OHSRP Newsletter

Sept 2025

A Letter from the Director

A central ethical obligation in conducting research with humans is the avoidance of exploitation. The first reaction of most clinical researchers to this statement is usually something like; "Of course! I would never exploit a research participant or anyone else!". I believe them. However, I think a more honest statement might be "I would never knowingly or intentionally exploit a research participant (or anyone else)".

Conducting clinical research carries an inherent risk of exploitation. To at least some degree, it is using people as a means to an end. Sometimes that end has little chance of benefitting the individual participant. If we are honest with ourselves about who does stand to benefit from the research, it is not just the "future patient", it is the researcher. Successful clinical research leads to publications, grant funding and future clinical trials, the currency of academic success.

Recognizing the inherent potential for exploitation in research, the ethical codes and regulations that govern human subjects research have incorporated safeguards to reduce the risk. Things like informed consent, ensuring that risks are minimized and benefits maximized reduce the likelihood of exploitation. These only go so far, and I would argue exploitation in research can never be completely eliminated.

Inside this issue

Special points of interest

- NEW OHSRP website
- Policy 405 Research Involving American Indian/Alaska Native Persons, Their Data and Biological Materials

Periodically, I think about this problem, and it recently came to the front of my mind. I traveled with members of the Tribal Health Research Office (THRO) to meet with representatives of Tribal Leadership living in regions where the NIH conducts research. It was a fascinating and eye-opening trip. There were several important points that were consistently made by all the Tribal leaders with which we spoke.

Tribal communities want to be involved in NIH conducted and supported research. However, involvement does not mean only being enrolled as research subjects. It means being truly involved. It means being part of the process that determines what are the important problems facing their community that should be studied. It means being part of the development of the protocol to ensure the research is designed in a way that is aligned with their values, and it means Tribal review of the protocol prior to initiation to ensure compliance with Tribal laws, regulations, ordinances and cultural norms.

Equally important, it means leaving something behind, not just parachuting in, conducting the study and leaving. The Tribal community wants to know the outcome of the research and experience the benefit of the research conducted in and with their community. Depending on the nature of the study, this might range from sharing the results of the study all the way to creating sustainable programs that measurably improve individual and community well-being. It might also mean building research capacity within the Tribal community so that they can conduct their own research.

What became abundantly clear to me on this trip is that if we (NIH researchers) cannot meet these requirements, we are not welcome. Nor should we be. Failing to meet these legitimate asks is exploitation.

OHSRP recently published a new policy that applies to research involving AI/AN persons (*Policy 3014-405 Research Involving American Indian/Alaska Native Persons, Their Data and Biological Materials).* This policy establishes the minimal requirements to ensure appropriate Tribal Authority review and approval for NIH intramural research involving AI/AN persons. It also establishes the formation of a special panel within the NIH IRB to consist of a majority AI/AN persons when reviewing research that is within scope. If you are considering research that may fall within the scope of this policy, I encourage you to read this policy ahead of time and reach out either to OHSRP or THRO for guidance.

- Jonathan

GOLD STAR AWARD

"This issue's Gold Star award goes to Dr. Joshua Levy, MD, MPH, MS, Chief of the Sinonasal and Olfaction Program in NIDCD; Protocol Navigators, Dr. Mbuyi Madeleine Kabongo, MD, DrPH and Nancy Yeates; and the rest of the research team."

This issue's Gold Star award goes to Dr. Joshua Levy, MD, MPH, MS, Chief of the Sinonasal and Olfaction Program in NIDCD; Protocol Navigators, Dr. Mbuyi Madeleine Kabongo, MD, DrPH and Nancy Yeates; and the rest of the research team. In July, the research team submitted an initial review of a pilot study to investigate the mechanisms of parosmia, increasingly seen after COVID-19, using neuroimaging and biochemical analysis. Parosmia is a smell disorder that distorts how you perceive odors, often transforming natural smells into unpleasant ones. The study will examine functional and structural brain changes and peripheral inflammation. It aims to distinguish parosmia from other olfactory disorders and provide a foundation for future diagnostic and therapeutic approaches. The protocol went through two rounds of stips with the analyst. The analyst's stipulations were mostly related to administrative errors and missing NIH consent template language. The study was reviewed at the full board at the end of August. The IRB approved the IR with minimal stips that were focused primarily on consent changes. The IRB noted that the protocol was clearly written in terms of the background, justification and procedures. The study team returned the submission within six days, and it received final sign off on the 27th of August. Congratulations to Dr. Levy, Dr. Kabongo, Ms. Yeates, and the other members of the research team!

