NIH Office of Intramural Research
Office of Human Subjects Research Protection

OHSRP NEWSLETTER

Volume 4 • Issue 1 May 2022

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LETTER FROM THE OHSRP DIRECTOR

As we head into the middle of 2022, much of OHSRP's efforts are focused on the design and implementation of our new eIRB submission system. As you can imagine, this is a complex project with lots of moving parts. The Huron team and OHSRP have been meeting multiple times each week to go over all aspects of the system design. In addition, the teams are working closely with representatives of the Scientific Review Groups, Office of Protocol Services, Radiation Safety, Institutional Biosafety Committee, and the Deputy Ethics Counselors to address each group's requirements. We are excited about the system and are confident that in the end, the change will be a positive experience for all users. Please see the detailed update later in this newsletter. Keep an eye out for upcoming presentations and demos as our team hits the road to introduce you to the new system.

Elsewhere in the newsletter, we share more details about our successful reaccreditation effort. We were officially awarded the status in March 2022, although the site visit was back in December. AAHRPP accreditation is not a single event, but an ongoing process. We are committed to living the standards each day, not just when the site visitors are here.

We have developed a number of new resources to help investigators. A new investigator handbook is on the way that will be a quick and easy reference for research teams. Another area of focus is the informed consent process. We see lots of reportable events related to both the form and the process. I know all of us appreciate how essential informed consent is to the ethical conduct of research, so we want to do whatever we can to facilitate this for you and our research participants.

In the IRBO section of the newsletter, we review when a protocol should be closed with the IRB, and how to go about doing this. Once the research is complete, you should close your protocols. This doesn't mean the data/specimens are inaccessible forevermore…just you are done with the planned and approved research.

Lastly, congratulations to the NIAID Protocol Navigators and Protocol Development team and Dr. Hourigan, recipient of this quarters "Gold Star Award" for their recent initial submission. Way to go!

—Jonathan M. Green, MD, MBA
DIRECTOR

TO CLOSE OR NOT TO CLOSE (A PROTOCOL)

In this issue, we discuss a topic that we don't think gets discussed enough: When (and Why) protocols should be kept open or be closed with the IRB.

When Should a Protocol Remain Open with the IRB?

If any of the following seven conditions apply, the protocol should remain open with the IRB:

1. Enrollment will continue;
2. Research-related interventions are being conducted;
3. Subject follow-up is ongoing;
4. Biological specimens or data containing personally identifiable information (PII) or linked to PII are being used for research activities described in the protocol;
5. Manuscript preparation or responses to requests by the journal prior to publication are not yet complete (These activities may involve the need to access PII about the subjects);
6. If the protocol is part of a multi-site study with local IRB review, **and the sponsor has not provided permission to close the protocol with the IRB**; or
7. If the protocol is part of a multi-site study with single IRB review AND **research activities are ongoing at one of the sites** OR the sponsor has not provided permission to close the protocol with the IRB.

If the PI is serving as the lead investigator or the NIH is the Coordinating Center (a multi-site study with local IRB oversight at the NIH), the protocol must remain open with the IRB if the NIH is still receiving, studying, using, or analyzing identifiable private information from other sites (even if all interventions, interactions, observations, and data collection at NIH are complete).

When Should the Research Team Submit A Protocol Closure?

Although investigators may feel reluctant to do so, there are times when it is appropriate to close the protocol with the IRB. Per OHSRP Policy–3014-204 — Levels of IRB Review and Criteria for IRB Approval of Research, once the research team has completed all the procedures described in the protocol, collected all the necessary data and specimens, performed the planned data analysis to meet the research objectives, and published, it is likely time to close the protocol. At this point, they should submit a Progress Report to request that the study be closed. When a protocol prematurely ends, is stopped by the PI, or is stopped or closed by an outside sponsor or the IC, the PI must also request study closure. This request serves as notification to the IRB that continuing review of the protocol is no longer needed.

