Post-Webinar Questions and Answers
with Karen Hale, RPh, MPH, CIP, and Daniel Nelson, MSc, CIP

Q: Why can’t I determine if a study involves “human subjects” before I determine if it is “research”?
A: From a regulatory standpoint, the definition of a “human subject” requires one to have first determined that research is being conducted. Per Department of Health and Human Services (DHHS) regulations: “Human subject means a living individual about whom an investigator conducting research obtains (1) data through intervention or interaction with the individual, or (2) identifiable private information.” Per Food and Drug Administration (FDA) regulations the term refers to: “An individual who is or becomes a participant in research, either as a recipient of the test article or as a control.” It is implicit (and explicit) in both definitions that the activity must have already been determined to be research prior to looking at who is involved in that activity.

From a more practical standpoint, as stressed in the webinar, many activities involve human beings, but not all are research. Failure to consider these definitions in the proper order may lead to unintended or counterproductive situations. For example, if someone decided that participants answering polling questions during this webinar (or providing a course evaluation afterwards) defined them as “human subjects,” we might then be forced to obtain research consent for this webinar, which would be illogical and serve to protect no one.

Whether you rely on regulatory or practical lines of reasoning, it simply works better to first determine that an activity is “research” before you consider the status of the humans in that activity!

Q: You mentioned that what happens within a school classroom would not generally be considered observation of public behavior. What about more communal areas within a K-12 school setting, such as a playground? Must we assume that anything that happens with children on a K-12 school campus during the school day is not public behavior?
A: To our knowledge—and this has not been addressed in guidance—we agree that what happens on a K-12 school campus during the school day should not be considered to be public behavior. Given security concerns, the norm in most communities today is to require visitors to obtain permission to enter or observe on school property when school is in session. While it might be possible to sit on the boundary of the school property and observe the playground with binoculars, such behavior may undermine the authority of the researchers and may even warrant a warning from the school administration or police. Thus, since this would not be considered a location where the public is free to wander, activities occurring there would not generally be considered public behavior. The same arguments would not extend to observation on college campuses.

Q: Can classroom observations fall under exempt category 1?
A: If one first determines that the classroom observations are research activities involving human subjects (and not, for example, student teacher evaluations or other non-research activities), then these could be considered "normal educational practices" under Category 1.

Q: I’m confused by exempt Category 4, which includes "publicly available data." That would seem to imply that there are no human subjects involved—and thus not even exempt.
This is an example that illustrates why it is important to first determine whether an activity is human subjects research (i.e., one has already established that human subjects are involved) before looking at the exempt categories. For practical purposes, it is likely that research using publicly available datasets would involve only de-identified, aggregate data. In this case, if no other activities are included, it would not meet the definition of human subjects research. However, there may be rare examples of publicly available databases where identifiable information is included, in which case it is human subjects research but could still be considered for exemption. Consider the inclusion of “publicly available data” in Category 4 an example—like “information recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects” – of data that, if it is used in research, would not require the additional protections provided by applying the regulations.

Q: Can you provide a reference or guidance for further information on Category 4 exemption specifically regarding when it is coded for the sole purpose of linking to other medical records, etc?
A: This came from a slide used by Office for Human Research Protections (OHRP) and others when teaching on exemptions, which states: “OHRP has interpreted exemption 4 to permit the recording of identifiable information (without any private information) for the sole purpose of allowing investigators to use this identifying information to link it to other records of interest (e.g., to identify which charts to pull). However, once the records of interest have been identified, then OHRP has indicated that no identifying information may be recorded for the research analyses.”

Before posting this response, we checked with Julie Kaneshiro, policy team leader at OHRP, who confirmed that they are working right now to post this among Frequently Asked Questions on the OHRP website.

Q: Regarding exempt Category 4, the regulations do not provide guidance regarding the “when” of de-identification. Many researchers want to retain the identifiers until all their data is gathered in case they need to go back to check “outliers,” but our institution requires that the de-identification be immediate upon recording the data. Do you have any views on this?
A: Our understanding is that under Category 4, identifiers can be retained long enough to cross-link between multiple record sources (see preceding question, for example). However, once the records of interest have been located and linked, no identifying information may be retained or recorded for research analyses. If identifiers must be retained for other reasons, such as checking “outliers,” then we recommend that the project receive expedited IRB review.