ASSENT OF SUBJECTS WHO LACK THE CAPACITY TO CONSENT

Did you know that….

In November 2024, HRPP Policy 403 – Research Involving Adults Who Lack Decision-Making Capacity To Consent To Research Participation was revised to clarify the requirements for seeking assent from adults who lack the capacity to consent.

If an Investigator plans to enroll adults who lack the capacity to consent to the research, they must provide a scientific justification in the protocol. When considering whether to enroll this population, in general, the Investigator must make the case that the research is no more than minimal risk (or a minor increase over minimal risk), and that the research question cannot be

answered without including this population; **or** that the research is more than minimal risk, but offers the prospect of direct benefit to this population.

When meeting with a participant who may have a cognitive impairment, the Investigator will need to determine the participant's level of impairment and whether that impairment will likely be permanent or temporary. This decision may be made with input from a family member, Legally Authorized Representative (LAR) or guardian. Once the determination is made that the person lacks the capacity to consent, the expectation remains that their assent to the research will be obtained. It's important to state that a participant's *failure* to object to participating in the study or to undergoing a procedure, is not the same as "assent". Accordingly, the Investigator will need to decide if written assent, verbal assent or no assent is most appropriate, while ensuring consistency with what is currently allowable in the approved protocol. Ultimately, the Investigator must document their determination about the level of impairment and ability to assent in the medical record (or research record), along with the details of the assent process.

Accordingly, all active protocols which anticipate enrolling adults who lack or may lose their capacity to consent must address the topic of assent, when these individuals will be enrolled in a study (or remain on study). The required content associated with assent of this vulnerable population was added to the NIH protocol templates in November of 2024. The protocol must address whether some or all of the participants will be asked to assent to the research, provide a justification for not obtaining assent, when applicable, and describe *how assent will be obtained from all participants on the study who may lack the capacity to consent*, either via written assent, verbal assent or both. The protocol should also clarify that any expressions of dissent will be honored. If some participants have limited communication skills, the protocol should describe how the investigators will be able to recognize dissent in these cases.

When describing the assent plan, the PI should take into consideration the characteristics of the population; the trajectory of the subjects' disease/condition, when applicable; expectations regarding loss of capacity, e.g. temporary loss or permanent loss; the context; and the complexity of the research. For example, an individual's capacity to consent to a clinical trial involving an investigational drug may not be the same as it is with a minimal risk research study with few procedures. Keep in mind that it may be prudent to include different assent plans within the same protocol, if individuals with varying degrees of capacity might enroll.

If you have not yet updated your protocols (that allow for the inclusion of decisionally-impaired subjects) to address assent, you should submit a modification to do so now.

Here are some example text that could be used in protocols, but should be customized as needed:

Incapable of Providing Assent

Participants in this study who do not have consent capacity, are not capable of providing assent, due to the nature of <disease/condition> because <provide the justification>; therefore, assent will not be obtained.

Verbal and/or Written Assent

To have the capacity to assent, the participant must be able to understand the general purpose of the research, the nature of the research procedures and the concept of voluntariness. The Investigator, with input from the LAR/guardian, will determine the participant's level of impairment by assessing the participant's decisional abilities, their psychologic state, and their emotional state as well as their underlying disease or condition. The study team will obtain assent from adult participants without the capacity to consent, in consult with their legally authorized representative (LAR) or guardian. The investigator will then <determine, based on the participant's cognitive level, whether he or she will be able to understand the written assent or will be able understand a verbal assent process that is customized to the participant's cognitive level>.