GOLD STAR AWARD

This issue's Gold Star award goes to the Protocol Navigation/ Protocol Development Program of NIAID (PN/PDP of NIAID). Suchitra Hourigan, a PI in NIAID, submitted an initial review in March which went for full board IRB review at the end of that month. This study is a pilot focused on fecal microbiota transplantation for chronic granulomatous disease–associated colitis. The protocol was approved at the IRB meeting with minimal stipulations. The IRB was impressed with the quality and clarity of the writing in the protocol and consent form. Our experience with the program staff for this protocol was very similar to other experiences that we have had with them in the past. The IRBO staff and the IRB Chair are very pleased with the quality of interactions with these staff members and appreciate how quickly they respond to questions and requests. Their inquiries consistently demonstrate critical thought about how the research plan is designed and presented. **Congratulations to the PN/PDP of NIAID, Dr. Hourigan and all the other members of the research team!**

How Should Protocols be Managed when the PI or Lead Investigator Leaves NIH?

Principal Investigators who are departing the NIH are expected to close or transfer their projects to a new PI prior to leaving the NIH. Principal Investigators for fellow/student projects should ensure the fellows/students submit a Progress Report to close the study prior to leaving the NIH, unless the PI intends to continue to work on the study.

What Activities Must Cease Once a Protocol is Closed?

Once a Progress Report is processed to close a protocol:

- Contact with subjects for research purposes is no longer permitted;
- Specimens and data may no longer be collected; and
- No further analysis or other research-related activities can occur with identifiable (or coded and linked with access to a code key) specimens and data.

Can a Protocol Be Kept Open to Continue Analyses to Answer New Research Questions?

If all planned analyses are complete, but an investigator wishes to use the specimens or data to answer new research questions and conduct additional analyses while maintaining identifiers, these activities should not be conducted under the existing protocol. The use of identifiable specimens or data for new research questions constitutes *human subjects research* which must be described in a new protocol and IRB approved prior to moving forward. In addition, if the investigator plans to share the existing specimens or data with a collaborator who will conduct analyses and return individual level results that they can link back to subjects to answer these questions, this activity also constitutes *human subjects research* which must be IRB approved. In these cases, the investigator's activities are considered secondary research. Accordingly,

they must write a *secondary research* protocol and submit it for IRB approval. *Secondary Research* means the research use of information and biospecimens that were collected through interaction or intervention with living individuals for some other "primary" or "initial" purpose (e.g., a clinical purpose or a different research protocol). In other words, the materials were not collected from humans for the purpose of the specific proposed study.

Alternatively, the research team can remove all identifiers and codes from the study database and specimens and destroy the code key (i.e., everything is anonymized). Once the specimens and data have been anonymized, any research activities conducted with these materials would be considered "not human subjects research" and no further IRB oversight would be required.

A study closure can be submitted at any time; research staff do not need to wait for the time of continuing review or the end of the research approval period to close a protocol.

For more information, please review the secondary research protocol template and the following OHSRP presentations:

Secondary Research: Fact, Fiction, Fears and Fantasies **(videocast)** and **(slide deck)**

Using and Sharing Existing Specimens and Data for Secondary Research: Expectations for Consent and IRB Approval **(slide deck)**

Record Retention

Data from the completed protocol should be stored and protected in the manner approved by the IRB and consented to by the research subjects to maintain the privacy and confidentiality of the subjects. Whenever possible, the data should be permanently anonymized. Also, at a minimum, per the NIH Intramural Research Record Schedule, NIH investigators must maintain research records for seven years beyond the completion/ termination of the protocol. Investigators should be aware that certain categories of research (e.g., FDA-regulated research, research records that support intellectual property rights, (i.e. involving patents or inventions), records of intramural research projects of historical significance) may require a longer record retention period (see 21 CFR 56.115(b); 21 CFR 312.62(c); 21 CFR 812.140(d); NIH Intramural Research Record Schedule).

How is Closure Managed for Protocols that Do Not Require Submission of CRs?

