**1. PURPOSE**

1.1 This procedure establishes the process for review of Unanticipated Problems Involving Risks to Subjects or Others (UPs) in a manner that protects the rights and welfare of subjects.

1.2 This procedure covers the processes for investigator reporting, and IRB review, of such reports.

**2. REVISIONS FROM PREVIOUS VERSION**

2.1 None. (This is the first version of this Standard Operating Procedure (SOP)).

**3. POLICY**

3.1 Federal regulations require the Principal Investigator PI to promptly report UPs to the IRB.

3.2 Reports regarding potential physical and non-physical risks and harms to subjects and others that occur in human research studies, or a death of a subject in an interventional study, must be reported by promptly (within timelines indicated below) by the PI to the Rutgers IRB as defined in this SOP.

**4. RESPONSIBILITIES**

4.1 The PI bears the primary responsibility for the protection and well-being of human subjects in their research studies.

4.2. The PI must promptly report UPs, or a death of a subject in an interventional study, to the Rutgers IRB.

4.3 The Rutgers IRB is responsible for the review of UPs and for providing oversight monitoring of human subjects research that it approves.

**5. PROCEDURE**

5.1 UPsmust be reported by the PI, or designee, to the designated IRB that approved the study within five working days of the research team’s discovery of the event or incident. There are separate reporting requirements for the PI for reporting of serious adverse events (SAEs) and adverse events (AEs) to the sponsor (See HRP-103 – What Are My Obligations as an Investigator?).

5.2 Some AEs or SAEs meet the definition of a UP. Only those AEs/SAEs that were unexpected, possibly related, and place subjects/others (e.g., family member) at greater risk are UPs and need to be reported promptly to the IRB. If a researcher is told by a sponsor or Contract Research Organization (CRO) that they need to report a SAE or AE to the IRB, that the PI determines that the SAE/AE does not meet the definition of a UP, the PI can direct the sponsor/CRO to this SOP and inform them that the RU IRB will not accept the report (other than for inclusion in a summary of SAEs/AEs for continuing review).

5.3 A summary of all Adverse Events must be reported by the PI to the IRB with the Continuing Review submission.

5.4 It is important to note that UPs also include non-physical risks/harms such as potential or real breach of confidentiality of sensitive information (e.g., loss of a laptop with Protected Health Information (PHI), social security number, etc.), psychological stress (e.g., anxiety, embarrassment), financial loss, loss of employment, etc.

5.5 Each Unanticipated Problem should be reported to the designated IRB, whether or not a) it is serious or non-serious or b) it occurs at a site at which a RU investigator is conducting the research (an “***Internal Site***”), or a site at which a non-RU investigator is conducting the research (an “***External Site***”).

5.5.1 For research conducted at an Internal Site, the RU investigator should make the determination as to whether an incident, experience, or outcome constitutes an Unanticipated Problem.

5.5.2 For research conducted at an External Site, an incident, experience, or outcome generally should be reported to the IRB only if a Monitoring Entity or an External Site investigator has determined that it constitutes an Unanticipated Problem, which is subsequently reported to the RU investigator.

5.6 When reporting a UP, the PI or study staff will provide the following 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 any changes to the protocol and/or informed consent document(s) or other corrective actions that has been taken or is proposed in response to the unanticipated problem to minimize risks/harms or reoccurrence of the event.

5.6.7 For multicenter research protocol proposed changes in response to an unanticipated problem, the investigator should consult with the sponsor or the coordinating center in addition to the Rutgers IRB.

**V. IRB REVIEW AND REPORTING OF UNANTICIPATED PROBLEMS**

1. Upon receipt of the report, the IRB Administrator or the IRB Manager will begin an evaluation to determine if the unanticipated problem indicates a new or increased risk to study subjects or an urgent safety issue.

1.1 The IRB Chair, or designee, reviews all UPs and determines which ones require review by the convened full board versus expedited review.

1.2 UPs that constitute serious adverse events or harm that raise potential concerns regarding the safety and well-being of subjects and/or the integrity of the study and will be reviewed by the convened full board meeting.

 2. UPs requiring full board review will be reviewed at the next convened full board meeting.

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

 3.1 Informing enrolled participants of the UP.

 3.2 The research protocol still satisfies the requirements of the IRB approval, in particular whether the risks to subjects are still minimized and reasonable in relation to the anticipated benefits, if any, to the subjects and the importance that my reasonable be expected to result.

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

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

 3.5 Any proposed changes to the research study in response to the unanticipated problem must be reviewed and approved by the Rutgers IRB before being implemented, except when necessary to eliminate apparent immediate hazards to subjects.

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

4.1 If the report describes a serious increased risk or safety issue, the protocol may be suspended until the issue has been addressed

4.1.1 Suspension of enrollment of new subjects.

4.1.2 Suspension of research procedures in currently enrolled subjects.

4.1.3 The PI may be required to notify research subjects about the unanticipated problem and the newly recognized risks.

4.1.3.1 PI may be required to re-consent previously enrolled subjects.

4.2 The PI may be required to submit a *Protocol Modification* with the changes to the protocol to eliminate apparent immediate hazards to subjects.

4.3 The PI may need to modify the informed consent documents to include a description of newly recognized risks.

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.

4.5 All project team may be required to complete further education.

4.6 PI may be required to submit more frequent continuing reviews to the IRB.

 5. If the IRB proposes 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 discusses the proposed modifications with the study sponsor or coordinating center, if applicable, and submit a response or necessary modifications for review by the IRB.

6. Reporting of UP Reports to Institutional Officials and Regulatory Agencies - All UPs that result in a change in the protocol and/or the consent documents (either by the IRB, the investigator, or the sponsor) shall be reported to appropriate institutional officials, the supporting agency head (or designee), and for federally-supported or conducted research to OHRP within one month of the IRB’s receipt of the report. If the research is FDA-regulated, then the IRB will report the UP to the FDA (CDER for UPs resulting from drugs; CDRH for UPs resulting from devices; CBER for UPs resulting from biologics).

6.1 If the IRB suspends or terminates a study due to reported adverse experiences, the University notifies federal regulatory agencies, and/or the sponsor in accordance with Rutgers IRB SOPs.

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

* + - 1. At the time of continuing review of a protocol, the PI should submit a summary of all Unanticipated Problems and a summary of all adverse events that occurred during the review period and since the beginning of the study. The summary for each Unanticipated Problem should include:
	1. the number of subjects who experienced the Unanticipated Problem;
	2. the investigator’s determination of whether or not the Unanticipated Problem is serious;
	3. the investigator’s determination of the Unanticipated Problem’s relationship to the study

 procedures (e.g., definitely related, probably related, or possibly related).

* + - 1. If the study is a multi-center study and is subject to oversight by a Monitoring Entity, a current report from the Monitoring Entity may be submitted in lieu of the summary of Unanticipated Problems described above. The current monitoring report must indicate the date of the review and the Monitoring Entity’s assessment of the data reviewed. If not described in the data safety monitoring plan submitted to the IRB, the report should also identify what information was reviewed.
			2. Any Monitoring Entity reports that have not been previously submitted to the IRB should also be included with the continuing review submission.