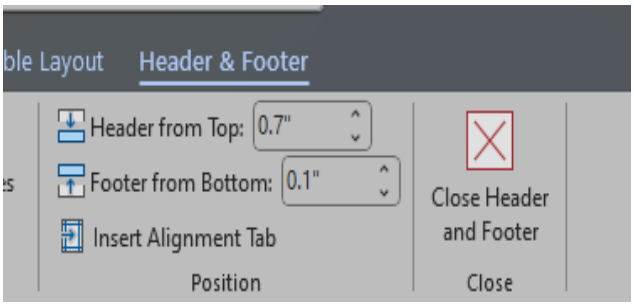
The LAR/guardian and adult participant will be included in all discussions about the study and cognitively-appropriate language will be used to describe the research procedures and tests, risks, discomforts and benefits, as applicable, involved in study participation. <Participants, who do not have consent capacity, but can read and understand the basic elements of the study and its implications, will be asked to provide written assent. Participants, who do not have consent capacity, but can understand the basic elements of the study and its implications, will be asked to provide verbal assent using a verbal assent script/the consent form to guide the discussion>. Accordingly, <a written assent process/verbal assent process> that is customized to the participant's cognitive level will be conducted. <To respect the participant's autonomy, the investigator will encourage the participant to communicate via common gestures, such as head-nodding, lifting arm to seek clarification or stop the discussion, and thumbs-up or down movements to engage with the investigator. However, the investigator is not limited to these techniques and may incorporate any reasonable methods.> Dissent will be respected in all participants. <Verbal assent will be documented via a signature on the consent form/will only be documented in the medical/research record>. The assessment of the participants' ability to provide <verbal/written assent, as applicable>, the consent process with the LAR, and the assent process with the participant will be documented in the participant's <medical/research record>.

As part of the IRB's review of the protocol, it must consider whether to require assent and, if so, the appropriate process for a given cohort, depending on the nature of the protocol and unique circumstances of the subjects being targeted for enrollment. It must approve the plan for seeking assent to the research, including any justification as to why some or all of the subjects may not be able to assent. For example, it may be ethically appropriate to obtain assent from individuals who develop a moderate cognitive impairment and lack consent capacity but still have more general decision-making capacity. However, it would likely not be possible to obtain assent from a potential participant who has always had profound cognitive impairment due to a developmental disability or who is temporarily unresponsive due to head trauma.

For additional information about the enrollment of subjects who lack the capacity to consent, please check out this page on the OHSRP website, along with the Guideline For Enrolling Adults Who Lack The Capacity To Consent For Research.

TIPS & TRICKS

SPACING MATTERS IN CONSENTS FORMS



The IRBO has been receiving consents where the formatting is not consistent with our template. When revising consent forms, please be careful to retain the spacing in the headers and footers of the posted version of our consent templates. The header should read 0.7" from the top, and the footer should read 0.1" from the bottom. The spacing matters. If you add extra carriage returns, it might add a blank page to the consent, once it is approved and turned into a PDF. In addition, changes to the spacing in the header or footer might lead to the approval stamp being positioned on top of some of the text in the footer.

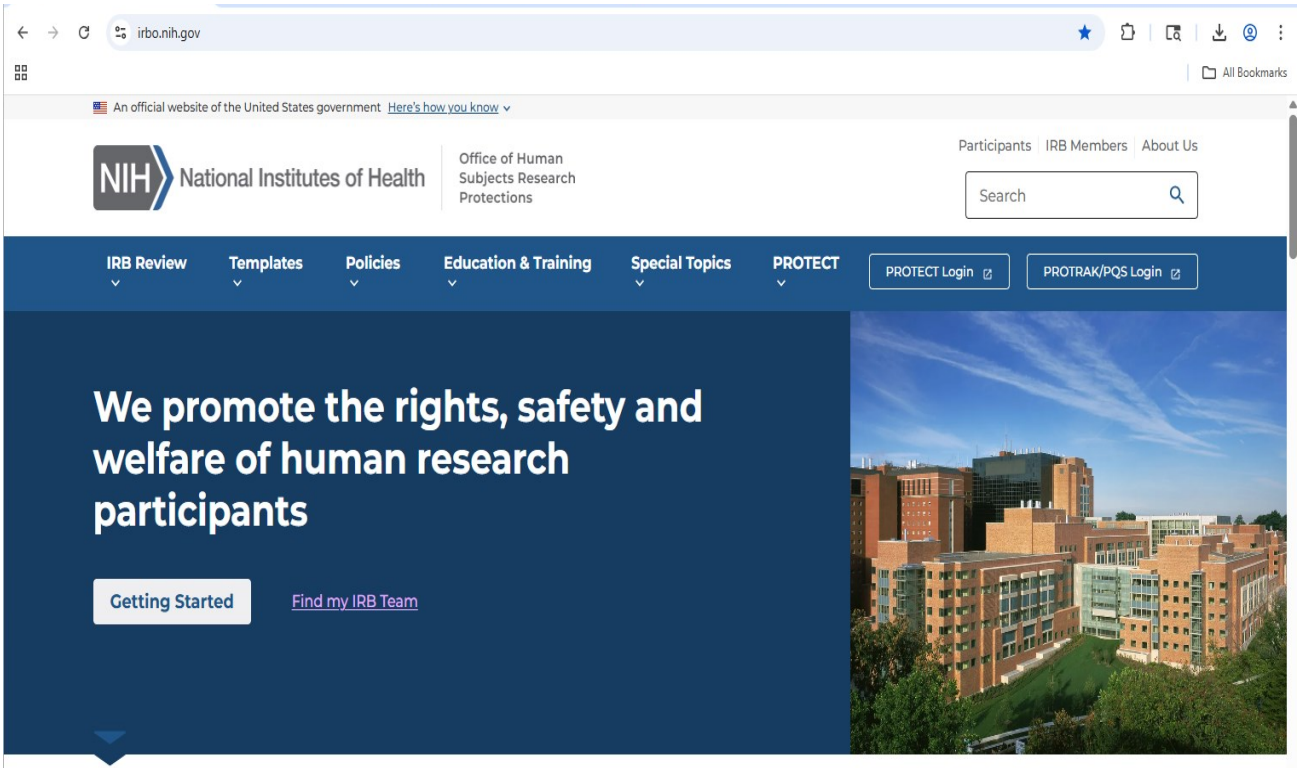
If these problems arise, Protocol Services Section (PSS) will not post your consent form. In this situation, the team will have to fix the spacing in the consent form and then submit a new MOD with the revised document. Always remembering to double-check the spacing in your consent forms when you revise them can help the team avoid unnecessary work and delays in the posting of consent forms.

