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 human subject research reviewed by Advocate Aurora Health's (AAH) IRB and conducted by researchers on staff at or affiliated with AAH, conducted at any AAH facility, or utilizing individually identifiable data of AAH patients.

For Research Ceded to an External IRB, review of the reported problem to determine if an UPIRSO is the responsibility of the IRB of Record. The AAH RSPP reviews the reported incident to determine if any immediate action is needed to protect AAH subjects.

3. DEFINITIONS

External Unanticipated Problem is an Unanticipated Problem that occurs on a multi-center study that AAH is engaged in but does not occur at an AAH facility (i.e., the Unanticipated Problem occurs at another center).

Local Unanticipated Problem is an Unanticipated Problem that occurs at a site for which AAH 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 IV.B.7.a) &b), IV.B.8.a) and IV.B.10 of AAH System Policy– *Research Involving Humans or Their Identifiable Data or Biospecimens*.

5. PROCEDURE

5.1 Review of UPs for studies overseen by the AAH IRB
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 AAH's IRB. If an AAH 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 in IRBNet, the problem will also be logged into the RSPP database for tracking purposes. The report will be provided to an RCA for review.

a) *UPIRSO determination.*

IRB Chair or designated, qualified IRB member (designee) will be provided the UP Report. He/she 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 RSPP *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) complete the *UP Reporting* form with UPIRSO decision;

ii) publish the completed *UP Reporting* form in IRBNet. Correspondence within IRBNet is available to all who are shared access to the study in the IRBNet system, including the reporter of the event, the Principal Investigator, and others as applicable.

iii) update RSPP database with review outcome; notify IRB of review and outcome via agenda of next available IRB meeting;

iv) 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 (see *Meeting Materials* and *Convened IRB Meeting Administration* guidance documents);

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 publishes copy of completed form in IRBNet. Correspondence within IRBNet is available to all who are shared access to the study in the IRBNet system, including the reporter of the event, the Principal Investigator, and others as applicable. RSPP database is updated with review outcome.

5.2 Review of Problems occurring at AAH for Research Ceded to an External IRB
Local problems reported in Research Ceded to an External IRB will be reviewed to determine whether immediate action on the part of AAH should be considered to protect AAH subjects.

Upon receipt of submissions in IRBNet, the problem will be logged into the RSPP database for tracking purposes. The report will be assigned to an RCA for review.

a) Immediate action and risk determination. For each reported problem,

i. the RCA will consult with a Chair or RSPP Director to determine whether immediate action is required to alleviate apparent immediate risks to AAH Subjects or Others;

1. the RSPP Director will consult with a Chair and/or Institutional Official as needed.

RSPP Office will:

ii. complete the *UP Reporting Form* with any immediate action decision;

iii. upload the completed *UP Reporting Form* in IRBNet. Correspondence within IRBNet is available to all who are shared access to the study in the IRBNet system, including the reporter of the event, the Principal Investigator, and others as applicable.

iv. Update RSPP database with review outcome.

b) The IRB of Record will determine whether the reported problem is an UPIRSO per their policies.

i. The AAH RSPP will receive a copy of UPIRSO decisions per terms of reliance agreement executed between AAH and the external entity.

5.3 Reporting to regulatory agencies and institutional officials

Findings of UPIRSO in research overseen by the AAH IRB 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.*

Reporting of UPIRSO findings in Research Ceded to an External IRB will be made per the terms of the executed reliance agreement.

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

CROSS REFERENCES:

SOP 12 – *External Reporting*

RSPP Guidance – *Meeting Materials*

Convened IRB Meeting Administration

Deferral/Ceding Of IRB Oversight To An External IRB

	AHC system policy – *AAH Record Retention, Storage and Destruction* *Research Involving Humans or Their Identifiable Data or Biospecimens*
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:	1/3/22 (effective 1/24/22)