

SOP#: PM-11

Processing of New Information Related to Risk

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William L. Dahut, M.D. 12/28/2020

POLICY

All new information received by the Principal Investigator (PI) about the drug/biologic agent or device being studied must be reviewed and retained in a regulatory compliant and consistent format. This information may come in the following forms:

- IND Safety Report, including SUSAR (Suspected Unexpected Serious Adverse Reaction)
- “Dear Investigator” letter identifying a new risk
- Request for Rapid Amendment
- Safety Monitoring Committee/Data Safety Monitoring Board report
- Interim analysis

The PI is responsible for reviewing all new information and making a determination about whether the new information represents an unanticipated problem (UP) and is reportable to the IRB.

The PI may delegate review of new information and determination of UP to a clinical physician associate investigator if the PI is unavailable to perform the task in a timely fashion. For the purposes of this SOP, the person delegated PI responsibilities will be considered the “PI designee.” Please see CCR SOP PM-1 *Principal Investigator (PI) Delegation of Tasks for Research Involving a Drug or Device* to determine what activities can be delegated to whom.

PURPOSE

This standard operating procedure (SOP) outlines the process for review, submission, and retention of all new information received by the PI from a study sponsor and/or manufacturer.

RESOURCES

- [Guidance for Industry and Investigators: Safety Reporting Requirements for IND and BA/BE Studies](#)
- [FDA Form 1572: Statement of Investigator](#)
 - (see page two of the Form 1572 for Commitments)
- NIH Office of Intramural Research Policies & Guidance [website](#)
 - Policy 801 - *Reporting Research Events*
- CCR Policies/Standard Operating Procedures [website](#)
 - PM-1: *Principal Investigator (PI) Delegation of Tasks for Research*

PROCEDURES FOR REPORTING SPONSOR (INCLUDING CTEP) OR MANUFACTURER NEW INFORMATION

STEP 1: Receive and Review New Information

1. Principal Investigator (PI) receives the new information from a study sponsor or manufacturer by mail, email, fax or via the Sponsor's or Manufacturer's electronic portal.
Important: Individual login information for access to these portals must not be shared. Each team member must request individual access.
2. As soon as possible, the PI/PI designee reviews the new information and determines whether the information meets the definition of a UP which includes potential increase risk to participants or others.
 - If the new information meets the definition of a UP, the IRB must be notified via a Reportable Event Form (REF) within 7 days - see Step 3.
 - If the new information is a UP, the PI/PI designee must also determine if a protocol amendment is needed and how participants will be contacted about the increased risk.
3. The PI/PI designee will inform all appropriate AIs and other research team members of his/her assessment of the new information and if it meets the definition of a UP. Two examples of how notification may occur are:
 - forwarding an email containing the new information including documentation of the determination of UP or not UP to team members.
 - reviewing new information in team meetings with documentation of determination in team meeting minutes.

STEP 2: Forward the New Information to the Protocol Support Office (PSO) Mailbox

1. After reviewing the new information, the PI/PI designee sends the new information to the PSO Manager or PSO mailbox at: NCICCRPSO@mail.nih.gov.
2. The email must include the protocol number to which the new information pertains and the PI/PI designee's determination of whether the new information is a UP. Please see Appendix A for sample language.
3. The PSO Manager assigned to the PI saves the new information and the PI's determination of UP or not UP in the regulatory files for the affected protocol(s).
 - If the Sponsor or Manufacturer (i.e., the source of the new information) indicates that the event does not change the risk profile of the agent, the PI is still required to make a determination of UP or not UP.

Note: If the PI receives multiple IND Safety Reports (INDSRs) regarding the same agent, the reports may be sent together as long as the PI assessment of each INDSR is clearly delineated.

STEP 3: If the New Information is a UP, Send New Information to IRB

1. The PI/PI designee is responsible for notifying the IRB of new information that meets the definition of a UP. The IRB must receive the REF identifying the UP within 7 days of the PI/PI designee becoming aware of the UP. A copy of the document identifying the new information should be attached to the REF in iRIS. The PI may delegate this task as appropriate – see CCR SOP PM-1.
2. The REF should include what steps have already been taken and what additional steps are planned as a result of this event. In addition, the REF must include a plan to manage the increase risk. For example, how and when will currently enrolled participants be notified of the new risk? See Step 6.
3. If the new information (e.g., INDSR) is not a UP but the Sponsor or Manufacturer REQUIRES reporting to the IRB, the team should contact the sponsor/ manufacturer to notify them of NIH policy on reporting research events (NIH Policy 801) and that the INDSR does not meet reporting requirements. If the sponsor/manufacturer still requests the INDSR submitted to the IRB, the research team will work with the PSO Manager to revisit the requirement and/or to submit the INDSR in a future submission to IRB.

STEP 4: File Documents in Regulatory File

1. The PI's PSO Manager will file the copy of the REF and the IRB outcome letter (the outcome letter from OHSRP Division of Compliance and Training, if applicable should also be included) in the regulatory file for the affected protocol(s).