ADDITIONAL INFO FOR STUDY CLOSURES

When submitting a study closure, please add a comment or upload a memo which provides some background information about the decision to close the study with the IRB including any information that is unique to the situation. Examples are as follows:

1. All analyses are complete and planned publications have been approved for publication.
2. PI is leaving NIH and there is no one in the IC who is able to take [interested in taking] over the PI responsibilities.
3. PI is leaving NIH and the specimens and data will be transferred to the PI's new institution to continue the research.
4. All human subject research activities are complete.
5. Insufficient resources to continue the research.
6. Difficulty recruiting subjects to the study.
7. Have not been able to obtain the study drug after a prolonged waiting period.
8. The research question is no longer considered scientifically important.
9. Concerns have been raised about [some aspect of the study].
10. The study requires the use of [a resource] which is no longer available to the study team because [reason].

PROTECT System Update



New OHSRP Website

This summer, we launched our new OHSRP Website (same URL). You should find our new site easier to use with:

- **Easy Navigation:** A simple layout, displaying most common content up front
- **Simple language:** Straight-forward instructions for your most common tasks
- **Robust search capability:** Improved searchability of content, instructions, policies, trainings, and templates
- **Organized regulatory/training/policy/process info:** A more intuitive layout of the resources you need to plan, submit, and conduct your human subjects research.
- **Latest News and Updates:** A "News" area to keep you apprised of recent HRPP announcements and news.
- **Staff Directory:** A newly designed staff directory with photos of our team and their contact info.
- **Events Calendar:** A newly designed events calendar to keep you aware of our upcoming trainings, community calls, system downtimes, and other events.

Policy Updates

OHSRP has completed its triennial review of policy series Manual Chapter 3014. These revisions included technical revisions such as fixing or removing broken links or obsolete references. For example, we recently removed the links to the "Common Rule Bulletins" from *Policy 3014-301 Informed Consent*. As you may remember we used these bulletins to explain the key consent changes implemented during the transition to the 2018 Common Rule and before our new policy series 3014 was published. By now you should have a solid grasp of these requirements such as presenting "Key Information" a participant would want to know before presenting other information about the study. These requirements are already included in the policy. You can see news about policy revisions without having to wait for the next OHSRP newsletter on the refreshed website (https://irbo.nih.gov). From the home page of our website, scroll to the bottom of the page to see Policy updates. Be sure to check our newsfeed to see the latest updates.

Here are the latest policy revisions to Manual Chapter 3014 of interest to study teams:

- **Policy 3014-105 IRB Reliance** was revised effective 02/13/2025 to specify that all external IRB approval letters and approved documentation must be submitted to IRBO no later 2 weeks from study team receipt.

- **Policy 402 Research Involving Children** was revised 3/20/2025 with the addition of a footnote letting study teams know that they can direct questions about the legal decision maker for a child to the NIH Office of Legal Counsel. Be sure to submit your questions as early as feasible to allow counsel time to respond before the participant arrives at the NIH.

