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1. PURPOSE

To outline RSPP and Institutional Review Board (IRB) review processes and requirements after receipt of initial submissions.

2. SCOPE

This SOP applies to all initial submissions to the Advocate Aurora Health (AAH) RSPP.

3. DEFINITIONS

See Glossary

4. APPLICABLE POLICY STATEMENTS

This SOP implements requirements at sections IV.B.2., IV.B.3., IV.B.7-14, and portions of sections IV.C. and IV.D.2.-3. of AAH System Policy– *Research Involving Humans or Their Identifiable Data or Biospecimens*.

5. PROCEDURE


RSPP Office and IRB processes for review of initial submissions are detailed under the header for each type of submission.

5.1 Human Subject Research (HSR) and Research Engagement Determinations


- a) An RSPP team member will review the submitted HSR Determination Form, request additional information as needed, and make and document in writing the determination as to whether the activity constitutes HSR.
- b) The RSPP Office will:
 - i) provide written notification of the determination to the individual who submitted the HSR Determination Form. Notification (letter) and the finalized form will be uploaded into IRBNet.

5.2 Exempt Human Subject Research

- a) **Administrative Review.**
 Upon receipt of an *Exempt Submission Application*, RSPP team member(s) will complete activities on the *CHECKLIST – Exempt Submission*. This includes but is not limited to:

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- i) Confirming receipt of RAPR preauthorization from AARI,
 - ii) Confirming education and significant interest disclosure questionnaire is complete for Investigators and Key Personnel, issuing an IRB number and adding the activity to the IRB database,
 - iii) Reviewing the submission for completeness/conflicting information and request clarification, additional information/materials or revisions as deemed necessary
- b) Review of Exempt Application will be conducted by one of the following individuals:
- i) an RSPP Research Compliance Analyst (RCA) who is also a voting member of AAH's IRB
 - ii) an IRB Chair
 - iii) the Director of RSPP
- c) The individual conducting review will:
- i) request additional information from the submitter or request assistance from others in making the exemption determination, as necessary
 - ii) only exempt from IRB review those activities in which the involvement of human subjects is limited to one or more of the categories listed at 45 CFR 46.104 or 45 CFR 56.104
 - iii) conduct limited IRB review as necessary
 - iv) document the determination, including the specific exemption category(ies), utilizing the *Exempt Determination Checklist*
 - v) Address HIPAA privacy requirements by:
 - (1) ensuring the activity includes plans to obtain HIPAA authorization from study subjects or use a limited data set with a Data Use Agreement; or
 - (2) reviewing and documenting on the RSPP *Waiver or Alteration of HIPAA Authorization* form the decision to waive HIPAA authorization in accordance with AHC System Policy - *Use and/or Disclosure of Protected Health Information for Research*

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- d) The RSPP Office will:
 - i) provide written notification to the individual who submitted the RSPP *Exempt Submission Application* of the exemption determination and, if applicable, HIPAA authorization waiver or requirement to obtain HIPAA authorization from subjects. Notification (letter) and finalized forms if appropriate will be uploaded into IRBNet.
 - ii) notify the submitter of the obligation to account for any disclosure of Protected Health Information if a waiver of the requirement to obtain HIPAA authorization is granted.
 - iii) upload into IRBNet a copy of the finalized checklists.
 - iv) Update the RSPP database with appropriate Exempt category.

5.3 Request to Rely on an External IRB

- a) **Administrative Review and IRB review**
 Upon receipt of *Request to Rely on an External IRB form*, RSPP team member(s) will complete activities on the *CHECKLIST – Request to Rely*. This includes but is not limited to:
 - i) Verification that the activity meets criteria for review by an external IRB, as outlined in *Deferral/Ceding Of IRB Oversight To An External IRB Guidance*. If not, the submitter must submit an exemption to the ceding requirements as noted in RSPP SOP #1, section 5.3.a.
 - ii) Confirming receipt of RAPR preauthorization from AARI
 - iii) Confirming human subject education and significant interest disclosure questionnaire is complete for all key personnel, issuing an IRB number, and adding the activity to the IRB database
 - iv) verification that a satisfactory assessment of the proposed IRB of record /external institution's human research protection program (i.e., external accreditation, OHRP quality assurance review or equivalent) has occurred within the past five years
 - v) in cases where the use of a Legally Authorized Representative is requested, review the study to ensure the proposed use of a LAR is in compliance with State law, as outlined in *Deferral/Ceding Of IRB Oversight To An External IRB Guidance*

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- vi) reviewing and documenting on the RSPP *Waiver or Alteration of HIPAA Authorization* form the decision on any request to waive HIPAA authorization in accordance with AHC System Policy - *Use and/or Disclosure of Protected Health Information for Research*
 - vii) if not already completed, establish a reliance agreement with the External IRB in accordance with the retention and documentation of responsibilities outlined in *Deferral/Ceding Of IRB Oversight To An External IRB* Guidance
 - viii) communicate any differences in retained responsibilities to those impacted
 - ix) issue written ceding authorization or denial (letter) to the requester which includes communication of State or local laws, regulations, policies, and/or standards to the External IRB. Notification (letter) and the finalized form will be uploaded into IRBNet.
- b) The RSPP office will upload into IRBNet a copy of the finalized Request to Rely checklist.


