

SOP: RR 403 Version No.: 08 Effective Date: 1/21/11	ONGOING OVERSIGHT OF APPROVED RESEARCH AND REPORTING OF PROBLEMS/EVENTS	Supersedes Document Dated: 1/19/11
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1. POLICY

Steering Committee approved 1/21/11

Human Subject Research regulations require ongoing oversight of research activities involving human subjects.

Ongoing oversight includes, reviewing and responding appropriately to the following activities:

- Reported problems
- Adverse events
- Changes to previously approved research
- Violations and Protocol Exceptions
- Significant new information
- Complaints
- Noncompliance (See Policy CO 601)
- Site visit results and third party verification

Specific Policies

Terms used in this policy, but not defined herein shall have the meanings set forth in the Glossary.

1.1. Definitions

“Administrative Hold” is a request to the Investigator by the convened IRB, IRB Chair or Administration to voluntarily place some or all research activities on a temporary hold to allow the IRB to obtain and review additional information.

“Complainant” means any individual(s) asserting a complaint to the IRB.

A “Protocol Exception” means a one-time, intentional, time-sensitive action or process that departs from the IRB-approved study protocol, intended for one occurrence. Protocol Exceptions are classified as minor or significant.

“Local” events are those that occur at a site for which the Aurora IRB has oversight.

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“External” events are those that occur at a site for which the Aurora IRB does not have oversight.

An “Unanticipated Problem” means any incident, experience, or outcome that is (1) unexpected (in terms of nature, severity, or frequency) given the research procedures described in the protocol and related documents and the characteristics of the population being studied; (2) related or possibly related to the participation in the research. For example, exposure of a technician to increased levels of radiation due to a malfunctioning investigational imaging device would be an Unanticipated Problem. The IRB would review the report of such event as a possible UPIRSO [Unanticipated Problem Involving Risk to Subjects or Others] (see discussion later in Policy) if it involves increased risk to subjects or others.

“Others” may include subjects’ family members, health care providers, and research staff.

“Unexpected” means that the specificity and severity are not accurately reflected in the information previously submitted to the IRB (e.g. protocol, Investigator Brochure and/or informed consent document). [Note an event is considered “unexpected” if it occurs at a specificity or severity that is inconsistent with prior observations, such as what is described or addressed in the information previously submitted to the IRB.]

“Possibly Related Or Related To The Research Procedures”. Possibly related means there is a reasonable possibility that the incident, experience or outcome may have been caused by the procedures involved in the research. Reasonable means a strong temporal relationship to the study protocol, and implies that an alternative etiology is unlikely or significantly less likely. Related means related to the use of the research procedure and implies a definitive relationship.

“Violation” means any action affecting a research subject (or potential subject) which deviates from, or does not comply with, the conduct of a research study as reviewed and approved by the IRB, or Noncompliance with Aurora policies or federal regulations. Protocol violations are classified as minor or significant violations.

1.2. Reporting Unanticipated Problems

Upon becoming aware of any problem/event occurring in the research (whether drug/biologic, device, or procedure related research, occurring at a Local site or site External to Aurora), an Investigator should determine whether the problem/event constitutes a potential Unanticipated Problem that needs to be reported to the IRB per this Policy. In order to meet the Policy definition of an Unanticipated Problem, the Sponsor/Investigator must determine that **BOTH** of the following conditions exist: 1) “Unexpected” **AND** 2) “Possibly Related or Related To The Research Procedures”.

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1.2.1. Reporting timeframe

(A) Local and External Unanticipated Problems must be promptly reported by Principal Investigator to the IRB as soon as possible, but in no case **no more than 5 working days following discovery of the event [local] or determination of event by the sponsor/investigator as an Unanticipated Problem [external].**

(B) In some cases, it may be appropriate to submit a preliminary report in order to meet the required timeframe for reporting under this Section and to submit a follow-up report at a later date when more information becomes available. If this reporting option is taken, it must be **clear** in the report to the IRB that the problem/event meets the Policy definition of Unanticipated Problem, and that more information is forthcoming.