- **Policy 404 Research Involving NIH Staff as Study Subjects** was revised effective 3/12/2025 to:

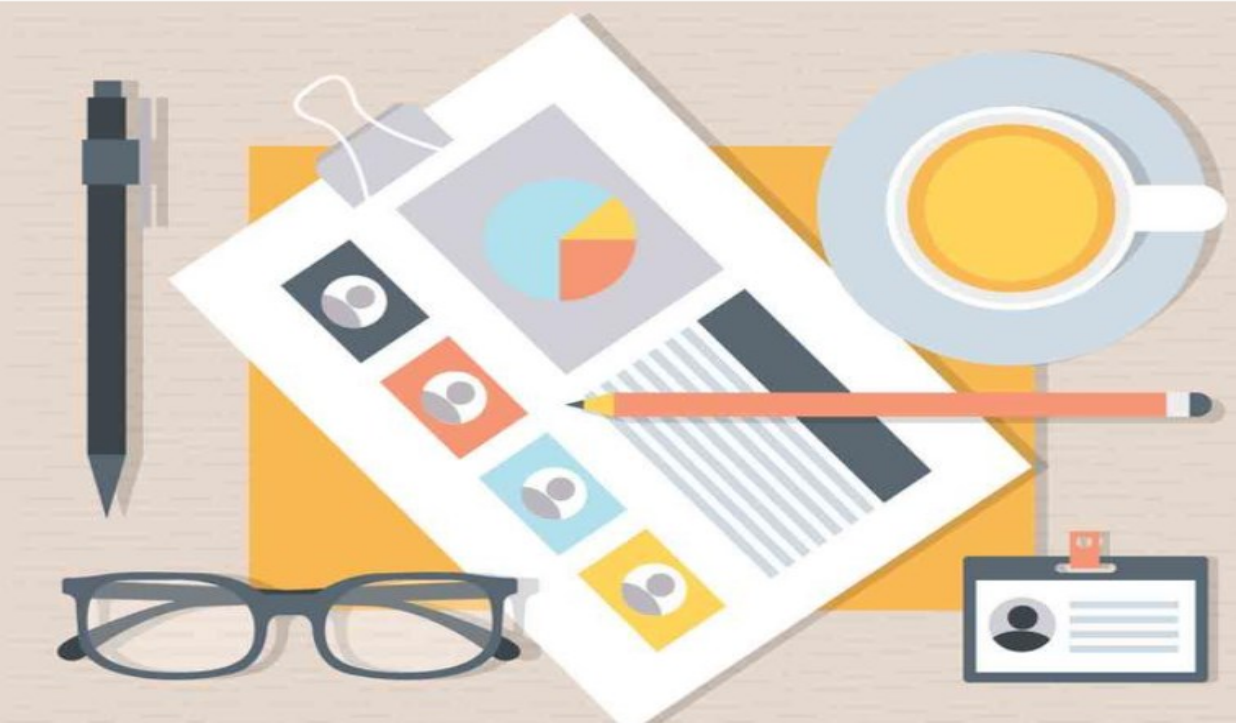
  1) Expand the title of this policy to *Research Involving NIH Staff or Immediate Family Members of Study Team Members as Subjects*.

  2) Clarify at Section C.2. that only NIH federal employes must review *NIH Manual Chapter: 2300-630-3 - Leave Policy for NIH Employees Participating in NIH Intramural Research Program (IRP) Biomedical Research Studies* when considering participation in NIH research, and

  3) Section C.9. was revised to specify when enrolling an immediate family member of a study team member, informed consent may not be obtained by the study team member who is related to the potential participant.

- ***New*** **- Policy 405 Research Involving American Indian/Alaska Native Persons, Their Data and Biological Materials** was published and is effective as of 7/9/2025. We introduced this new policy last December at an OHSRP Education Session, you can view that video and slides on the AI/AN information page on the OHSRP website. This information page also explains how this policy is being implemented and who to contact for help.

Policy updates (cont.)



- **Policy 500 Research Involving Drugs, Biological, and Nutritional Products** was revised effective 8/5/2025 to remind investigators to notify the IRB when the Sponsor has withdrawn the IND, consistent with Policy 801 Reporting Research Events.

- **Policy 502 Expanded Access, Including Emergency Use of Investigational Drugs, Biologics, and Medical Devices (Test Articles)** was revised effective 3/19/2025 to direct investigators to Policy 801 for more details about event reporting for expanded access protocols.

