1. PURPOSE

1.1 This procedure outlines the process for reviewing Unanticipated Problems Involving Risks to Subjects or Others (UPs) to ensure the protection of subjects' rights and welfare.

1.2 This procedure outlines the process for reviewing Unanticipated Problems Involving Risks to Subjects or Others (UPs) to ensure the protection of the rights and welfare of subjects.

2. REVISIONS FROM PREVIOUS VERSION

2.1 6.3.2021

3. POLICY

3.1 Federal regulations require the Principal Investigator (PI) to promptly report any Unanticipated Problems (UPs) to the Institutional Review Board (IRB).

3.2 Principal Investigators (PIs) must promptly report any potential physical or non-physical risks and harms to participants, as well as any incidents of death occurring in interventional studies, to the Rutgers Institutional Review Board (IRB). This reporting should be completed within the timelines specified in the Standard Operating Procedures (SOP).

4. RESPONSIBILITIES

4.1 The Principal Investigator (PI) is responsible for the protection and well-being of human subjects in their research studies.

4.2 The Principal Investigator (PI) must quickly report any unanticipated problems (UPs) or the death of a subject in an interventional study to the Rutgers Institutional Review Board (IRB).

4.3 The Rutgers Institutional Review Board (IRB) is responsible for reviewing research proposals and providing oversight and monitoring of approved human subjects research.

5. PROCEDURE

5.1 Unanticipated Problems (UPs) must be reported by the Principal Investigator (PI) or their designee to the designated Institutional Review Board (IRB) that approved the study within five working days after the research team discovers the event or incident. The PI also has separate reporting obligations for Serious Adverse Events (SAEs) and Adverse Events (AEs) to the study sponsor. For more details, please refer to 1.002 (HRP-103) – What Are My Obligations as an Investigator?

5.2 Some Adverse Events (AEs) or Serious Adverse Events (SAEs) may be classified as Unanticipated Problems (UPs). AEs or SAEs are considered UPs if they are unexpected, potentially related to the research, and pose a greater risk to subjects or others, such as family members. These must be reported promptly to the Institutional Review Board (IRB).

If a researcher is notified by a sponsor or Contract Research Organization (CRO) that they need to report a Serious Adverse Event (SAE) or Adverse Event (AE) to the Institutional Review Board (IRB), but the Principal Investigator (PI) determines that the SAE or AE does not meet the criteria for a Unanticipated Problem (UP), the PI can refer the sponsor or CRO to this Standard Operating Procedure (SOP). The PI should inform them that the Research University's IRB will not accept the report, except for inclusion in a summary of SAEs/AEs during the continuing review process.

5.3 The principal investigator must report all adverse events to the IRB with the ongoing review submission.

5.4 It is important to recognize that unintentional exposures (UPs) encompass not only physical risks but also non-physical risks and harms. These may include potential or actual breaches of confidentiality involving sensitive information, such as the loss of a laptop containing Protected Health Information (PHI) or social security numbers. Additionally, UPs can lead to psychological stress, including feelings of anxiety or embarrassment, as well as financial losses and even job loss.

5.5 All unanticipated problems must be reported to the designated Institutional Review Board (IRB), regardless of whether they are classified as serious or non-serious. This requirement applies to incidents that occur at sites where a Rutgers University (RU) investigator is conducting research, known as "Internal Sites," as well as at sites where a non-RU investigator is conducting research. erred to as “External Sites.”

5.5.1 For research conducted at an internal site, the RU investigator must determine if an incident, experience, or outcome qualifies as an Unanticipated Problem.

5.5.2 When conducting research at an external site, an incident, experience, or outcome should only be reported to the Institutional Review Board (IRB) if a monitoring entity or an investigator from the external site has determined that it qualifies as an unanticipated problem. This determination must then be communicated to the principal investigator at the research unit (RU).

5.6 When reporting an Unanticipated Problem (UP), the Principal Investigator (PI) or study staff must provide the necessary information.:

5.6.1 The protocol title, investigator’s name, and the IRB project number.

5.6.2 Date, location, and a detailed description of the adverse event, incident, experience, or outcome.

5.6.3 An explanation of the basis for determining that the adverse event, incident, experience or outcome represents an unanticipated problem.

5.6.4 Date and means by which the PI became aware of the incident, experience, or outcome.

5.6.5 Entities to which the incident, experience, or outcome was reported.

5.6.6 A description of changes made to the protocol or informed consent documents, along with other corrective actions taken or proposed, in response to the unanticipated problem, to minimize risks or harms and prevent recurrence of the event.

5.6.7 In multicenter research protocols, when changes are proposed due to an unanticipated problem, the investigator must consult with the sponsor or coordinating center, as well as the Rutgers IRB.

