator, study team, or DUHS personnel becomes aware of the event, but no later than 24 hours after becoming aware. A formal submission in the electronic IRB system must be completed within 10 working days, unless otherwise specified.	Report	Report to DUHS IRB, and IRB of record as applicable.
Unapproved inclusion or involvement of vulnerable populations, including post-enrollment changes in status (e.g., prisoner, pregnant woman, neonate, child, adult with impaired decision-making capacity) • This includes incarceration of a subject in a research study not approved to enroll or otherwise involve prisoners.	Report	Report to IRB of record as required, do not report to DUHS IRB unless otherwise reportable.
Holds, suspensions, or terminations of a study, in part or in full, by an investigator, sponsor, or others	Report	Report to DUHS IRB, and IRB of record as applicable.

Information or Event	DUHS is the IRB of Record	Non-DUHS IRB is the IRB of Record
Changes that impact the ability of the PI to conduct or supervise the study, temporarily or permanently	Report	Report to DUHS IRB, and IRB of record as applicable.
Changes that impact the qualifications of investigators or research staff members such as actions taken by regulatory authorities, licensing boards, or credentialing committees, including but not limited to: • State medical board or hospital medical staff actions, (denial, revocation, suspension, reduction, limitation, probation, non-renewal, relinquishment, sanction, fine, or discipline) regarding any of the following for the PI or research staff, or if research staff are added, a past history of such action: • Clinical privileges at any site • DEA licensure • Fellowship/board certification • Medical licensure in any state, nation, or province • Membership on any hospital staff • Prescribing privileges • Professional sanctions including fines and public reprimands • Professional society membership • Research privileges at any site • Written report by study monitor.	Report	Report to DUHS IRB, and IRB of record as applicable.
Unresolved Subject Complaint, see Section 8 Participant Complaints	Report	Report to DUHS IRB, and IRB of record as applicable.

6. SUSAR & Adverse Event Reporting

Adverse events that occur in FDA-regulated clinical trials must be reported to the sponsor in accordance with applicable FDA regulations and the sponsor's reporting requirements. The DUHS IRB does not accept routine adverse event reports solely because they have been reported to the sponsor. However, IND Safety Reports that meet the reporting criteria for a Suspected Unexpected Serious Adverse Reaction (SUSAR) under 21 CFR 312.32 are generally considered reportable to the DUHS IRB because they meet the definition of an Unanticipated Problem Involving Risks to Subjects or Others (UPIRTSO). Unless the IRB has specifically required additional adverse event reporting for a particular protocol, only events that meet the criteria for IRB reporting, such as a UPIRTSO, should be submitted.

The DUHS IRB does not accept reports of adverse events unless they are otherwise reportable to the IRB (e.g., they meet the criteria for an Unanticipated Problem Involving Risks to Subjects or Others (UPIRTSO). Adverse events that are classified by the sponsor as a Suspected Unexpected Serious Adverse Reaction (SUSAR) must be submitted to the DUHS IRB per the reporting requirements in Section 4.1 if any of the following conditions are met:

- the DUHS IRB serves as the IRB of Record for the study and the event is reportable; or

- If the IRB of record makes an Unanticipated Problem Involving Risks to Subjects or Others (UPIRTSO) determination and the event directly impacts a DUHS participant. The submission to the DUHS IRB must include documentation of the reviewing IRB's UPIRTSO determination.

As described in Section 4.0, reporting requirements are based on the role and oversight of the IRB of record. External SUSARs may be reportable to the DUHS IRB when they meet the criteria outlined in this document per the FDA's requirements; however, when an external SUSAR (a SUSAR that is not a DUHS participant or we are not the site's IRB of record) involves a death, the 24-hour notification requirement to the DUHS IRB does not apply. External SUSAR's involving death do not need to be reported to the DUHS IRB as the 24-hour requirement is intended to allow the IRB with oversight of the participant and site where the event occurred to take immediate action, as appropriate.