- **Policy 801 Reporting Research Events** was revised effective 4/3/2025 to clarify expectations for event reporting for expanded access protocols to the IRB. Events related to Intermediate-size Patient Population INDs and Treatment INDs must be reported consistent with Section E.1.b of Policy 801. Events related to Single Patient INDs do not need to be reported to the IRB. Regardless of the type of expanded access IND, PIs are still expected to comply with FDA reporting requirements to the Sponsor and to the FDA.

The policy was revised effective 5/5/2025 to clarify reporting requirements for minimal risk protocols that do not require continuing review. For these studies, the PI is expected to track minor deviations and only report them to the IRB if they rise to the level of a reportable event, such as a major deviation, non-compliance, or unanticipated problem. These events are to be reported consistent with Policy 801. The policy was revised effective 8/6/2025 to specify that investigators must report to the IRB within 7 days of Sponsor notification that the IND has been withdrawn.

Accreditation Updates

My how time flies by! It has been almost 4 years since our last Association for Accreditation of Human Research Protection Programs (AAHRPP) reaccreditation site visit at the end of 2021. Thanks to everyone involved, NIH easily received full accreditation in March 2022. We want to do that again in 2026!

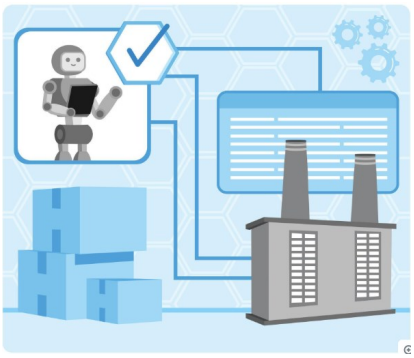
You might ask, why do we need to get accredited? AAHRPP sets common standards for high-functioning Human Research Protection Programs (HRPPs) worldwide. The goal of accreditation is to engender trust in the research process. After all, we can't do clinical research without research participants. This peer review process independently confirms that we prioritize the rights, safety, and welfare of our research participants at all times.

Here is an example of how we strive to meet an accreditation standard. Standard I.1.H. focuses on how HRPPs protect research participants during and immediately following an emergency. In Fall 2023, we gathered key stakeholders from OHSRP, the Division of Emergency Management, CC Pharmacy and ORSC to tell investigators how to manage protocols following an emergency. As part of the education, we explained how to obtain investigational agents after a major emergency so that participants can continue to receive them. If you are conducting a clinical trial and missed this important education session, you can watch it on our website.

The accreditation process focuses both on our written materials and our practices. In March 2026 we will submit the Step 1 application for reaccreditation. The process of preparing the application has started already. This Fall, we will start collecting the necessary data to support the application. While most of that data can be gathered from PROTECT and from within OHSRP, we will also need collect some data from Institutes and Centers (ICs) or other offices.

For example, we are currently moving the annual QAQI survey to the OD instance of RedCap. This gives us the opportunity improve the survey. We will work with the ICs to gather needed information. Like last year, we anticipate that our request will be largely focused on changes in resources that affect the conduct of clinical research studies or impact the Intramural Human Research Protection Program (HRPP). Much of this activity takes place behind the scenes, since we work with IC staff designated by their Clinical Directors.

The most visible part of the accreditation process is the Site Visit. Once AAHRPP peer reviewers have reviewed our written application and policies and agree that they meet accreditation standards, then the site visit will be scheduled. The site visit will likely take place late 2026. Once the site visit schedule is confirmed, we will start preparing interviewees. If you are selected to be interviewed by the site visitors, we will prepare you, so you know what to expect during an interview. We promise to keep you updated as we move through the application process. We cannot do this without you. We thank you for your continued dedication to clinical research, human subjects protections and for your support!



REPORTING USE OF SHORT FORM CONSENT PROCESS VIA REPORTABLE NEW INFORMATION (RNI) FORM

Policy 301, *Informed Consent* requires IRB notification when a short form consent process is used to obtain consent from a non-English speaking potential participant. Notification occurs by submitting an RNI form within seven calendar days. The policy also states, "The notification must provide the rationale for the use of the short form." This means that for studies that are greater than minimal risk and those that are no greater than minimal risk, information in the RNI form must explain why it was in the best interest of the potential participant to use the short form consent process rather than waiting to enroll them after the English long form consent has been translated into their language and approved by the IRB. Study teams are reminded that even for protocols that are no greater than minimal risk, this explanation must be included when the RNI is submitted.