5.4 Request for External Parties to Rely on AAH's IRB

The RSPP Director or team member will:

- a) review the email request and make a study-specific determination as to AAH IRB's capacity to serve as the IRB of Record (see *Advocate Aurora Health (AAH) IRB as the IRB of Record for External Sites* Guidance for factors affecting the decision)
- b) issue written reliance authorization or denial to the requester.

If determined that the AAH IRB will serve as the IRB of Record for an external site, in most cases, the addition of the external site will be conducted using the Change process (see RSPP SOP #9 and RSPP guidance: *Advocate Aurora Health (AAH) IRB as the IRB of Record for External Sites*) once the study is approved by the AAH IRB. In very few instances will the AAH IRB allow external sites to be added to an initial review. Consult the RSPP office with questions.


Below are actions that will be required when an external site is added to a study that is being overseen by the AAH IRB:

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- a) establish a reliance agreement with the external institution in accordance with the retention and documentation of responsibilities outlined in *Advocate Aurora Health (AAH) IRB as the IRB of Record for external sites* guidance
- b) communicate any differences in retained responsibilities to those impacted
- c) IRB review will be conducted in accordance with other applicable sections of this SOP or SOP #10.

5.5 Non-Exempt Human Subject Research


- a) **Administrative Review.**
Upon receipt of an RSPP *IRB Application*, RSPP team member(s) will complete all activities on the *CHECKLIST – New Submission*. This includes but is not limited to:
 - i) Confirming receipt of RAPR preauthorization from AARI
 - ii) Confirming human subject education and significant interest disclosure questionnaire is complete for all key personnel, issuing an IRB number, and adding the activity to the IRB database,
 - iii) Reviewing the submission for completeness/conflicting information and request clarification, additional information/materials or revisions as deemed necessary
 - iv) Determining whether the study qualifies for expedited review (see *Expedited Review* Guidance) or whether the submission requires convened board review. If expedited review can occur, process in accordance with b) below. If convened board review is needed, process in accordance with c) or d) below.
 - v) Process the submission for IRB Chair or designated expedited reviewer if the study qualifies for expedited review, or schedule for convened IRB review
- b) **Expedited Review.**
For submissions determined to qualify for expedited review, designated expedited reviewer will review all materials submitted and:
 - i) Request additional information, clarification or materials as deemed necessary

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- ii) Verify and document on the RSPP *Checklist for Review Using the Expedited Procedure* that the activity qualifies for expedited review including the applicable regulatory citation
- iii) Document on the appropriate RSPP checklist (e.g. *Primary Reviewer Checklist; Expedited Reviewer Checklist*) that the activity meets/ applicable regulatory criteria for approval or if not meeting criteria for approval, document conditions necessary to secure approval (see *IRB Decisions* guidance)
- iv) If conditionally approved, determine and document who will review responsive materials to determine whether condition(s) is met
- v) If conditions cannot be met, determine whether approval criteria are met with any alternative proposed by the PI or if proposed alternative does not meet approval criteria, defer to convened IRB for review
- vi) Address HIPAA privacy requirements by:
 - (1) ensuring the activity includes plans to obtain HIPAA authorization from study subjects or plans to use a limited data set with a Data Use Agreement; or
 - (2) reviewing and documenting on RSPP *Waiver or Alteration of HIPAA Authorization* form the decision on any request to waive HIPAA authorization in accordance with AHC System Policy - *Use and/or Disclosure of Protected Health Information for Research*


RSPP Office will:

- i) communicate the outcome of each review in writing to the PI. Notification (letter) will be uploaded into IRBNet.
 - ii) upload into IRBNet a copy of the finalized checklists.
 - vii) update IRB database with appropriate expedited approval category.
 - i) notify IRB members of actions taken via expedited review by listing on the IRB meeting agenda
- c) Prior to Convened IRB Review.
- i) IRB Chair or RSPP Director will designate a Primary Reviewer for each research proposal based on the expertise required of the protocol and the member's IRB experience
 - ii) RSPP team member will ensure: (1) none of the proposed Primary Reviewers have a Significant Interest in the research under review; (2)

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membership with appropriate expertise is scheduled to be present at the meeting or obtain an outside consultant to provide expertise; (3) verify and document that voting IRB physician member privileges are not suspended or terminated; (4) obtain a signed confidentiality agreement for any consultant or visitor that will be in attendance, other than invited study team members/leaders.