Q: What is the difference between online public observation (Facebook profiles, Twitter feeds) and observation in real life, such as at a park?
A: There is no difference (from a regulatory perspective) between public observation in “real life” and public observation online. However, investigators and IRBs should consider the site and the reasonable expectations of participants in determining when an online venue should be considered public. Depending on their level of sophistication, it may not be equally apparent (or transparent) to online participants that their behavior is visible to others. One suggestion would be to consider a site’s published privacy/confidentiality policy. When establishing policies, institutions might also want to consider whether or not approval is required for an individual to participate in an online activity and whether a site is intended for public viewing, or if online participation is limited in some way (e.g., to individuals who share a particular condition or interest).

Q: Can video or audio taping of interviews ever be considered for exempt review? What if the audio recording is for transcription purposes only?
A: OHRP has stated that even when audio taping is used, research involving human subjects (non-prisoner adults) may be considered for exemption under Category 2, provided the information is not sensitive and would not reasonably place the subject at risk of criminal or civil liability or be damaging to the subjects’ financial standing, employability, or reputation. In other words, Category 2 does not limit or define the medium used to record information, so it could be pencil and paper, audiotaping, or other.
Remember that exempt category 2 does not require “anonymity,” if responses are not potentially damaging.

Q: What resource should you referring to when determining engagement of institutions in human subjects research?

Q: If professors at our institution partner with other institutions, we assume our institution is not engaged in research. Yet, how do we know that all proper review occurred at the other institution without asking to see that paperwork?
A: The first sentence is not necessarily true, if it was intended as a blanket “rule,” since engagement depends on the nature and level of involvement. Merely partnering with other institutions does not mean that your institution is not engaged (or that it is). We would advise institutions to use the OHRP engagement guidance to determine if/when the institution is engaged in non-exempt human subjects research. When an institution is not engaged, there are no requirements to determine what reviews (if any) are occurring at a collaborating institution. However, when two or more institutions are engaged, this presents an opportunity for institutions to cooperate or streamline IRB review. Often this takes the form of an IRB authorization agreement, which should spell out the responsibility of both institutions (including sharing of “paperwork”). See also OHRP’s Terms of the Federalwide Assurance for the Protection of Human Subjects for more information.

Q: Please clarify the requirement surrounding federal employees’ participation in a study, particularly with regard to surveys and program assessments related to their professions.
A: We are not entirely clear to which requirement this question applies, but will answer with regard to exempt categories 3 and 5. Category 3 applies to elected or appointed officials, but not to all public employees. It does not, for example, apply to all federal or state employees, the majority of whom are not elected or appointed. Category 5 is limited to projects conducted by or subject to the approval of federal agencies (not state or local projects), and should not be used without authorization or concurrence by the funding agency. The focus here is on public benefit programs, and not on federal employees.

Q: Can you provide the answers to cases #9 and #10?
A: In Case 9, Dr. A. Orta, a cardiac surgeon, wants to conduct research using 25 leftover tissue specimens from routine biopsies he will obtain during open heart surgeries on his patients. No additional information from medical records is needed for the planned analysis.

We determined that this is human subjects research (because the research involves specimens that are identifiable to the investigator/surgeon), and is eligible for expedited review under Category 5. Please note: The research does not fit into exempt Category 4 because the specimens aren’t “existing” (as they will be obtained over the next 2 months).

In Case 10, researchers want to contact patients who were treated for pneumonia with an FDA-approved drug, asking them to complete a short survey and undergo a chest x-ray at their next clinic visit. The researchers will also obtain the patients’ age, height, weight, adverse effects, and overall health status from their medical records. The information will be recorded so that they cannot link the data back to an individual patient.”

This is human subjects research that requires convened meeting review. The research doesn’t qualify for expedited review under Category 4 because an x-ray is involved.