When Continuing Review is not required (i.e., per the Revised Common Rule), the IRBO will send out annual reminders stating that all other requirements continue to apply and that the protocol should be closed if all research activities are complete. If the IRBO does not receive a reply, the protocol may be closed administratively by the IRB.

eIRB SYSTEM IMPLEMENTATION UPDATES

Naming Campaign

Our system naming campaign has concluded and we are excited to officially announce that "ProtECT" has been selected as the name of the Huron eIRB system at NIH! This stands for "Protocol Electronic Capture Tool." Thank you to the research community for your input, as the name "ProtECT" came from your suggestions! Going forward, we will be using this name in communications, and it will be included in branding throughout the new system.

Implementation Progress

Our eIRB implementation team has been very productive in working with our vendor, Huron, these past several months, completing onboarding and design sessions for the major areas of the system that we are building. These meetings took place with key stakeholders for each business area of the system. Our progress is noted below, as well as estimated time frames for upcoming testing and training with the community, and a tentative Go-Live timeframe of Oct 2022* (subject to change).

COMMUNITY ENGAGEMENT: *TIME TO "GO OUT ON THE ROAD"*

Our training team is prepared to begin going out into the community to deliver what our OHSRP Director, Jonathan Green, has affectionately named our "Roadshow"- an *eIRB System Intro & Demo of the IRB Module*. We will be targeting all of NIH in the following ways:

System demos to Clinical Directors/ICs

OHSRP leadership has reached out to all Clinical Directors of all ICs to begin scheduling this system overview and demo. We will reach out to all who responded to schedule a visit to your IC. We look forward to showing you our progress and answering your questions.

	Onboarding	Design	Development	Testing	Training	Migration	Deployment
IRB	✓	✓	✓	May–Aug	Aug–Sept	Oct	Oct
SRC	✓	✓	In Progress	May–Aug	Aug–Sept	N/A	Oct
RSC	✓	✓	In Progress	May–Aug	Aug–Sept	N/A	Oct
"Ancillary Lites" PRIA/DEC/IBC	✓	In Progress	In Progress	May–Aug	Aug–Sept	N/A	Oct

Matrix table showing where major system areas are in the implementation process. Cells in the table reflect that: all major modules have had Onboarding and Design complete—IRB, SRC, and RSC; that the IRB module has been developed; and that SRC, RSC, and Ancillary Lites – PRIA/DEC/IBC development and design are In Progress. User Testing is slated for May–Aug. User Training is slated for Aug–Sept. Migration for IRB is slated to be complete in Oct. And Deployment is slated tentatively for Oct 2022.

**subject to change.*

System demos to Research Community

Our trainers will schedule regularly occurring sessions for the research community to go over the system overview and demo. Look for an email blast announcing upcoming dates soon.

System demos to Special Groups

OHSRP wants to interact with and demo the system to as many business groups at NIH as possible. If you have a group or department or business need that you feel would benefit from our scheduling a separate session for your group, please let us know by completing the following availability survey and we will get back to you about setting that up.

Special Groups: eIRB Demo Availability Poll

User Testing

We will be conducting live facilitated testing with our end users of various roles through this summer. Please consider being a tester in our end-to-end user testing experience. We really value your feedback, the feedback we collect from testing will be considered in our final iteration of the product. To volunteer to be a tester, complete this poll below and let us know how to best include you:

eIRB System - End User Testing Interest Poll

Questions & Comments

We have created an eIRB Project Mailbox for the community to send general questions and comments. This is monitored by our eIRB Project Manager, Meredith Mullan, and our eIRB Change Management Lead, Sue Tindall. Send your questions here and one of us will respond to you: OHSRPeIRBProject@od.nih.gov.