- iii) RSPP Office will distribute to assigned Reviewers, consultants and IRB members scheduled to attend the convened IRB Meeting the materials noted in the *Meeting Materials* Guidance generally no less than 5 working days in advance of the meeting
 - iv) Primary reviewer: (1) will thoroughly review all submitted materials; (2) will request the engagement of a consultant if additional expertise is needed; (3) will consult with investigators and research staff as needed; and (4) is encouraged to complete the Primary Reviewer Checklist.
- d) During the convened IRB meeting.
- i) Primary Reviewer will: (1) lead the IRB discussion on the submission; (2) take the IRB through the regulatory determinations outlined in the applicable RSPP *Primary Reviewer Checklist* to determine whether the submission can be approved; (3) recommend specific actions to the IRB to ensure that regulatory criteria of approval are met
 - ii) IRB Chair will: (1) present any written reviews submitted by members not able to attend; (2) call for a vote from members who were present for the entire review and deliberation and attended in person, via conference call, or via video conference (no proxy voting)
 - iii) IRB members will: (1) raise any concerns not addressed by Primary Reviewer; (2) participate in discussion of any controverted issues; (3) determine whether all regulatory criteria are satisfied; (4) record their vote on the provided ballot which is coded to ensure no member with a Significant Interest votes;
- e) After the convened IRB meeting
- RSPP Office will:
- i) document outcome of review in meeting minutes;

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- ii) as applicable, communicate in writing any conditions of approval within two days of the meeting whenever possible. Upon receipt of responsive material, the individual designated by the IRB will review responsive material and grant final approval or defer to next IRB meeting if condition(s) cannot be met. (See guidance on *IRB Decisions*).
- iii) promptly issue the final determination letter once conditions are met. Letter and any finalized forms are uploaded into IRBNet.
- iv) upload into IRBNet a copy of the finalized checklists;
- v) update IRB database.

5.6 Compassionate Use/Expanded Access (Not Research)

- a) **Administrative Review.**
Upon receipt of a RSPP *IRB Application* noting Expanded access use, RSPP team member(s) will complete all activities on the *CHECKLIST – New Submission*. This includes but is not limited to:
 - i) Issue an IRB number; add request to RSPP database
 - ii) Reviewing the submission for completeness/conflicting information and request clarification, request additional information/materials or revisions as deemed necessary
 - iii) NOTE as compassionate use/expanded access uses are not research, human subject education and significant interest disclosure questionnaire are not required by key personnel.
- b) **Individual Patient Expanded Access Review – Investigational Drug/Biologic**
 - i) **FDA Waiver of Convened IRB Review Requirement**

If a waiver of convened IRB review was granted by the FDA, federal regulations allow the review process to include concurrence of IRB Chair or designated IRB member before treatment use occurs (ie. a form of expedited review).

IRB Chair or designated IRB member will document the following in writing:
 - (a) whether the activity meets the criteria for single patient expanded access

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- (b) whether the use meets the criteria for review by the IRB Chair rather than review of the convened IRB.
- (c) convened board review will be conducted in accordance with 5.5.c)-e) above.

RSPP Office will:

- (a) promptly communicate the outcome of the concurrence review in writing to the requester. Notification (letter) will be uploaded into IRBNet.
- (b) notify the IRB of the action at the next available IRB meeting via the meeting agenda.

ii) No FDA Waiver of Convened IRB Review Requirement

If a waiver of convened IRB review was not requested of/granted by the FDA, process the submission for convened IRB review before treatment use occurs.

Convened board review will be conducted in accordance with 5.5.c)-e) above

c) Intermediate Expanded Access – Investigational Drug/Biologic

Convened board review will be conducted in accordance with 5.5.c)-e) above.

d) Widespread Expanded Access/Treatment Use – Investigational Drug/Biologic

Convened board review will be conducted in accordance with 5.5.c)-e) above.


e) Individual Patient Expanded Access – Investigational Device

Federal regulations allow the review process to include concurrence of IRB Chair or designated IRB member before treatment use occurs.

IRB Chair or designated IRB member will document the following in writing:

- i) whether the activity meets the criteria for single patient expanded access
- ii) whether the use meets the criteria for review by the IRB Chair rather than review of the convened IRB.
- iii) Convened board review will be conducted in accordance with 5.5.c)-e) above.