1.2.2. Types of Unanticipated Problems that must be submitted to the IRB. The following problems are reported to the IRB through various mechanisms which are discussed later in this policy:

- Adverse events/reactions (that are either Serious or Nonserious per the FDA’s definition (see section 1.3).
- Injuries to subjects or Others as a result of research procedures (see section 1.4)
- New information that indicates a change to the risks or potential benefits of the research (see sections 1.4-1.9). For example:
 - An interim analysis or safety monitoring report indicates that the frequency or magnitude of harms or benefits might be different from those initially presented to the IRB.
 - A paper is published from another study that shows that the risks or potential benefits of the research might be different from those initially presented to the IRB.
 - Change in FDA labeling or withdrawal from marketing of a drug, device, or biologic used in a research protocol.
 - Changes to the Investigator Brochure/Device Manual that affects the risks or benefits of the study.
 - Change to the protocol done without prior IRB review to eliminate an apparent immediate hazard to a subject.

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- Incarceration of a subject in a protocol not approved to enroll prisoners.
- Event that requires reporting to the sponsor.
- Sponsor imposed suspension for risk.
- Complaint of a subject when the complaint indicates unexpected risks or cannot be resolved by the research team.
- Complaints by employees or staff which involve risks to subjects or others.

1.3. Adverse Events (as defined in the Glossary)

Any Local adverse event that has been determined by the local Investigator to meet the definition of Unanticipated Problem as defined in section 1.1, or an external adverse event that the sponsor has determined to be an Unanticipated Problem, must be promptly reported (per section 1.2.1) to the Aurora IRB..

1.3.1. Local adverse events. These events may meet the FDA’s definition of either Serious or Nonserious. The events meeting the Policy definition of Local Unanticipated Problems must be reported to the Aurora IRB using form RR 403-A.

1.3.2. External adverse events. When the local research site receives a report of an External adverse event from the Sponsor, and the Sponsor has determined the event to be an Unanticipated Problem, the event must be reported to the IRB using form RR 403-B.

1.3.3. NOTE: Only those External Adverse Events for which the Sponsor has made an Unanticipated Problem determination should be reported to the Aurora IRB. Aurora IRB form RR 403-B must be received in the RSPP Office no more than 5 working days following receipt of the Sponsor’s determination that the event meets OHRP and FDA guidance on reporting of Unanticipated Problems.

Individual IND safety reports from external sites are generally not reportable to the IRB because their implications for the study cannot be sufficiently understood.

External adverse events reported to the IRB as Unanticipated Problems should be accompanied by the Sponsor’s Risk Mitigation Plan that addresses how re-occurrence of the problem is being prevented.

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1.3.3. For those events and reports that are not reportable to the IRB under this Policy, a summary (i.e., not individual reports) of all adverse events that have occurred within the last approval period may be submitted to the IRB at the time of continuing review.

1.4. Injuries to Subjects or Others as a Result of Research Procedures

Injuries or problems that meet the Policy definition of Unanticipated Problem but affect Others (e.g. hospital employee, subject’s family member) must be also reported using form RR 403-A. Such report must be submitted to the Aurora IRB within 5 working days from discovery whether the injury/problem occurred in a subject or other individual

1.5. Changes to Previously Approved Research

1.5.1. Changes in approved research, during the period for which approval has already been given, **may not be initiated without prior IRB review and approval** (full or expedited review, as appropriate), except where necessary to eliminate apparent immediate hazards to human subjects. Changes to eliminate apparent immediate hazards to human subjects will be reviewed as Unanticipated Problems as described above in Section 1.2.

1.5.2. Reporting timeframe. Although there is no regulatory timeframe for reporting changes to a research study, the Aurora IRB requires any changes that may affect subject safety or the risk benefit analysis be submitted within thirty (30) days after notification from the sponsor. All other changes must be submitted within ninety (90) days after notification from the sponsor. Failure to notify the IRB of changes in approved research within these time frames may be considered a Protocol Violation per section 1.7 of this policy, and may be handled in accordance with the Noncompliance policy (Policy CO 601). Notwithstanding these time frames, all changes must be submitted to and approved by the Aurora IRB before the change is implemented.

