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Special Edition of the Advocate Aurora Health Research Subject Protection Program (RSPP) newsletter

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Contents

2022

2022 has been a very action-packed year for the AAH RSPP/IRB. With your help and understanding, we:

- received full accreditation from our accrediting body, AAHRPP;
- successfully merged the two legacy IRBs into the AAH IRB;
- transitioned all open research studies from legacy Advocate IRB to the AAH IRB;
- became proficient in the use of our (new for some) submission portal, IRBNet.

We acknowledge that there have been some growing pains, but the gains were many. So, **thank you** very much for your support in making these outcomes successful! We look forward to even more success in 2023!

Holiday RSPP office hours

The RSPP Office will be closed on Monday December 26, 2022 and Monday January 02, 2023 in observance of the holidays.

2023 IRB meeting schedule

The 2023 IRB convened board meeting schedule and associated submission deadlines can be found in the IRBNet library as well as the RSPP website.

Educational article - Regulatory Criteria for Approval

In addition to using the RSPP newsletter as a resource in outlining what's new in the RSPP – forms, processes, etc. – the RSPP has been including educational articles in the newsletter with the intent to help researchers better understand aspects of Human Subject Research.

In this last newsletter of 2022, we provide the following article on the Regulatory Criteria of Approval of Human Subject Research. It is our hope that this article will provide: 1) a better understanding of the AAH IRB's responsibility in reviewing non-exempt HSR projects, 2) assistance for researchers when designing investigator-initiated research studies, and 3) help in responding to questions on the AAH IRB submission application and from the RSPP/IRB about research activities.

Regulatory Criteria for IRB approval of Human Subject Research

An IRB (Institutional Review Board) is the review board who's task it is to minimize risk and protect individuals taking part in human subject research (HSR). The proposed HSR project must be found by the IRB to meet an established set of criteria before it can be approved, and the IRB's approval must be granted before the HSR is initiated. The reviewing IRB may be internal, that is, part of the institution (e.g. the AAH IRB) or external, that is, outside of the institution (e.g. a commercial, central or another institution's IRB). The points below outline the federal regulatory criteria (found at 45 CFR 46.111 and 21 CFR 56.111) that the IRB must find are met when considering whether a non-exempt HSR study is approvable.

If the IRB determines that any of the criteria are not met, the HSR study must not be approved. The IRB has the option of outright disapproving the study or deferring/tabling the IRB's review of the study until a later date when the investigator has had the opportunity to revise the project and address the missing criteria.

Criteria for IRB Approval of Human Subject Research

45 CFR 46.111 and 21 CFR 56.111

(a) ...IRB shall determine that all of the following criteria are followed

1. Risks to subjects are minimized by using:
   i) procedures consistent with sound scientific design* and which do not unnecessarily expose subjects to risk
   ii) whenever appropriate by using procedures already being performed on subjects for diagnostic or treatment purposes
2. Risks to subjects are reasonable in relation to the anticipated benefits ...
3. Selection of subjects is equitable ...
4. Informed consent will be sought from each prospective subject or the subject's legally authorized representative ... as required by 45 CFR 46.116.
5. Informed consent will be appropriately documented... to the extent required by §46.117
6. When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects
7. When appropriate, there are adequate protections to protect privacy of subjects and to maintain the confidentiality of data.

(b) When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, individuals with impaired decision-making capacity, or economically disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of the subjects.

*NOTE that "Procedures consistent with sound research design" require that the investigator demonstrate they are capable of conducting the study and producing scientifically valid results. Some protocols, particularly those that are investigator initiated, provide insufficient evidence of sound scientific design.

We'll go into further depth on each of the individual criteria.

Minimizing Risk

The IRB is not only required to assess the risks and benefits of the research, it must also ensure that the risks of the research have been minimized. Even when the research is minimal risk, the potential risks to the subject must be minimized. For example, a retrospective data collection study might include identifiers in the database when they aren't required, or an intervention study might unnecessarily require extra blood draws. These actions would require justification for inclusion in the study, or the IRB should require that they be removed/revised. Careful planning/study design is the key to minimizing risk.