ACCREDITATION NEWS

We are happy to announce that on March 15, 2022, the Association of for Accreditation of Human Research Protection Programs (AAHRPP) Council awarded the NIH Intramural Research Program "Full Accreditation" for the next 5 years. The full accreditation of the program confirmed that "All Standards are Met." We'd like to share with you three (3) areas of strength for the NIH Human Research Protection Program (HRPP) identified by the AAHRPP Site Visitors and commended by the Council:

1. The NIH consolidated its HRPP by establishing one centralized administrative office supporting a new intramural IRB and a standing research compliance review committee (RCRC) serving 22 institutes and centers in 2018. Under the leadership of the Office of Human Subjects Research Protections Director, the transformative NIH HRPP is equipped with strong leadership, knowledgeable, and dedicated staff and has provided consistent guidance and timely assistance to the NIH research community. It was well received and appreciated by researchers, research staff, and administrators from all institutes and centers. (Standard I-1)
2. Given the wide range of protocols and researchers from many institutes, the scientific review process has not only facilitated but also enhanced IRB review. For example, all protocols (both convened board and expedited reviewed protocols) underwent scientific review at local institutes. The scope of the review included not only scientific merits but also resources to conduct the study under review. (Element I.1.F.)
3. The IRBs and researchers and research staff instituted exemplary practices in

reviewing/approving and obtaining/ assessing informed consent. For example:

- When research involved participants who cannot give consent or whose decision-making capacity is in question, IRB members considered whether additional safeguards were needed as part of the consent process. For example, the National Institute of Mental Health clinical research advocate from the Human Subjects Protection unit routinely provided independent assessment for research participants with potentially impaired decision-making capacity. (Element II.4.B.)
- Researchers and research staff understood the difference between the consent process and documentation of the consent process. They understood consent to be an on-going process throughout the participant's involvement in the research. For example, many researchers used the "teach back" approach to verify participants' understanding of what they were informed of; they routinely provided the consent form in advance to allow sufficient time for prospective participants to ask questions; when new research staff on-board, the senior staff observed the consent process as part of the training for new staff. (Element III.1.F.)

Keep up the good work that you do! Thank you to our interviewees from all across our HRPP who represented the best of this institution and to our staff and IC Liaisons who assisted us to make this reaccrediation a success.

Springing Forward

OHSRP will not be resting on its laurels. We will file Annual Reports each March for the next 3 years to keep AAHRPP apprised of our progress and in 2026 we'll initiate the next reaccreditation application. In January we told you about the new AAHRPP Standard I.1.H. that is going into effect in 2023. Emergencies like Hurricane Katrina or the COVID-19 pandemic can cause disruption to HRPPs, stop research, and place research participants at risk. AAHRPP has asked that their accredited institutions establish emgergency management plans to respond to emergencies. We are developing a continuity of operations plan (COOP) that will fit into the larger NIH COOP to ensure that the NIH IRB and its critical functions can continue during and following an emergency. NIH's response to the COVID-19 pandemic is only one example of an emergency an HRPP can face, there are other types of emergencies (natural disasters, supply chain issues, infrastructure failures, etc.) We are taking lessons learned from COVID-19, government shutdowns and other NIH experiences to develop the COOP. Being prepared will serve to strenghen our program, ensure that critical research can continue, and that the rights, safety and welfare of our research participants will continue to be protected even in the face of an emergency.

What's Next for HRPP Policies

As you know IRBO and OHSRP have been working hard to implement the new Huron system. This may result in some minor policy changes. We will be sure to update you as the system falls into place.

OHSRP has been working closely with the NIH Ethics Office to simplify and streamline DEC submissions. Have you checked out the DEC Ancillary Review Page? We developed a checklist for study teams to make sure submissions go more smoothly and hopefully cut down on clearance timeframes. Check out the new FAQs for study teams and the link to the DEC iRIS User Guides for Ethics offices. Currently, we are working to combine our two Conflict of Interest (COI) Certifications into a single form that can be provided to any investigator or statistician working on a covered research protocol who is not an NIH ethics filer. Look for that to come in the near future. We hope that by having only one COI certification, that the clearance process can be further streamlined.

OHSRP EDUCATION SERIES SESSIONS

During the first few months of 2022, our OHSRP Education Series provided members of the NIH community with a number of opportunities to expand their knowledge on a variety of interesting research-related topics and to hear about details and updates regarding OHSRP processes. As noted in the past newsletter, the January session started 2022 off with a town hall that reviewed the past and present state of the OHSRP and 2021 IRBO metrics. The session also provided details about the AAHRP reaccreditation of our Human Research Protection Program (HRPP) and an update on the status of the pending Huron eIRB implementation.

During the February 2022 session, HRPP Director, Dr. Jonathan Green, tackled the topic of regulatory considerations and IRB review of natural history studies. These types of studies have significant differences from clinical trials testing investigational drugs and/or devices. Understanding the issue of research vs. the practice of medicine is critical to recognizing what specific information needs to be included in the protocol and consent form. Dr. Green also discussed the unique considerations when children and family members are included in natural history protocols as well as tracking research-related events that occur during the conduct of such studies.

OHSRP was very fortunate to have a guest speaker, Dr. Aisha Langford, from NYU's Grossman School of Medicine at NYU Health for our March session. Dr. Langford spoke on the topic of *Health Literacy Considerations for Clinical Trial Communication* and shared lessons learned from her experience serving as co-director of NYU's Recruitment and Retention Core at their Clinical and Translational Science Institute. She discussed health literacy and the importance of using plain language as related to informed consent. Dr. Langford provided a conceptual model for enhancing trial participation, and she also reviewed methods and resources to promote equity and inclusion in research.

Most recently, the April session covered issues related to use of investigational devices in human subjects research (HSR). During this presentation, Dr. Jonathan Green spoke about the relevant federal regulations and review and approval processes for investigational device exemptions (IDEs). Following his presentation, Lisa Goldfeder, Section Head, Regulatory Support Section, Office of Research Support and Compliance, addressed sponsor and investigator responsibilities when HSR involves devices used under IDE.

Links to the videocasts and slides from our monthly OHSRP Education Series Sessions are posted in the Presentation Archive section of the OHSRP website.

Investigator Handbook

Our Compliance and Training group is working on an Investigator Handbook to be posted on our website that will address various processes with which investigators need to be familiar when conducting HSR. Each section starts with key points, and topics include distinguishing HSR from research that is not HSR as well as which types of HSR may be exempt from IRB review. The handbook covers the investigator's role throughout the lifecycle of a protocol from preparing a protocol for IRB review, subsequent staff training and other important steps prior to study initiation, the consent process, and additional investigator responsibilities throughout the duration of the protocol.

Relevant details that investigators should understand when conducting HSR with specific populations such as pregnant women, prisoners, children, adults that lack capacity to consent to research and NIH staff are also included. FDA regulated research and NIH protocols being conducted at non-US sites are also addressed in the handbook. *Stay tuned!*

Optimizing the Informed Consent Document

We continue to schedule training sessions for the OHSRP *How To Write An Effective Consent Form: A Workshop for Investigators, Protocol Navigators and Research Staff*. Since this workshop has an interactive component involving small breakout groups, workshop attendance size is limited and advance registration is required. Sign-up for the next session in May is now closed, but be on the lookout for announcements about future sessions. Information about upcoming sessions will be announced on the Protocol Navigator listserv, and anyone at NIH who is interested in issues related to human subjects research can sign up to be part of this listserv. To subscribe, go to the landing page for the OHSRP website and scroll to the bottom of that page to where it says, "Join Protocol Navigation Listserv" and click on the green button that says "Subscribe."

With the revised Common Rule comes a renewed focus on the informed consent process. Have you attended an Informed Consent Readability Workshop and want to move to next steps? Are you interested in making your consents more readable, or wondered if you can improve the effectiveness of the informed consent process/discussions with your participants? Coming Soon, IRBO is committed to partnering with you to help you improve the readability of your consent forms, and improve your consent discussions with participants. Stay tuned for more information!

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