1.5.3. Investigators must submit requests for changes to the protocol or to the IRB-approved informed consent form to the IRB by completing and submitting an Aurora IRB Modification Form and, if necessary, an Addition of a Site Form (form RR 403-C and RR 403-D). Upon receipt of the protocol change, the IRB Chair or his or her designee, will determine if the revision meets the criteria for expedited approval (Policy RR 401). If the change does not qualify for expedited approval, it must be reviewed and approved by the full IRB at a convened meeting. Failure to notify the IRB of changes in approved research prior to implementation of such changes, except where necessary to eliminate apparent immediate hazards to human subjects is a Protocol Violation and

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Unanticipated Problem, and will be handled in accordance with this policy and the Noncompliance policy (Policy CO 601).

1.5.4. Investigators will be notified in writing as soon as possible as to action taken by the IRB for changes to approved research.

1.6. Protocol Exceptions

The terms “protocol deviation” and “protocol exception” are not defined by either the HHS human subjects regulations (45 CFR 46) or the FDA human subjects regulations (21 CFR 50). For Aurora IRB purposes, a Protocol Exception is a one-time, intentional, time-sensitive action or process that departs (“deviates”) from the IRB-approved study protocol.

NOTE: Eligibility exceptions (or eligibility waivers granted by a sponsor) for enrollment of a specific individual who does not meet the inclusion/exclusion criteria in the IRB approved protocol **are not** exceptions. Eligibility exceptions are considered changes in research that require IRB review and approval **before** a subject who does not meet the approved protocol inclusion/exclusion criteria may be enrolled.

1.6.1. Protocol Exceptions are classified as either Minor or Significant, based on both the actual or potential effect of the action or process on the specific subject(s), the entire subject population, and/or the overall integrity of the study design and results. It is the Investigator’s responsibility to determine whether the Protocol Exception is minor or significant, based on the following criteria.

A Significant Protocol Exception is an event that actually or potentially meets one or more of the following criteria:

- impacts subject safety, welfare or rights;
- alters the risks or the benefit to the subject in a significant serious or negative way;
- impacts the integrity of the data; and/or
- affects a subject’s willingness to participate.

A Protocol Exception that does not meet one or more of the criteria above is considered Minor.

1.6.2. Minor Protocol Exceptions

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(A) **Minor or Administrative Protocol Exceptions** are exceptions to the approved protocol that should be reported to the Aurora IRB at the time of continuing review. NOTE: this category of exceptions does not apply for IDE studies (see section 1.6.3.D).

Examples of Minor or administrative exceptions include: follow up visits that occurred outside the protocol required time frame because of the participant’s schedule, or blood samples obtained at times close to but not precisely at the time points specified in the protocol.

1.6.3. Significant Protocol Exceptions

(A) **Major, Non-Emergent Protocol Exceptions** are **planned** exceptions that are non-emergent and represent a major change in the protocol as approved by the IRB. The Sponsor should approve the Protocol Exception prior to submission to the Aurora RSPP Office.

The IRB must approve the request before the proposed change is implemented. The PI must submit non-emergent exceptions to the Aurora IRB by completing and submitting an Aurora IRB Modification Form and, if necessary, an Addition of a Site Form (form RR 403-C and RR 403-D) (see section 1.5). A copy of the written approval document from the Sponsor must be provided with the Modification form.

If a Major, Non-Emergent Protocol Exception occurs without prior IRB approval, the event is considered a Significant Violation of the protocol, along with an UPIRSO. The Significant Violation must be reported to the IRB per section 1.7 of this policy. The event will be reviewed as a UPIRSO under section 1.12 of this policy, and as an instance of noncompliance under Aurora IRB policy 601. An investigator’s failure to report promptly any major, non-emergent exception for which prior IRB approval is not obtained is itself an incident of noncompliance.

(B) **Emergency Protocol Exceptions** are departures from the protocol that are required to protect the life or physical well-being of a subject. Prospective IRB review of the request is not possible. The sponsor and the Aurora IRB must be notified as soon as possible, but no later than 5 working days after the **emergency** situation occurred (21 CFR 812.150(a)(4)).

