1. PURPOSE

To outline the processes for review of Unanticipated Problems and communication of any action necessary to address the problem.

2. SCOPE

This SOP applies to all nonexempt human subject research reviewed by Aurora's IRB and conducted by researchers on staff at or affiliated with Aurora Health Care, conducted at any AHC facility, or utilizing individually identifiable data of AHC patients.

3. DEFINITIONS

External Unanticipated Problem is an Unanticipated Problems that occurs on a multi-center study that Aurora is engaged in but does not occur at an Aurora facility (i.e., the Unanticipated Problem occurs at another center). [External Unanticipated Problems are not Unanticipated Problems in studies ceded to non-Aurora IRB.]

Local Unanticipated Problem is an Unanticipated Problem that occurs at a site for which Aurora IRB has oversight.

Minimal Risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

Others may include but is not limited to research subjects' family members, health care providers and research staff.

Significant New Information is any information not previously reported to the IRB about the research that may relate to subject's willingness to continue participation. Significant new information may be revealed in publications, data safety monitoring reports, interim study results, revised package inserts, or other material.

Subject is a living individual(s) about whom an investigator conducting research obtains: (1) data through intervention or interaction with the individual; or (2) identifiable private information.

Unanticipated Problem (UP) is any incident, experience or outcome that is:
a) unexpected in terms of its nature, severity or frequency given the research and the characteristics of the Subject population being studied;
b) regarded as unwelcome or harmful and something that may need to be dealt with or overcome; and

c) is related or possibly related to the research.

UPs might include but are not limited to:
(1) Complaints from Subjects or Others
(2) Breaches of privacy or confidentiality
(3) A series of adverse events and rarely a single adverse event (see FDA and OHRP guidance for a description of on those adverse events FDA and OHRP consider Unanticipated Problems Involving Risks to Subjects or Others requiring reporting to the IRB)
(4) Events determined by a sponsor or multi-center lead PI to be meet the definition of a UPIRSO
(5) Changes made to research without prior approval in order to eliminate apparent immediate harm
(6) An unintentional change in the study plan for an individual Subject or series of Subjects
(7) Subject noncompliance (e.g., missed dosing, refused appointment)
(8) Significant New Findings
(9) Other incidents, experiences or outcomes that are unexpected, related to the research, and unwelcome or harmful and something that may need to be dealt with or overcome.

Unanticipated Problem Involving Risks to Subjects or Others (UPIRSO) is an Unanticipated Problem that the IRB Chair/designee determines involves a new or increased risk to Subjects or Others (including physical, psychological, economic or social) that either might affect Subjects' willingness to continue participation or requires some action (e.g., modification of the consent process, informing participants, modifying the study protocol or procedures, etc.).

4. POLICY

This SOP implements requirements at sections 4.2g)i) & ii), 4.2h)i) and 4.2j) of AHC System Policy #811 – *Research Involving Humans or Their Identifiable Data or Biospecimens*.

5. PROCEDURE

5.1 Review of UPs

Local and External UPs will be reviewed in the same manner (as described below) except that the review and any action required related to External UPs will be specific only to Subjects under the oversight of Aurora's IRB. If an Aurora PI is the lead PI of a multi-site study, the review and any action required will consider Subjects at all sites.

Upon receipt of submissions, the proposed change will be logged into the RSPP database for tracking purposes. The tracking number will be entered onto the submitted form.

a) *UPIRSO determination.*

IRB Chair or designated, qualified IRB member (designee) uses the document "Review Considerations for Unanticipated Problems Involving Risk to Subjects or Others ('UPIRSO')" to review, within 5 working days whenever possible, both Local and External UPs submitted and make a determination of whether the reported UP meets the criteria of a UPIRSO.

b) *Immediate action and risk determination*. For each UPIRSO, the Chair/designee will:

i) assess and communicate verbally with the PI, with follow up in writing, any immediate action required to alleviate apparent immediate risks to Subjects or Others;

ii) document decision on *UP Reporting* form or in another permanent record as determined appropriate by RSPP;

iii) determine whether the UPIRSO involves more than minimal risk to Subjects or Others.

c) *Review of no more than minimal risk UPIRSO*. For UPIRSO determined not to involve greater than minimal risk to Subjects or Others, the Chair/designee will:

i) review and approve action proposed by the PI and/or sponsor to address the problem;

ii) consider whether additional action not proposed is required to address the problem, document decision on the *UP Reporting Form.*

RSPP Office will:

i) communicate outcome of review to reporter of the UP, Principal Investigator and others as applicable

ii) notify IRB of review and outcome via agenda of next available IRB meeting;

iii) schedule the item for convened IRB review if reviewer is unable to agree with the PI on necessary action.

d) *Review of greater than minimal risk UPIRSO* For UPIRSO determined to involve greater than minimal risk to Subjects or Others:

i) RSPP team member schedules the item for review at the next available convened IRB meeting following standard procedures for assignment of reviewers and distribution of meeting material (additional information on IRB roles in reviewing UPIRSOs and materials to be distributed may be found in *Unanticipated Problem* guidance);

ii) convened IRB reviews and determines action required to address the UPIRSO;

iii) RSPP Office documents decision in meeting minutes and on the *UP Reporting Form*, and communicates outcome of review to reporter of the UP, Principal Investigator and others as applicable. RSPP database is updated with review outcome.

5.2 Reporting to regulatory agencies and institutional officials

Findings of UPIRSO will be reported via written communication to regulatory agencies and institutional officials, and others as applicable, in accordance with the RSPP SOP #12 – *External Reporting.*.

5.3 RSPP Office will retain submitted materials and documentation of determinations in accordance with AHC record retention requirements as noted in AHC system policy #223 - *Record Retention, Storage and Destruction.*

CROSS REFERENCES:

SOP 12 – *External Reporting*

RSPP Guidance – *Unanticipated Problem*,

IRB Reliance for Multi-center Research

OWNER:

Director, Research Subject Protection Program

REFERENCES:

45 CFR 46.103(b)(5)

21 CFR 56.108(b)

AAHRPP Element II.2.F. & II.2.I

PRIOR REVIEW / REVISION DATES: