Title
IRB Review of Promptly Reportable Information

1. Purpose
This SOP establishes written procedures for ensuring prompt review and reporting of any Unanticipated Problems Involving Risks to Subjects or Others (UPIRSO), Serious Noncompliance, Continuing Noncompliance, Suspension or Termination of IRB approval in accordance with 45 CFR 46.103(a) and (b)(5), and 21 CFR 56.108(b). This SOP begins when the UNC Office of Human Research Ethics (OHRE) receives a Promptly Reportable Information (PRI) submission. This SOP ends when the Principal Investigator (PI), and if applicable, the Institutional Official (IO) and designee, and Federal Regulatory Agencies have been notified of the outcome of the PRI review.

In previous versions of the UNC-Chapel Hill SOPs and electronic submission system this was known as New Safety Information (NSI), however, as not all information that requires prompt reporting is due to safety issues or changes in risk the nomenclature has been revised to Promptly Reportable Information (PRI). Definitions for terms used in the is SOP can be found in SOP 6001: Definitions.

2. Responsibility
The convened IRB; the Safety and Welfare Analysis Group (SWAG); the Institutional Official (IO) and designee; the IRB Chair, Co-Chairs, and Vice-Chairs; OHRE leadership; and the Compliance team are responsible for carrying out the procedures described in this SOP.

3. Procedures
3.1 PRI Triage
Upon receipt of PRI, the OHRE Compliance team, in consultation with OHRE leadership as necessary, will promptly triage the PRI, including assessing whether the information reported has a basis in fact / is credible. PRI that suggests that participants or others may be at risk of imminent serious harm is triaged to an IRB Chair, Co-Chair or Vice-Chair, and the OHRE Director is notified. Direct risk mitigation will be considered to eliminate the risk of immediate harm, such as reviewing the CAPA plan and, if necessary, revising the plan, and considering interim suspension of study activities as needed. All other reports of PRI are managed by the Compliance team or referred to SWAG. External safety events submitted as Suspected Unexpected Serious Adverse Reaction (SUSAR) reports which have been submitted to the FDA will be reviewed by the Compliance Manager and resolved if there is no risk of harm to local subjects. Investigator’s Brochure (IB) updates, new safety information, clinical holds, or other information that does not require additional analysis will be resolved by the Compliance team or referred for review by the convened IRB as applicable. Information that does not represent PRI or that represents noncompliance or other reportable events per SOP 1401 without increased risk of harm to
subjects or others may be resolved by the Compliance team and/or re-triaged within the IRB. PRIs are resolved by issuing a letter of acknowledgement to the PI and designated personnel. PRIs may be re-triaged or referred to other IRB personnel as applicable, if for example, a study modification is needed along with the PRI.

3.2 Interim Suspension
The IRB Chair(s) will review the referred PRI or external information. If it is determined that participants may be at risk of imminent serious harm, the IRB Chair, Co-Chair or Vice-Chair will initiate an interim suspension of IRB approval of all or a subset of activities. The Compliance team will notify the PI and designated personnel, the IRB Chair or Co-Chair of the IRB that will review the interim suspension, and OHRE leadership.

3.3 Suspension
When an interim suspension is initiated by the IRB Chair, Co-Chair or Vice-Chair, the associated PRI will be referred for review by the convened IRB to either uphold or lift the suspension. At the direction of the IRB Chair and OHRE leadership, selection of the reviewing board will be based on the expertise of the board. The decision to uphold or lift the suspension should be based on the potential risk to subjects and the interim CAPA plan in place. The IRB should consider (1) actions to protect the rights and welfare of currently enrolled participants, (2) whether procedures for withdrawal of enrolled participants take into account their rights and welfare (e.g., making arrangements for medical care outside of a research study, transfer to another Researcher, and continuation in the research under independent monitoring), (3) informing current participants of the suspension, and (4) if any adverse events or outcomes have been reported to the IRB. The Compliance team will notify the PI and designated personnel, the IRB Chair who issued the interim suspension, and OHRE leadership of the IRBs decision to uphold or lift the suspension.

3.4 SWAG PRI Review
SWAG membership includes a group of two or more individuals, an IRB Chair, and staff members with expertise in clinical research. The group will have sufficient expertise for actions or will obtain additional consultation as needed. SWAG reviews PRI and proposed CAPA plans and conducts fact-finding. If the PRI suggests that participants or others may be at risk of imminent serious harm, SWAG will follow the process for consideration of an interim suspension in Section 3.2.