RSPP Office will:

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- i) promptly communicate the outcome of the concurrence review in writing to the requester. Notification (letter) will be uploaded into IRBNet.
- ii) notify the IRB of the action at the next available IRB meeting via the meeting agenda.
- e) Intermediate Group Expanded Access – Investigational Device
 Convened board review will be conducted in accordance with 5.5.c)-e) above.
- f) Widespread Expanded Access/Treatment Use – Investigational Device
 Convened board review will be conducted in accordance with 5.5.c)-e) above.

5.7 Humanitarian Use Devices ('on-label' use; Not Research)

- a) Administrative Review
 If part of a research study, then follow processes outlined in section 5.5.c) -e) of this SOP. If for non-research processes continue with this section.
- b) Upon receipt of *Request for Use of Humanitarian Use Device (HUD) for Non-Research Purposes*, RSPP team member(s) will complete activities on the *CHECKLIST – New HUD Submission*. Review will be conducted in accordance with 5.5.a) with the following exceptions:
 - i) Confirming receipt of RAPR preauthorization from AARI– unless the use of Humanitarian Use Device is part of a human subject research project.
 - ii) Confirming human subject education and significant interest disclosure questionnaire is complete for all key personnel - unless the use of Humanitarian Use Device is part of a human subject research project
 - iii) Consideration of expedited review status (5.5.iv and 5.5.v) as all initial reviews of HUDs must be completed by the convened board.

RSPP Office will:

- iv) Verify the approval status of the HDE (see *Humanitarian Use Device (HUD) guidance*)
- v) Verify, if applicable, that the holder of the HDE has or will be provided training on the use of the device, prior to its use.
- c) Prior to the convened IRB Meeting
 Steps outlined at 5.5.c) will be followed

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- d) During convened IRB meeting


The steps outlined at 5.5.d) will be followed with the following exceptions:

 - i) The *HUD Primary Reviewer checklist* will be used for the review. The IRB will review the submission to that the criteria at 21 CFR 56.111 and other applicable sections of Part 56 to the extent practical are met, and will take one of the following actions: (1) approve the use for an unlimited number of patients; (2) approve the use in a specific number of patients; (3) approve the use on a case-by-case basis; or (4) deny the application.
 - ii) After convened IRB meeting

The steps outlined at 5.5.e) will be followed

5.8 Emergency Use (Not Research) of Investigational Drug/Biologic/Device

- a) See *Emergency Use of a Test Article* Guidance to determine whether the use meets the criteria for an emergency use;
- b) If reported during normal operating hours, a RSPB Office team member will immediately review any submitted informed consent form to ensure appropriate elements of informed consent as noted in 21 CFR 50.25 are included and notify the submitting physician immediately via email and/or phone call of the outcome of that review. Notification via phone will be documented.
- c) If the manufacturer requests acknowledgement from the IRB prior to shipping the investigational agent for emergency use, an RSPB team member will issue a letter indicating that the IRB is aware of the proposed use under the provisions at 21 CFR 56.104(c).
- d) Upon receipt of the *Emergency Use Report*, the IRB Chair or designee will conduct a review of the submitted information within 5 working days of receipt whenever possible. The IRB Chair/designee will determine whether the use of the investigational agent met the Emergency use regulations.
 - i) The IRB Chair or designee will document his/her review outcome on the Emergency Use Report..
 - ii) The RSPB will upload a copy of the finalized Emergency Use Report to IRBNet.
- e) The IRB will be notified of the emergency use at the next available IRB meeting via the meeting agenda.

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f) The RSPP office will notify the Institutional Official and the AAH Specialty Patient Accounts representative of the Emergency Use as soon as possible so appropriate billing procedures may be followed.

5.9 RSPP Office will retain a copy of all materials submitted and/or distributed to IRB members as well as documentation and correspondence generated by the IRB or RSPP Office, in accordance with AHC record retention requirements as noted in AHC system policy *AAH Record Retention, Storage and Destruction*

CROSS REFERENCES:

RSPP Guidance: *Is My Project Research/Human Subject Research?*

Advocate Aurora Health (AAH) IRB as the IRB of Record for external sites, Deferral/Ceding Of IRB Oversight To An External IRB IRB Decisions

Informed Consent

Emergency Use of a Test Article

Exemptions

Expedited Review

Humanitarian Use Device (HUD)

Meeting Materials


AHC system policy Use and/or Disclosure of Protected Health Information for Research

AHC system policy –AAH Record Retention, Storage and Destruction

AAH system policy Research Involving Humans or Their Identifiable Data or Biospecimens

OWNER: Director, Research Subject Protection Program

REFERENCES: 45 CFR 46.104
21 CFR 50.25

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21 CFR 56.104
 21 CFR 56.111
 AAHRPP Elements

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