6. IRB REVIEW AND REPORTING OF UNANTICIPATED PROBLEMS

6.1. Upon receiving the report, the IRB Administrator or Manager will assess whether the unanticipated problem presents a new or increased risk to study subjects or constitutes an urgent safety issue.

6.1.1 The IRB Chair, or their designee, reviews all UPs and determines which require either review by the convened full board or expedited review.

6.1.2 Unanticipated Problems or harm that poses significant concerns regarding the safety and well-being of subjects, as well as the integrity of the study, will be reviewed by the convened full board meeting.

6.2. Unanticipated Problems (UP) requiring full board review will be reviewed at the next convened full board meeting.

6.3. When reviewing the report of an unanticipated problem, the IRB should consider the following:

6.3.1 Informing enrolled participants of the Unanticipated Problem (UP).

6.3.2 The research protocol continues to meet the requirements for IRB approval, particularly regarding whether the risks to subjects are minimized and are reasonable in relation to the anticipated benefits, if any, to the subjects, as well as the expected importance of the research outcomes.

6.3.3 Revising the informed consent document(s) to disclose information regarding new risks of the research.

6.3.4 Other corrective actions by the institution (e.g., addressing a data security policy).

6.3.5 Any changes proposed to the research study due to Unanticipated Problem (UP) must be reviewed and approved by the Rutgers IRB before implementation unless they are necessary to eliminate immediate hazards to subjects.

6.4. The IRB may take/recommend the following actions:

6.4.1 If the report describes a serious increased risk or safety issue, the protocol may be suspended until the issue has been addressed
6.4.1.1 Suspension of enrollment of new subjects.
6.4.1.2 Suspension of research procedures in currently enrolled subjects.
6.4.1.3 The PI may be required to notify research subjects about the unanticipated problem and the newly recognized risks.
6.4.1.3.1 PI may be required to re-consent previously enrolled subjects.
6.4.2 The PI must submit a protocol modification to address immediate hazards to subjects.
6.4.3 The principal investigator may need to submit a protocol modification to address immediate risks to participants.
6.4.4 The PI may be required to submit a corrective action plan (CAPA) to address the rights, safety and welfare of the research subjects.
6.4.5 All project team members may be required to complete additional education.
6.4.6 PI may be required to submit more frequent continuing reviews to the IRB.

6.5. If the Institutional Review Board (IRB) suggests changes to the protocol or informed consent, in addition to those proposed by the study sponsor, coordinating center, or local investigator, the IRB should request, in writing, that the local investigator discuss the proposed modifications with the study sponsor or coordinating center, if applicable. The investigator should then submit a response or any necessary modifications for the IRB's review.

6.6. Reporting Unanticipated Problems (UPs) to Institutional Officials and Regulatory Agencies: All Unanticipated Problems that result in changes to the research protocol or consent documents must be reported to the appropriate institutional officials and the head of the supporting agency (or their designee). This requirement applies regardless of whether the changes are initiated by the Institutional Review Board (IRB), the investigator, or the sponsor.
6.6.1 For research that is federally funded or conducted, these reports should also be submitted to the Office for Human Research Protections (OHRP) within one month of the IRB's receipt of the report.
6.6.2 If the research falls under FDA regulations, the IRB is responsible for reporting the UP to the appropriate FDA division: the Center for Drug Evaluation and Research (CDER) for UPs related to drugs, the Center for Devices and Radiological Health (CDRH) for UPs concerning devices, and the Center for Biologics Evaluation and Research (CBER) for UPs associated with biologics.
6.6.3 If the IRB suspends or terminates a study due to reported adverse events, the University will notify federal regulatory agencies and/or the sponsor according to Rutgers IRB SOPs.

7. IRB REVIEW AND REPORTING OF UNANTICIPATED PROBLEMS SUMMARY REPORTS DURING CONTINUING REVIEW

7.1 During the ongoing review of a protocol, the Principal Investigator (PI) is required to submit a summary of all Unanticipated Problems and all adverse events that occurred during the review period, as well as since the start of the study. Each summary for an Unanticipated Problem should include:
7.1.1 The number of individuals who encountered the unexpected issue.
7.1.2 The investigator's assessment of whether the Unanticipated Problem is serious or not.
7.1.3 The investigator's assessment of the Unanticipated Problem's relationship to the study procedures (e.g. definitely related, probably related, or possibly related).

7.2 If the study is a multi-center trial and is supervised by a Monitoring Entity, you may submit a current report from that entity in place of the summary of Unanticipated Problems mentioned earlier. This report must include the date of the review and the Monitoring Entity's assessment of the data that was reviewed. Furthermore, if the information reviewed is not detailed in the data safety monitoring plan submitted to the IRB, the report should specify what information was assessed.

7.3 All Monitoring Entity reports that have not been previously submitted to the IRB must be included with the continuing review submission.