Follow-up reports to previously submitted SUSARs do not require submission to the DUHS IRB when all the following conditions are met:

- the follow-up information does not indicate an increase in risk beyond that described in the initial report;
- the follow-up information does not result in new or revised corrective or preventive actions; and
- the follow-up information does not directly involve DUHS participants or participants enrolled at sites for which the DUHS IRB serves as the IRB of Record.

7. Sponsor Coordinating Center Reports, DSMB Reports, Internal & External Audit Reports

Reports issued by the Sponsor, Coordinating Center, Data and Safety Monitoring Board (DSMB), quality assurance programs, compliance offices, or internal and external auditors do not require immediate submission to the IRB solely because they have been received by the Investigator or research team.

These reports must be submitted within 10 working days to the IRB only when the report contains information that meets the IRB's definition of a Reportable Event, including:

- An Unanticipated Problem Involving Risks to Subjects or Others (UPIRTSO);
- Serious Noncompliance;
- Continuing Noncompliance; or
- Any other event that meets the reporting criteria outlined in this policy; or
- Submission is specifically required by the Sponsor, funding agency, regulatory authority, or if requested by the IRB.

When submitting such reports, the Investigator is responsible for reviewing the findings or observations and providing an analysis that identifies which observations, findings, or deviations meet the IRB's reporting definitions and explains the basis for that determination. Submission of monitoring, DSMB, audit, or inspection reports without Investigator analysis is generally not sufficient to satisfy reporting requirements and will be returned to the study team for additional information.

The Investigator may document this assessment using Appendix A and identify any observations or findings that constitute a Reportable Event, including a UPIRTSO, Serious Noncompliance, or Continuing Noncompliance.

If the report does not contain findings that meet the prompt reporting criteria and immediate submission is not otherwise required, the report should be retained in the study records and may be submitted to the IRB at the time of continuing review or other periodic review, as applicable.

8. Participant Complaints

The DUHS IRB will be responsive and sensitive to the complaints or concerns expressed by subjects or others and will respond to all complaints or concerns in a confidential and timely manner. The PI and all other research team members are responsible for the safety and welfare of all subjects enrolled in their studies. When investigators or team members hear complaints or concerns from subjects, they will try to resolve them.

Investigators conducting research under the oversight of the DUHS IRB report complaints unable to be resolved by the investigator using the Event Report form in the IRB electronic system. All complaints, including those resolved by the investigator, should be summarized at the time of continuing review in the Continuing Review Request Form, when continuing review is applicable. Investigators conducting research under the oversight of an external IRB must comply with the reporting requirements of the external IRB and the internal reporting requirements outlined in Section 5.

Investigators are encouraged to contact the Executive Director or Compliance Director in the DUHS IRB when they are having difficulty resolving a complaint or concern, and whenever circumstances warrant (e.g., immediate attention is needed).

8.1 DUHS IRB and Direct Participant Complaints

When the DUHS IRB Office is the direct recipient of complaints or concerns, if minor in nature and can be resolved easily the IRB Office Staff may resolve the complaint or concerns themselves, notifying the

DUHS IRB Executive Director or Director of Compliance. If the complaint or concern is not minor or cannot be easily resolved it will be referred to the Executive Director or Director of Compliance who will proceed with the following:

- Document the complaint or allegation. When appropriate, the staff may request that the subject submit the complaint in writing.
- Reassure the subject that the DUHS IRB will take all necessary measures to inquire into the circumstances and to address the issue.
- Provide written confirmation of receipt of the complaint to the Participant if the Participant requests confirmation and is willing to provide contact information.
- Convey the information to the IRB of record as applicable in a timely manner.
- When appropriate, contact the investigator for additional information or to assist with resolution.
- When appropriate, contact other resources or institutional offices (e.g., Research Compliance, Risk Management, Patient Relations, Privacy, Research Integrity Officer) to assist with information-gathering, resolution or conduct any additional required reviews or investigations.
- For research under the oversight of the DUHS IRB, will consider the complaint or concern and take any reasonable steps necessary to investigate and/or resolve the issue, as appropriate. If the concern or complaint rises to a level that adversely effected the participants rights or welfare a report will be provided to a convened IRB meeting or provided to the designated expedited reviewer if the research is eligible for expedited review. When reviewing complaints, the IRB will consider whether the complaint was the result of, or related to, an UPIRTSO or noncompliance, and, if so, will follow the relevant procedures. The IRB Chair or designated expedited reviewer may refer any complaint for review to the convened IRB, and the outcome of this review will be documented as noted in the IRB Review and Reporting of Promptly Reportable Information.
- The IRB will maintain written copies of any complaints and concerns that could not be resolved by the investigator or requires review by the IRB and will document the relevant information, any outcomes of the investigation, if applicable, and resolution. The complainant will be notified promptly following resolution of the complaint or concern, when appropriate, if contact information has been provided.

Regarding suggestions or offers of input from a participant concerning a research study, the correspondence is forwarded to the Executive Director and Director of Compliance. Where the suggestion or input affects the conduct of the study by the Principal Investigator or study staff, the suggestion or input is forwarded to the investigator.

9. Immediate Actions to Mitigate Risk of Harm

Investigators are responsible for taking prompt and appropriate actions to protect research participants whenever an unanticipated problem, noncompliance, or other event indicates that participants may be at risk of harm. This includes, but is not limited to:

- Stopping or modifying study procedures that may increase risk;

- Ensuring that affected participants receive appropriate medical evaluation or treatment;
- Implementing interim safety measures to prevent further harm; and
- Notifying relevant study personnel, including research staff, clinical teams, and sponsors, as necessary to protect participants.

These actions must be taken immediately upon recognition of the risk, without waiting for IRB review or determination, submission of a formal report, or completion of a corrective and preventive action (CAPA) plan.

After taking immediate protective measures, investigators must submit a report of the event through the electronic IRB submission system in accordance with DUHS reporting requirements. The report should include a description of the actions taken to mitigate risk and any additional plans to protect participants while the IRB conducts its review. Failure to take timely action to mitigate risk may constitute serious noncompliance and may result in IRB or institutional action.

10. Responsibilities

10.1 DUHS Investigator Responsibilities

DUHS investigators and study personnel are responsible for the prompt identification, documentation, and reporting of UPIRTSOs, serious noncompliance, continuing noncompliance, and other reportable information within required timelines. When DUHS relies on another IRB, investigators must ensure that required determinations from the reviewing IRB are submitted to the DUHS IRB in accordance with this policy. The DUHS Principal Investigator retains ultimate responsibility for ensuring compliance with all reporting obligations, including those carried out by delegated study personnel.

10.2 DUHS IRB Responsibilities

The DUHS IRB is responsible for maintaining, implementing and providing training on this policy, and reviewing the reported events as outlined in the IRB Review and Reporting of Promptly Reportable Information, to ensure consistent application in accordance with applicable federal regulations, AAHRPP standards, and institutional requirements.

11. Revision

11.1 Revision

- Version 1.1 Effective Date: 09/03/2026-Minor Clarification in Section 6 regarding external SUSAR's and 24 hour reporting in reference to Section 4 and IRB of record. The version was not changed as this was a minor clarification, not a substantive change.
- Version 1.0 Effective Date: 09/01/2026- Original Document-Combined "Non-Compliance with the Requirements of the Human Research Protection Program (03/25/2021)", "Problems or

Events That Require Prompt Reporting to the IRB (11/20/2023)" and "The Review of Problems, Complaints, Comments, Concerns, or Allegations of Noncompliance from Investigators or Research Participants (11/22/2023)" Revised timeline for consistency, and provided additional information on SUSAR's based on "Investigator Responsibilities-Safety Reporting for Investigational Drugs and Devices (December 2025-FDA)"