The investigator must report the Emergency Protocol Exception to the Aurora IRB as a Significant New Finding (see section 1.8 of this policy). The event will be reviewed as an UPIRSO per section 1.12 of this

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policy. A copy of the written approval document from the Sponsor must be provided with the Significant New Finding form (RR 403-F).

(C) Investigational Device Exemption (IDE) studies. FDA device regulations at [21 CFR 812.150\(a\)\(4\)](#) require **prior** approval **from the Sponsor** of all planned exceptions, including administrative and Minor Exceptions. Planned exceptions of an IDE study must be submitted and approved by the Aurora IRB prior to implementation of any such planned exceptions from the IRB approved protocol.

The PI must submit all planned exceptions to the Aurora IRB by completing an Aurora IRB Modification form and, if necessary, an Addition of a Site form (form RR 403-C and RR 403-D) (see section 1.5). A copy of the written approval document from the Sponsor must be provided with the Modification form.

(D) Investigator-Initiated Research. In the case of Investigator-Initiated Research, the Investigator serves as the Sponsor of the research. Therefore, **ALL** requests for Protocol Exceptions must be submitted to the Aurora IRB **prior** to implementation by completing and submitting a Modification Form (form RR 403-C), except those that are required to protect the life or physical well-being of a subject. The Aurora IRB must be notified as soon as possible, but no later than 5 working days after the emergency situation occurred.

A **second** request for the same Protocol Exception in an Investigator-Initiated research protocol will necessitate that the Investigator modify the protocol.

1.6.4. IRB Review

(A) Significant Protocol Exceptions

(1) Major, Non-Emergent Exceptions. Upon receipt of a request for a Major, Non-Emergent Exception (see section 1.6.3.A), the Senior IRB Chair, or his or her designee, will determine if the Protocol Exception meets the criteria for expedited approval (Policy RR 401). If the Major, Non-Emergent Protocol Exception does not qualify for expedited approval, it must be reviewed and approved by the full IRB at a convened meeting.

(2) Emergency Protocol Exceptions. Upon receipt of notification of an Emergency Protocol Exception (see section 1.6.3.B), the Senior IRB Chair, or his or her designee, will send the

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notification to the fully convened IRB determination of appropriate action related to the UPIRSO.

Investigators will be notified in writing as soon as possible as to action taken by the IRB for a Significant Protocol Exception.

(B) Minor Protocol Exceptions. Minor Protocol Exceptions are reported to the IRB at the time of Continuing Review (see section 1.6.3.A and SOP RR 404). The Minor Protocol Exceptions will be reviewed by a Primary Reviewer and/or the full committee, and consideration given to them in the context of study conduct relative to the Criteria for Approval (see SOP RR 402).

1.7. Protocol Violations

Protocol violations are classified as Minor or Significant.

1.7.1. **Minor Violations** are defined as non-compliance with the approved protocol or any Aurora IRB policy or federal regulation that usually does **not**:

- Have any substantive effect on the safety or well-being of research subjects;
- Change the risk/benefit ratio;
- Affect the value of the data collected (meaning the violation does not confound the scientific analysis of the results);
- Result from willful or knowing misconduct on the part of the investigator(s) or study coordinator; or
- Violate any basic ethical principles.

This list of examples is intended as a guide and is not all-inclusive:

- Implementation of unapproved recruitment procedures
- Use of invalid consent form, i.e. consent form without IRB approval stamp, or outdated/expired consent form which did not contain unapproved language (a document comparison must be done to determine that no unapproved language was included in the incorrect consent document)

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- Missing original signed and dated consent form (only a photocopy available)
- Missing pages of executed consent form depending on the types and number of pages missed (may be deemed major)
- Failure to follow the approved study procedure that, in the opinion of the PI, does not affect subject safety or data integrity:
 - Study procedure conducted out of sequence
 - Omitting a IRB approved research activity on a protocol (e.g. mailing out or collecting QOL surveys, evaluating and documenting performance status)
 - Failure to perform a required lab test
 - Missing lab results
 - Study visit conducted outside of required timeframe
- Local over-enrollment to a multi-center protocol when the sponsor’s protocol limits have not been exceeded

These Minor Violations must be recorded and reported to the sponsor. Minor violations do not need to be immediately reported to the IRB, however, information regarding these minor violations will be requested by the IRB at the time of Continuing Review.