When the short form consent process is used for a study that has been determined by the IRB to be *no greater than minimal risk*, in the RNI please include the language of the short form that was used and the number of times that the short form in that language has been utilized. For protocols that are no greater than minimal risk, Policy 301 also requires the PI to have the English long form consent translated to a given language and to obtain IRB approval before use with any future subjects when the short form in that language has been used three times or if translation is directed by the IRB. Additionally, in these cases, when the IRB has approved the translated long form, that long form consent must be provided to any participants previously enrolled using the short form consent process who speak that language.

When a short form consent process is used for research determined by the IRB to be *greater than minimal risk*, translation of the English long form consent into the participant's language is required as is subsequent IRB approval of the form. In this case, the approved translated long form consent needs to then be provided to the participant. When an OHSRP Compliance and Training (C&T) staff member reviews the initial report of use of the short form consent process for a protocol that is greater than minimal risk, a request for clarification is sent telling the submitter to respond and let C&T know the date that the translated long form was provided to the participant. Please do not forget to respond to this request once it has been provided, so the RNI can be closed out.

2025 OHSRP EDUCATION SERIES SESSIONS

Sessions for this series for 2025 thus far have generally been related to topics and ancillary reviews relevant to protocol submissions.

In March, Ms. Celeste Dade Vinson, Chief, Privacy Policy Branch and NIH Senior Official for Privacy, familiarized the NIH IRP community with the basic requirements of the Privacy Act. She also discussed how to identify potential Privacy Act concerns and where to go for assistance. Finally, Ms. Dade-Vinson provided helpful links to relevant privacy resources and the list of NIH Privacy Act Contacts.

In May, Ms. Teresa Fisher, M.S., the NIH Radiation Safety Officer, provided a brief history of radiation safety at NIH and explained how radiation is used here. She also addressed the protocol review process from a radiation safety perspective for those studies that require review by the Radiation Safety Committee.

Education Session (cont.)

The June session featured an outside speaker, Dr. Camille Nebeker, Director of the UC San Diego Research Ethics Program. She is also a Professor of Public Health, with faculty appointments in the UC San Diego Design Lab and the Herbert Wertheim School of Public Health and Human Longevity Science. Dr. Nebeker outlined the key characteristics and challenges of digital health research for behavioral and clinical studies. The presentation also identified ethical considerations associated with participant privacy, informed consent, and the return of individual research results in digital health contexts. Finally, Dr. Nebeker provided practical approaches and tools, such as digital health checklists and decision support aids to improve consent communications and protect participant rights.

The presentation in July addressed the Protocol Resource Impact Assessment process (more commonly known as PRIA). For this session, Anela Kellogg and Dr. M. Schuyler Deming, PRIA Analysts in the Clinical Center Office of the Chief Medical Officer, addressed the PRIA review process and metrics, and the PROTRAK Query System (PQS). They also emphasized the relevance of Protocol Expectations (and) Actions (for) Real Life Scenarios (PEARLS) sheets which are prepared by research teams as part of study start up. PEARL sheets are a one-page synopsis of the "need to know" information that any provider not familiar with a particular protocol could use at the bedside to best care for the participant.

In August, Dr. Harry Malech and Dr. Rick Baumann presented *NIH Institutional Biosafety Committee (IBC) Review of Clinical Protocols.* Dr. Malech is the Chair of the IBC, and Dr. Baumann is the NIH Biological Safety Officer. During their session, they discussed the function and composition of the IBC and applicable regulations. They also addressed which clinical protocols require IBC review and details related the review process, how IBC review relates to other reviews (e.g., IRB, FDA), and investigator responsibilities at the time of IBC review.