Q: What wrinkles should one be aware of when the research is not occurring in the United States? For example, a faculty member at our institution is doing work that qualifies as research (low-risk), it does involve human subjects, is not federally funded, we have unchecked the box on our Federalwide Assurance (FWA), and the research is happening in China. Am I right that she does
not need IRB approval?
A: There are no US federal regulatory requirements for review in the circumstances described above (assuming FDA regulations do not apply); however, many institutions have policies that do require IRB (or other) review of human subjects research that otherwise falls outside of the regulatory requirements or is not required under the terms of the institution’s FWA. Institutions should also be aware of local review requirements in the country/location where the research will take place and may want assurance that the investigator has obtained any necessary approvals or permissions before the research begins.

Q: My question concerns records based studies. We are currently engaged in a public health surveillance collaboration with the Centers for Disease Control and Prevention (CDC) to develop a data repository. This is a retrospective study and no subjects will be consented. Medical charts will be reviewed and the data will be de-identified. The data will be linked later by the CDC, but it will remain de-identified. Is there a resource or a set of rules that we can reference to address this kind of study? Ultimately, we had to start over with our submission and submit a data repository submission for review, but is there a resource available that addresses public health surveillance studies, for instance?
A: Here, we would ask some of the same questions regarding the purpose of developing the data repository to determine if the data will be collected and retained for future research purposes. If so, since medical records (the data source in this case) contain private, identifiable information, it appears that the study involves human subjects. However, if the purpose of the repository is to collect information to potentially identify and implement prevention and/or interventional strategies for public health issues, then creating the repository may not constitute research. Often, since repositories are created for multiple purposes, one of which may be research, obtaining IRB review for developing a repository provides additional flexibility for future research projects.

Note: Subsequent “secondary” uses of the data from the repository may not meet the definition of human subjects research if the data will be coded or de-identified. For more information, see OHRP’s Guidance on Research Involving Coded Private Information or Biological Specimens.

Q: What are your thoughts on IRB review of capstone projects from graduate students where the focus is quality improvement projects related to an evidence-based interventions?
A: It does not appear that there is a universal or common definition of “capstone projects,” so this may vary across institutions and disciplines. Therefore, we would not be in position to make a blanket determination about whether these represent human subjects research or not. We would advise institutions to make the determination in the same way as described during this webinar, using the regulatory definitions of “research” and “human subject,” applied in that order. Based on the information above, if the “quality improvement project” is used solely for quality improvement within the institution, we suggest that it would not be “research.” However, if another intended purpose is for the graduate student to use the project as a thesis that is made available for citation by others, we would likely consider this activity “designed to contribute to generalizable knowledge” and determine that it is research.

Q: The Cystic Fibrosis (CF) Foundation has a national registry of patients. Clinical data is stored in this database and is used by local centers for clinical care of their patients following various health trends, recent visit data, etc. This data is also made available by application for research purposes. The Foundation created a two page research protocol that accredited CF centers can submit to their respective IRBs to collect this data. However, I'm not convinced this necessarily would be described as research. The two-fold purpose of the patient registry is described as: 1) So epidemiologic research can be performed; and 2) So current and accurate data can be provided to researchers and clinicians regarding practice patterns, age, and gender distributions, clinical outcomes, mortality and morbidity rates. To me this is not a “systematic investigation.” There is no plan for data analysis in the protocol or anything like that. It seems to me that the Foundation is trying to comply with regulations, but it may be a case of over-compliance. I would really appreciate some feedback on this because I feel it could save a considerable amount of time for hundreds of clinics throughout the country if IRB approval and informed consent are not necessary.
A: This is a good example of activity that typically occurs as a prelude to research, and therefore falls in a gray zone. Accordingly, you have even more discretion than usual in your handling, depending on your point of view. On the one hand, this activity would not likely be happening in this way if it were not being done for research purposes. Organizations such as foundations or patient advocacy groups are not in the business of delivering clinical care, nor is it quality assurance activity for in-house improvements. Finally, one would not usually enter patient-subjects into a registry like this without their consent (i.e., their voluntary consent will be sought). All of these points argue for treating it like research. On the other hand, it is true that there is no “systematic investigation” immediately at hand, so it technically fails the regulatory definition of research. The dilemma is, if it isn’t research, what is it? For these reasons, many IRBs treat these activities that “gather the subjects” as a first step in research (we might broaden the examples to include tissue banks and student pools, as well as registries). That said, review need not be burdensome, and could potentially be handled under exempt Category 2 or (worst case scenario) expedited review Category 5.