1.7.2. **Significant violations** are defined as actions of non-compliance with the approved protocol or any Aurora IRB policy or federal regulation that:

- Have or pose a significant risk of harm to research subjects;
- Have a likelihood of causing damage to the scientific integrity of the data collected;
- Result from evidence of willful or knowing misconduct on the part of the investigator(s) or study coordinator; and/or
- Ignore or violate the established research, medical, and ethical principles.

This list of examples is intended as a guide and is not all-inclusive:

- Failure to obtain informed consent, i.e., there is no documentation of informed consent
- Informed consent obtained after initiation of study procedures
- Inappropriate documentation of informed consent, including:
 - missing subject or LAR signature
 - missing signature of person obtaining consent
 - copy not given to the person signing the form

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- someone other than the subject or LAR dated or initialed the consent form
- Use of a consent document containing language that was not approved by the IRB
- Enrollment of a subject prior to IRB approval or who did not meet all inclusion/exclusion criteria
- Performance of a study procedure not approved by the IRB
- Failure to report events in accordance with IRB policies and/or sponsor requirements
- Failure to perform a required study visit or procedure that, in the opinion of the PI, may affect subject safety or data integrity
- Study visit or procedure is conducted outside of required timeframe that, in the opinion of the PI, may affect subject safety or data integrity
- All drug/study medication dispensing or dosing errors regardless of the percentage of the error.
- Breaches of confidentiality
- Inappropriate destruction of study records
- Failure to follow safety monitoring plan
- Over-enrollment to an investigator-initiated protocol
- Repeated or continued negligence in performance of study procedures
- Repeated or continued inability of a subject to comply with the research activity
- Dosing or treatment plan change with the potential for altered therapeutic efficacy and/or adequate evaluation of toxicity
- The number of missed oral medication doses indicates a problem with compliance with study procedures on the part of the subject, a problem with the ability of the study staff to monitor subject compliance, and/or the number of missed oral doses impacts the risk/benefit ratio.
- Enrollment of subjects after IRB-approval of study has expired
- Failure to submit continuing review application to the IRB before study expiration
- 3 or more minor exceptions for the same subject, or of the same type, that impacts the safety of participants, compromises the integrity of the study data and/or affects subject's willingness to participate in the study.

These Significant Violations must be reported to the Aurora IRB **within 10 working days discovery of the Violation** by completing and submitting Form RR 403-G. The Significant Violation will be reviewed according to the procedures outlined in section 1.12 of this policy and Aurora's Noncompliance Policy (SOP 601) as necessary.

1.8. Significant New Findings

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During the course of a study, the research staff may receive new information on the research that must be reported to the Aurora IRB. Such information may include: Data and Safety Monitoring Board (DSMB) or Data Monitoring Committee (DMC) reports, annual reports from sponsors, revised Investigator’s Brochures/Device Manuals, current literature. This information should be submitted to the Aurora IRB on form RR 403-F. The IRB expects that the Sponsor will make a determination whether any of the new information contained in these reports indicates an Unanticipated Problem and/or requires a change to the IRB-approved research. Changes to the IRB-approved research must be reported in accordance with Section 1.5 above.

If the new information is reporting a problem/an event determined by the Sponsor to be an Unanticipated Problem, the form must be submitted to the Aurora IRB **within 5 working days from receipt**. The information will be reviewed as described in section 1.12 of this Policy to assess whether or not the risk/benefit balance is still acceptable.

1.9. Complaints

Complaints may come from any source, including but not limited to IRB members, Investigators, subjects, personnel of the Facility where the research is conducted, the Quality Assurance Review process, the media, anonymous sources, or the public. The Aurora IRB and Aurora Health Care shall not intimidate, threaten, coerce, discriminate against or otherwise take other retaliatory action against the Complainant or those individuals participating in the review or investigation of any complaint. If the complaint is made to the IRB by oral communication, the individual(s) asserting the complaint shall be encouraged to file a written statement regarding the complaint with the IRB.