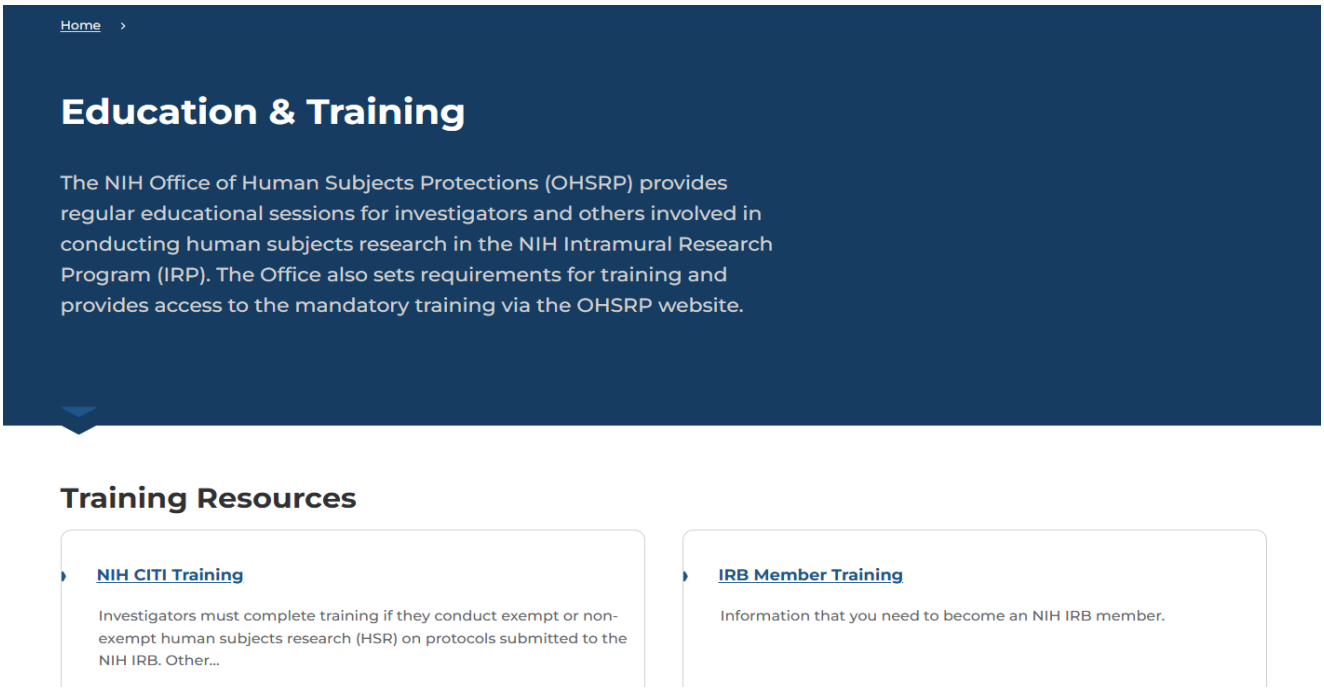
Links to the NIH videocasts and slides for the all of the OHSRP Education Series sessions can be found in the OHSRP website Educational Presentation Archive by date. The presentations thus far for 2025 (discussed above) are listed below.

- March 6, 2025: *The Privacy Act and the NIH Intramural Research Community* (Celeste Dade-Vinson)
- May 1, 2025: *Overview of the Radiation Safety Program at the NIH* (Teresa Fisher)
- June 6, 2025: *Foundations and Frontiers: Navigating Ethics in Digital Health Research* (Dr. Camille Nebeker)
- July 10, 2025: *Study Start-Up at the NIH Clinical Center Site* (Anela Kellogg and Dr. M. Schuyler Deming)
- August 14, 2025: *NIH Institutional Biosafety Committee (IBC) Review of Clinical Protocols* (Drs. Harry Malech and Rick Baumann)

Upcoming sessions for 2025 include a presentation in October on the role of the Office of Technology Transfer (OTT) in the NIH IRP, and the speaker will be Dr. Tara Kirby, Director of the OTT. The November session will address the ethical concerns related to early study closure and will be presented by Drs. Annette Rid and Robert Steele of the NIH Clinical Center Department of Bioethics.

COMPLIANCE AND TRAINING RESOURCES ON THE NEW OHSRP WEBSITE

- The Education and Training page of the website provides links to the NIH CITI training page, Educational Presentation Archive, Investigator Seminar Series information, IRB membe training, PROTECT training and Regulatory Resources.



- The topic page titled Reporting Research Related Events explains which events require expedited reporting via a Reportable New Information (RNI) form vs. events that can be reported at the time of continuing review. It also covers reporting requirements when NIH is not the Reviewing IRB as well as information about handling complaints from participants. There is also a page the explains how one can Report a Complaint.

- Consent Process FAQs can also be found on the website.

We invite your questions and suggestions

We would love to hear your ideas or requests for training! Please email any suggestions, comments or questions that you have for the OHSRP Compliance and Training staff to OHSRPCompliance@od.nih.gov.