STEP 5: Protocol Amendment

1. If the new information is determined to be a UP, the PSO Manager will work with the PI and research team to amend the protocol and/or consent form as soon as possible to revise the risk profile of the agent or device as appropriate. The PSO Manager and/or PI will consult with study sponsor as needed for protocol amendments.
2. If the new information requires a protocol amendment with changes to the consent, please ensure that the iRIS amendment form, accurately reflects how and when participants will be notified of changes and specify which groups of participants need to be notified.

STEP 6: Study Participant Notification

1. If the risk profile is changed, the PI and/or appropriate team member must:
 - a. Contact all currently enrolled research participants receiving treatment to discuss the new risk.
 - b. Share what will be done in terms of extra surveillance or procedures.
 - c. Ask if the participant would like to continue on the study and continue to receive the study treatment.
 - d. Document the discussion in the medical record.

Note: If the new information indicates a potential long-term risk, study participants that have completed treatment may need to be notified as above.

Step 7: For Multi-Institutional studies including CTEP-Sponsored Studies where CCR is the Coordinating/Corresponding Center

1. The PI's PSO manager will forward a copy of the new information, including the PI's determination of UP or not UP to each participating site PI for review.
2. The PI's PSO manager will save a copy of the communication in the regulatory file.

Note: Appendix B offers guidance for processing new information from updated Investigator Brochures.

Appendix A: Sample email language for documentation of PI/PI designee determination of UP

1. If the new information does indicate an increased (or new) risk to participants on an NIH research study:
“I have reviewed the attached {name document containing new information: IND Safety Report, manufacturer memo, Safety Monitoring Committee Report, etc.} and the information provided indicates an increased {or new} risk for participants on XXX protocol which uses this drug (or device). I will submit a Reportable Event Form in iRIS to notify the IRB of this increased (or new) risk. I will draft a protocol amendment to include this increased (or new) risk in the protocol and informed consent document.

2. If the new information does not indicate an increased (or new) risk to participants on an NIH research study:
“I have reviewed the attached {name document containing new information: IND Safety Report, manufacturer memo, Safety Monitoring Committee Report, etc.} and the information provided does not increase the known risk for participants on XXX protocol which uses this drug (or device).”

Appendix B: Guidance for Processing Updated Investigator Brochure

If the Sponsor is CCR and updated Investigator Brochure (IB) is received from the Office of Sponsor and Regulatory Affairs (OSRO):

- OSRO will indicate which studies are affected and they will include their recommendations regarding whether the consent and/or protocol need to be amended.
- The Regulatory Submissions Coordinator (RSC) in the Protocol Support Office (PSO) will save the IB in the Central IB folder, ensure that the IB is saved in the applicable Regulatory File(s) and ensure that the PSO Manager(s) assigned to the PI(s) and Clinical Center Pharmacy Department received the updated IB.

If the Sponsor is CCR and IB is received from a source other than OSRO:

- RSC receives an updated IB from any source other than OSRO. RSC saves the IB in the Central IB folder and in the Regulatory File(s) for each CCR-Sponsored study using the agent.
- RSC sends the updated IB (via email) to OSRO and includes in the email a list of all applicable studies. RSC copies the following in the email to OSRO:
 - PI, Research Team and PSO Mgr. for each CCR-Sponsored study using the agent
 - Clinical Center Pharmacy Dept.
 - Rita Misra, Stacie Jeter and Natalie Washington
- OSRO assesses the changes in the IB, distributes the assessment to all PIs with CCR-Sponsored studies using the agent and copies the PSO Mailbox. The assessment will include recommendations regarding whether the consent and/or protocol need to be amended.
- The RSC will ensure the OSRO determination has been sent to the PSO Manager for each CCR-Sponsored study using the agent.

If the Sponsor is CTEP:

- RSC receives an email from CTEP that an updated IB for a specific agent is available for download.
- RSC downloads the IB from the CTEP website and saves it in the Central IB folder and in the Regulatory File(s) for each CTEP-sponsored (or CTEP-associated) study using the agent.
- RSC distributes the updated IB to the PI, Research Team and PSO Manager for all CTEP studies using the agent and reminds the PI to determine if he/she agrees with CTEP's assessment of amendment needed.
- RSC sends the IB to Clinical Center Pharmacy Dept.

If the Sponsor is other than CCR or CTEP (e.g., Pharmaceutical Company):

- Sponsor sends the IB to PI or PSO Manager for a specific study. PI or PSO Manager sends the IB to RSC.
- RSC saves the IB in the Central IB folder and ensures that the IB is saved in the applicable Regulatory File(s).
- RSC ensures the IB has been sent to the PSO Manager for the applicable studies and to the Clinical Center Pharmacy Dept.

ALL ACTIONS – PSO MANAGER

- If no amendment is needed, the PSO Manager will submit the IB in iRIS as an attachment to any other iRIS amendment action or with the next CR Form, whichever comes first.
- If an amendment is needed, the PSO Manager prepares the amendment and submits the updated IB with the amendment in iRIS.
- The PSO Manager saves the IRB Outcome Letter in the IB Folder.