Any oral or written complaint will be reviewed by the RSPP Manager, who will investigate the complaint, take steps necessary to protect subjects, and involve appropriate parties to resolve it. . If the complaint involves failure of the research team to follow the protocol, the regulations, or the requirements or the determinations of the IRB, the matter will be handled under the Noncompliance policy (SOP CO 601) and/or as an Unanticipated Problem in accordance with this policy, if appropriate. RSPP staff may take action to resolve issues related to complaints that are not related to noncompliance or an Unanticipated Problem Involving Risk To Subjects or Others.

The RSPP Manager will contact the Complainant and inform him or her of the outcome of the review of the complaint.

1.10. Reports From Subjects, Employees, or Staff.

It is the responsibility of the RSPP staff and IRB members to act on information or reports received from any source that indicate a study being conducted at any Facility under the jurisdiction of the Aurora IRB could adversely affect the rights and welfare of

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research subjects. These reports will be investigated according to section 1.12 of this Policy, and if applicable, the Noncompliance Policy (CO 601).

1.11. Site Visits and Third Party Verification

The IRB has the authority to observe, or designate an employee of Aurora Health Care to observe the informed consent process of research it has approved, and to verify that the study is being conducted as required by the IRB and in accordance with Aurora’s policies and procedures and site-specific procedures, as appropriate. Also, the Aurora IRB may determine that it needs to verify from sources other than the Investigator that no material changes have occurred in the protocol since its last review (see Policy RR 404 section 1.6). An “IRB designee” (a RSPP staff member, IRB member, consultant to the IRB, or other employee of the Aurora Health Care) may perform site visits to verify information in the study application, or in any interim or continuing review submissions.

Other means of verification include queries sent to research staff to verify information submitted by the Investigator or contacting the Sponsor for answers to the IRB’s questions/concerns. Also, investigators or Sponsors should submit copies of monitoring reports if they indicate significant violations have occurred. Sponsors may be requested to address queries regarding the protocol and/or the investigative site.

A copy of an FDA form 483 or any notations from federal regulation requirements must be submitted to the IRB within 5 working days of receipt.

Investigators may be asked to submit copies of signed informed consent forms or other documents to ensure their compliance with IRB requirements. The IRB designee may conduct interviews with screened and/or enrolled subjects as deemed necessary. The findings related to Site Visits and Third Party Verification will be communicated to the IRB.

1.12. IRB Review of Unanticipated Problems and Other Ongoing Oversight Reports

1.12.1. The Senior IRB chair, in conjunction with RSPP staff, review each report of a Unanticipated Problem to determine if the Unanticipated Problem is a Unanticipated Problem Involving Risks To Subjects Or Others (UPIRSO).

1.12.2. External UPIRSOs

The UPIRSO will be reviewed by the Senior Chair, Primary Reviewer and/or the IRB to determine whether: the risks to subjects remain reasonable in relation to the anticipated benefits (per 46.111 Criteria for Approval); the corrective action plan/Risk

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Mitigation Plan provided is appropriate; and if other action per section 1.12.3.D of this policy is necessary.

1.12.3. Local UPIRSOs

(A) If the UPIRSO involves no more than minimal risk to subjects or others, the matter will be handled by the Senior IRB chair and RSPP staff, as they deem appropriate. The receipt of the report and the action taken by the IRB chair and RSPP staff will be reported to the IRB at the next meeting. The Senior IRB Chair and RSPP staff will consider whether one or more of the actions described in section 1.12.3.D are appropriate.

(B) If the UPIRSO involves more than minimal risk to subjects or others, it will be reviewed by the convened IRB, as further explained below.

(C) For UPIRSOs that involve more than minimal risk to subjects or others, the matter is placed on a meeting agenda. The Senior Aurora IRB chair serves as a primary reviewer or designates another IRB reviewer (Primary Reviewer). The Primary Reviewer reviews the materials as outlined below, and presents a summary of the UPIRSO to the IRB members.

(1) All IRB members are provided and review:

- A copy of the reported problem/event and any additional materials.
- The most recent IRB Submission Form (FO 301-A) (if relevant to the event).
- The current consent document (if relevant to the event).