If the PRI may represent an Unanticipated Problem Involving Risks to Subjects or Others (UPIRSO), Serious Noncompliance, or Continuing Noncompliance, SWAG will refer the PRI to the convened IRB for review and notify the PI and designated personnel, and the IRB Chair(s) of the IRB that will be assigned the PRI.

If the PRI represents Noncompliance or other information that is not an UPIRSO, Serious Noncompliance, or Continuing Noncompliance, SWAG will work with the PI to ensure that the proposed CAPA plan is appropriate and notify the PI and designated personnel of the determination and the approved CAPA plan.
If the reported information is not PRI, SWAG or the Compliance team will notify the PI and designated personnel and provide education on reporting requirements.

If SWAG is uncertain about what the reported information represents, it may request additional information from the study team to assess whether to refer an event for board consideration of UPIRSO, Serious or Continuing Noncompliance or SWAG will refer the information to the convened IRB for review.

SWAG identifies recommendations for consideration by the convened IRB. The Compliance team facilitates the IRB review by providing consultation to the board before the review as appropriate, corresponding with study personnel for additional information as needed, and is available if the board has questions.

3.5 PRI Review by the Convened IRB
The convened IRB serves in accordance with 45 CFR 46, and 21 CFR 50 and 56 (See SOP 401 for more information about the function of the convened IRB). PRI review follows the same processes as outlined in SOP 701, in addition to the following: (1) PRI referred to the IRB and any supporting documentation will be distributed to IRB Chair(s) and members with sufficient time for members to review the information, (2) the PI and study team may be invited to participate to answer questions or to clarify information, (3) the IRB support personnel will document the PRI review, including discussion, controverted issues, determinations or deferrals, the approved CAPA plan, stipulations, motions and votes, and (4) following PRI Review, the Compliance team will notify the PI of the outcome of the review which will include the IRB's determinations, approved CAPA plan, and stipulations. The IO and applicable parties will be copied on the notification.

The IRB may make a determination of UPIRSO, Serious Noncompliance or Continuing Noncompliance. Further, the IRB may suspend or terminate IRB approval of research that is not being conducted in accordance with the IRB's requirements and/or has been associated with unexpected serious harm to participants. In making determinations and taking actions, the IRB should consider whether notification of current participants is required when such information might relate to participants’ willingness to continue taking part in the research. Other IRB considerations may include: a modification to the protocol or consent form, notification to past participants, a reconsent plan of current or past participants, a modification to the continuing review schedule, monitoring of the research or the consent process, referral to other UNC Parties (e.g., University Counsel, UNC Hospitals Risk Management, Research Integrity Office).

3.6 Notification of Federal Agencies
Federal regulations require that the IRB follow written procedures for ensuring prompt reporting of any determination of UPIRSO, Serious Noncompliance, Continuing Noncompliance, Suspension or Termination of IRB Approval to the appropriate federal agencies. The Department of Health and Human Services (HHS), Office of Human Research Protections (OHRP), is promptly notified when research is supported by an HHS agency. The Food and Drug Administration (FDA) is promptly notified when the research is FDA-regulated. The Department of Defense (DoD) human research protections officer is notified when the research is regulated or funded by DoD. Other federal agencies are promptly notified.
when the research is overseen by those agencies, and they require reporting separate from OHRP. If an event has been reported to a regulatory agency through other mechanisms, such as reporting by the Researcher, Sponsor, or another Organization, the UNC OHRE need not report the same event.

The Compliance team, in collaboration with the IRB Chair/Co-Chair and OHRE leadership, as applicable, will prepare a notification that includes the elements as required by the appropriate agency. Notifications will include general study information (title, PI, IRB number), a description of the event, the IRB findings, and the approved CAPA plan or plans for continued investigation or action. The reports will be sent within 30 days of the PI notification of an event meeting the reporting criteria.

The Compliance team will send the draft notification to the IO and designee(s) and the OHRE director for review.

If UNC is the reviewing IRB for another institution, and the PRI involves researchers or participants at that institution, the relying institution will be notified and provided a reasonable opportunity to review and comment on the report as per the governing reliance agreement.

Correspondence from Federal Agencies will be disseminated to the appropriate parties and will be maintained on file in the OHRE.

Reports to funding agencies (e.g., NIH) is separate from IRB review and will be completed by the IO or designee (e.g., OSR with the PI).

3.7 Notification of Other UNC Parties

If the PRI is applicable to other UNC parties (e.g., University Counsel, Office of Sponsored Research, UNC Hospitals Risk Management, Research Integrity Office, Privacy Office), the Compliance team will notify the appropriate parties.