- Scientifically unsound research design exposes subjects to risk without any possibility for achieving useful results. Under the federal regulations an IRB cannot approve research where the proposed research does not have an achievable, meaningful objective or where the research design is inadequate to answer the proposed objectives. The IRB is therefore required to assess the design of the research and assess its ability produce something of scientific and social value.

  Who at AAH assesses the soundness of the scientific design?
  Not only does the IRB assess study design aspects of a project, but at AAH, all proposed research to be conducted at AAH must be reviewed and authorized by the Advocate Aurora Research Institute (AARI) RAPR [Research Authorization and Protocol Review] board. [See AAH Policy Tech for the RAPR system policy.] As part of the RAPR authorization process, a Protocol Review Committee, composed of research/scientific and clinical experts, will

review each proposal for soundness and ability to satisfy criteria according to a uniform set of scored items. RAPR authorization is required as part of submission to the AAH RSPP/IRB. Contact RAPR with questions on their review/authorization process.

NOTE: AARI RAPR authorization is **NOT** the same as IRB approval. Once you have secured RAPR authorization, you must still submit the study for IRB (either internal or external) approval. Only after IRB approval may the study be started at AAH.

- How does one go about minimizing risks associated with procedures?
  - Eliminate unnecessary procedures;
  - Utilize opportunities to decrease the risk, pain, discomfort, burden or other untoward impact of the research on subjects;
  - Combine research procedures with clinical care.

Risk/Benefit Assessment

In addition to ensuring that the risks to subjects are minimized, the IRB must also ensure that the risks to subjects are reasonable in relation to the anticipated benefits. Risk is measured in terms of probability of harm while benefit is a 'hope' whose probability generally can't be measured. The research may be approved by the IRB provided that it is determined that the benefits outweigh the risks to participants.

In consideration of this criterion, the IRB proceeds by:

- Assessing all risks associated with the research by identifying all potential harms that could befall a subject and the magnitude and the probability of those harms;
- Ensuring that the appropriate steps have been taken to minimize the risks that are identified; and
- Assessing the possibility and importance of potential benefits to subjects (if any) and to science and society in general.

Equitable Selection

The requirement for equitable selection flows from the Belmont Report's ethical principle of Justice. The IRB must determine that no one group is unduly burdened or will unfairly benefit from the research. Equitable selection does not mean that all groups are represented in proportion to the population. This means that selection criteria should be both fair and appropriate to the research question.

Informed Consent Document and Process

Informed consent is not just a document, it is a process – a process that begins with recruitment and continues until the subject's participation in the research is complete. Even after all subjects have completed active participation in the research, if subject's private identifiable information continues to be used in the study, IRB oversight must be maintained to protect the rights/welfare of the subject.

Obtaining research subject informed consent is fundamental to the ethical conduct of human subject research. The informed consent of the subject demonstrates Respect for Persons, another Belmont Report ethical principle. Only in rare circumstances will the IRB waive the requirement for obtaining the subject's informed consent.

The consent process involves providing information that a reasonable person would want to know in language that is understandable to the subject. 'Understandable' means at a grade level that the potential subject can understand and provided in in a language spoken/understood by the prospective subject. If the prospective subject cannot demonstrate that they comprehend the basic elements of informed consent, then the investigator should not enroll the subject.

The consent process is normally conducted in a face-to-face discussion. However, the IRB will consider other methods for holding the consent discussion (for example, by telephone, or remote or video technology, etc.). A subject's consent to participate in the research study is typically documented by their wet ink signature on the consent document. However, the IRB will consider an informed consent process that utilizes some other method of obtaining the subject's permission (e.g. electronic consent/signature). Any alternative method used in the informed consent process should be disclosed in the submission application to the IRB. Under some circumstances the IRB can waive the requirement for documentation ('signature') of consent. See the RSPP Guidance document *Informed Consent* located on the RSPP website.

A few things to note about the informed consent document/process when using the AAH IRB:

- The AAH IRB provides informed consent_authorization templates that include all of the regulatorily-required elements of informed consent as well as research HIPAA authorization. These are available in AAH IRBNet Library.