(2) The Primary Reviewer is also provided and reviews:

- The current, complete protocol (if relevant to the event).
- The current investigator brochure or device manual, when one exists (if relevant to the event).

(D) At the convened meeting, the IRB considers whether: the risks to subjects remain reasonable in relation to the anticipated benefits (per 46.111

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Criteria for Approval); the corrective action plan/Risk Mitigation Plan (if provided) is appropriate; and any actions (listed below), other than those presented in the corrective action plan/Risk Mitigation Plan, are necessary to protect subjects:

- Suspension of the research.
- Termination of the research.
- Suspension of research privileges.
- Notification of current subjects when such information may relate to subjects' willingness to continue to take part in the research.
- Modification of the protocol.
- Modification of the information disclosed during the consent process.
- Providing additional information to past subjects.
- Requiring current subjects to re-consent to participation.
- Modification of the continuing review schedule.
- Monitoring of the research by the Research Quality and Compliance Specialist.
- Monitoring of the consent process.
- Send a "warning letter" to the Investigator.
- Referral to other organizational entities (e.g. Radiation Safety Committee, Risk Management, Medical Staff Office).
- Other action(s) as the IRB deems appropriate.

For issues of Noncompliance, the IRB will follow Policy CO 601.

1.12.4. After IRB review, UPIRSO determinations and corresponding action will be reported to regulatory agencies and other individuals according to the IRB's External Reporting Policy (SOP 408).

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1.13. Administrative Holds on Research

An Investigator may voluntarily suspend research activities of an approved protocol while an Investigation into a situation or allegation of noncompliance is conducted by the IRB or other appropriate Facility department. This could be at the recommendation of the IRB, IRB Chair, Aurora Administration, or by the Sponsor. If the Investigator agrees to such a recommendation, the Investigator must submit the Administrative Hold as a modification to the research study. A Modification Form (form RR 403-C) should be submitted to the RSPP office for expedited review. Such a suspension does not need to be reported to OHRP, FDA or other federal agency. (See Aurora IRB policies RR 407 and RR 408.)

1.13.1. The IRB may recommend the Investigator to place some or all research activities related to a currently approved protocol on hold until additional information can be obtained, in order to determine if:

- (A) A change in the risk-benefit profile has occurred, or
- (B) Potential areas of noncompliance exist.

Concerns giving rise to an Administrative Hold may arise in various ways, including:

- A complaint received by the IRB;
- An allegation of non-compliance to the IRB;
- A discovery by the Investigator of potential additional risks; or
- IRB committee deliberations.

1.13.2. The RSPP Manager notifies the Investigator by e-mail or in writing of the recommendation for “Administrative Hold”, giving a reasonable timeframe for submitting the modification form along with the specific activities to be placed on hold.

1.13.3. When further information is received, it is evaluated to determine the course of review (either section 1.12 of this policy or Policy CO 601, as appropriate).

1.13.4. Once resolved to the satisfaction of the IRB, the RSPP Manager notifies the Investigator in writing that the study may return to active status.

1.13.5. If the Investigator does not respond within the requested timeframe, the study is suspended, and reported per policy RR 408.

SOP: RR 403 Version No.: 08 Effective Date: 1/21/11	ONGOING OVERSIGHT OF APPROVED RESEARCH AND REPORTING OF PROBLEMS/EVENTS	Supersedes Document Dated: 1/19/11
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2. SCOPE

These policies and procedures apply to all research submitted to the IRB.

3. APPLICABLE REGULATIONS AND GUIDELINES AND STANDARDS

21 CFR 312.32, 312.64

21 CFR 812.3(s)

21 CFR 56.108, 56.109, 56.113

45 CFR 46.103, 46.109, 46.115

FDA Information Sheets, 1998

OHRP Guidance on Written IRB Procedures (July 11, 2002)

OHRP Guidance on Continuing Review (July 11, 2002)

4. REFERENCES TO OTHER APPLICABLE SOPS

SOP 304

SOP 401

SOP 404

SOP 407

SOP 408

SOP 601

SOP 902