3.8 Notification of the Association for the Accreditation of Human Research Protection Programs (AAHRPP)

AAHRPP requires notification of the following information, within 48 hours after the institution or researchers become aware of the information: (1) Any negative actions by a government oversight office, including, but not limited to, FDA Warning Letters, FDA 483 Inspection Reports with official action indicated, FDA Restrictions on Investigators, and any corresponding compliance actions taken under non-US authorities related to human research protections, (2) Any litigation, arbitration, or settlements initiated related to human research protections, and (3) 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 UNC-CH or about UNC-CH’s Human Research Protection Program (HRPP).

Reportable information received by OHRE outside of IRBIS is triaged to the Compliance team and OHRE leadership. The Compliance team and OHRE leadership will promptly notify AAHRPP.

3.9 Reconsideration
As required by regulations, any decision of the IRB with respect to research involving human subjects is final. However, the PI may request that the convened IRB reconsider its determination and/or CAPA plan based on new information that was not available or considered at the time the determination was made. No other circumstances warrant a reconsideration. The petition must be made within 10 calendar days of notification of the IRB’s findings. At the IRB’s discretion, the PI may be invited to the IRB meeting at which his or her petition will be considered.

3.10 Complaint or Allegation of Noncompliance
Complaints or allegations for noncompliance may be made by participants, third parties, study staff, University personnel, or hospital personnel. Complaints or allegations of noncompliance may be received anonymously through the UNC Ethics Line or through contacting the OHRE.

Participants are encouraged to ask questions or voice any concerns or complaints they may have about the research. The PI is responsible for answering all questions, addressing all concerns, and responding to all complaints raised by participants to the best of his/her ability. The name and contact information of the PI responsible for the conduct of the research and the IRB’s contact information is required in all UNC consent documents (e.g., information sheets, scripts, consent forms) regardless of signature requirements. Participants are also encouraged to discuss their rights or to voice their concerns or complaints about the research with OHRE. OHRE contact information is available to participants and third parties on the OHRE website.

For complaints received by the PI or study personnel, the PI is responsible for ensuring that complaints are reviewed thoroughly and respectfully. Participants should not be penalized or lose any benefits they are receiving or have a right to receive as a result of the complaint. The PI will address the complaint promptly and communicate its resolution to the complainant, generally within 30 days. The PI must document all complaints received from participants or third parties and their resolution. If the complaint meets PRI reporting requirement per SOP 1401, a PRI submission is required. The PI and the study team will work with OHRE to resolve complaints.

For complaints received by OHRE, the Compliance team will review all complaints in consultation with the OHRE leadership and the IRB Chair(s) as applicable. OHRE will maintain privacy of the complainant where privacy is a concern or when requested by the complainant to the extent possible in order to appropriately investigate. Complaints received outside of IRBIS, regardless of point of origin, are provided to the Compliance Manager. The Compliance team will notify the PI of the complaint. If the complaint meets the criteria for PRI, a PRI submission with a response to the complaint is required. The PRI submission will be reviewed as described in this SOP. Complaints regarding minor administrative issues such as a brief delay in compensation does not require a PRI submission and will be referred to the study team for resolution.

When a complaint meets PRI reporting criteria, the OHRE Compliance team will work with the PI, the IRB Chair(s) and OHRE leadership to promptly resolve the complaint and will communicate its resolution to the complainant. OHRE will maintain records of complaints and their resolution, and a copy will be retained in the applicable protocol file.
3.11 PRI Review when UNC is Ceding IRB Review

If UNC is ceding review and oversight to another IRB and that IRB has made a regulatory determination of Serious Noncompliance, Continuing Noncompliance, an Unanticipated Problem Involving Risks to Subjects or Others that involve UNC participants or researchers, the determination and the approved CAPA is reportable as PRI (see SOP 1401).

SWAG will review the CAPA plan to ensure that it appropriately addresses the event and the root cause. If the CAPA plan is determined to be inadequate or if it is felt that the event is broader than the study, or requires additional actions to protect human subjects across studies that may be under the oversight of the UNC IRB, SWAG will provide additional recommendations for the PRI and will refer the recommendations to the convened IRB. If the CAPA is deemed adequate, SWAG will acknowledge the event and the reviewing IRB’s determinations.

The Compliance team will notify the IO and other relevant parties of the PRI.

If not previously received, the Compliance team will request a copy of the notification letter to Federal Agencies, as applicable.

Based on the review by SWAG, if it is felt that the event is broader than the study, or requires additional actions to protect human subjects across studies that may be under the oversight of the UNC IRB, the convened IRB will review the PRI, the approved CAPA plan and SWAG’s findings, and propose updates to the CAPA plan as required. The Compliance team will notify the reviewing IRB and the UNC IO and designee of the UNC IRB’s findings and proposed CAPA plan.