- If your research study population includes children, assent from the child, in addition to the permission of the parent(s), may be required. See the RSPP Guidance document *Vulnerable Populations* located on the RSPP website for more information. Parental permission and assent templates are available in the AAH IRBNet Library.
- If an adult potential subject is not able to provide informed consent for themself (for example the individual is decisionally incapacitated) the IRB has the ability to approve a process whereby a surrogate decision maker or legally authorized representative authorizes the subject's participation in the study. For more information on this topic, see the RSPP Guidance document on *Surrogate Decision Makers in HSR* located on the RSPP website.
- If the PI is aware that their subject pool has individuals with Limited English Proficiency (LEP), he/she should request inclusion of these individuals in the IRB submission application. If it is known that individuals with LEP will be enrolled in the research, the IRB will require approval of a certified translation of the informed consent_authorization document.
    - If the research team has not requested the inclusion of subjects with LEP but unexpectedly encounters such an individual, the research team does have the ability to include that person in the research study. However, before the informed consent process begins with the potential subject, the IRB must prospectively approve the inclusion of such individuals into the research study. This request can be made using the modification or Change process, and only needs to be made once (IRB approval will be for all unexpected encounters of individuals with LEP). If the study team can obtain a certified translation of the IRB approved informed consent_authorization document prior to subject enrollment, this is the preferred process. If, however, there is no time to obtain a certified translation of the document prior to enrollment, the IRB may approve the use of the 'short form' consent process. For more information on this topic, see the RSPP Guidance document *Enrollment of Subjects with LEP* located on the RSPP website.

Data-Safety Monitoring

All studies require some means to monitor data and subject safety. However, these plans should be tailored to the inherent risk of the study. For example, a retrospective chart review study that is no greater than minimal risk would not be expected to have the same data-safety monitoring plan as a greater than minimal risk clinical trial.

Most researchers consider subject safety in their monitoring plans, but all studies should also include plans for ensuring the accuracy, integrity and security of the collected data. Unless the collected data is accurate and secure, valid conclusions will not be possible. Conclusions based on faulty, invalid data fail to contribute to scientific knowledge, and will benefit no one.

- What does a data monitoring plan entail?
  These are the methods for monitoring and ensuring the accuracy, security and validity of the data.
- What does a safety monitoring plan entail?
  These are the methods used to ensure the safety of the subjects – for example, lab tests, strict enrollment criteria, etc. The details and protections for this part of the plan should be adjusted to the likely harms associated with the research.

Some studies (phase II and III randomized clinical trials) require a separate independent monitoring committee (DSMB or DMC). And some studies (phase I clinical trials and observational studies) require oversight by a single individual (the PI or medical monitor) or internal group (steering committee).

Privacy and Confidentiality

This regulatory requirement generally overlaps with the privacy and confidentiality protections in HIPAA. Generally speaking, privacy applies to the 'person' and confidentiality applies to 'information'. For any given study, the specific protections needed will depend on the nature of the study and the risks involved.

Privacy Protections

Careful consideration should be given to who approaches prospective subjects, how they are approached, the physical location or setting in which subjects are approached, and then the level of privacy needed to conduct the informed consent discussion.

Confidentiality of Data

The level of protections for the confidentiality of the person's information will vary from study to study. Not every study requires or can attain absolute confidentiality. At the same time, there should be a reasonable plan for limiting access to the information to only those who need to know.

- Care should also be taken not to promise to the subject more than can be truly attained. The AAH IRB is

typically fine with statements in the informed consent document that say, “Complete confidentiality cannot be guaranteed.”

Studies that require a higher than usual level of protection for subjects' confidential information (for example due to the sensitive nature of the study/situation/information collected) may be eligible for a Certificate of Confidentiality (CoC) issued by the NIH. CoCs allow the investigator and others who have access to research records to refuse to disclose identifying information about research subjects in any civil, criminal, administrative, legislative, or other proceeding, whether at the federal, state, or local level. More information can be obtained on the NIH website.

Vulnerable Populations

Additional regulatory protections (45 CFR 46, subparts B, C and D) apply to several categories of vulnerable subjects including children, pregnant women and the fetus, and prisoners. In addition, some groups need additional protections such as adults with diminished capacity. The RSPP has guidance on the inclusion of vulnerable populations in HSR on the RSPP website.

If you have questions on any of the regulatory criteria for approval, please contact the AAH RSPP office.

--Some content courtesy of the Children’s Hospital of Philadelphia (CHOP) IRB website, OHRP and NIH.

From your colleagues at the AAH RSPP…