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IRB Update

JANUARY 2013

THIS ISSUE

Reminder about COI Disclosure Requirement

Wendy Charles, MS, CIP, CCRP; Director, Research Regulatory Affairs

As a reminder, National Jewish Health implemented a new requirement for conflict of interest disclosures. All individuals (principal investigators, co-investigators, research coordinators, technicians and other research staff) listed on a protocol submitted to the IRB or IACUC must complete a study-specific Conflict of Interest and Scientific Misconduct form. Completion of this form by each individual listed on each protocol provides a more accurate and timely method for our institution to identify actual or potential conflicts of interest.

This requirement will be implemented for new human or animal protocols submitted or reviewed after January 1, 2013 or for personnel added to a protocol after January 1, 2013.

Incomplete Submissions May be Returned

Wendy Charles and Deb Clayton, MA, Regulatory Affairs Monitor

The IRB tries, whenever possible, to accommodate submissions in development. We follow personnel changes until training or education have been completed or are known to make a copy or two as a service to our customers. However, increasing numbers of submissions have been dropped off at the IRB office for review and approval with major components missing. For example, an IRB submission form, such as the Change/Update form, may indicate that the National Jewish Health Research Database will be utilized for the study, but the necessary forms to add the RDB to the protocol/research design were not included with the submission. The IRB cannot review or make determinations for incomplete submissions. Sometimes when missing portions of the initial submission are ready, they are often dropped off with no indication of the studies or submission forms with which they are associated.

In an effort toward enhanced quality control and to improve document tracking and accuracy of the review process, submissions will now be examined when they are dropped off at the IRB office. If submissions are incomplete, they will be returned to the Investigator or IRB Contact with an explanation of the missing items. Submissions for full committee review will not be scheduled for review until the submission is complete.

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Common Misunderstandings with NJH IRB Research Terminology

Wendy Charles and Deb Clayton

Some researchers have expressed confusion at the scope or definitions of terms used by the IRB. We are providing the following definitions as an attempt to reduce misunderstanding. We have paired and defined the most commonly misunderstood concepts.

"Research" vs. "Clinical Care"

"Research" means a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. A systematic, research protocol-driven approach for the best data collection might be quite different than a care-driven approach for the best interest of a patient. Therefore, when a research protocol lists specific procedures that should be performed at specific time intervals for consistency of data collection, the IRB considers these procedures to be part of research—even when the procedures themselves might otherwise be consistent with routine clinical care.

The IRB asks Investigators to carefully separate the activities that would be conducted for research from those procedures that would be performed for clinical care. Specifically, the IRB advises Investigators to include in the research protocol only those activities performed for research purposes. If some information could be gleaned from clinical care, Investigators are instead advised to specify that this information will be extracted from the medical record.

"Subject" vs. "Patient"

As noted above, there is an important distinction between research and clinical care. Consequently, the terms "subject" and "patient" are not synonymous. A "subject" is defined as a volunteer who participates in a clinical trial, either as a recipient of the experimental treatment, or as a control who receives the standard treatment, or as a healthy volunteer who receives no treatment. A "patient" is a person who receives clinical care and is not participating in research. An individual might serve as both a "subject" and a "patient" at different points in the same encounter with a Clinician Investigator, but a "subject" might not be a "patient."

Because the federal regulations refer to human volunteers as "subjects," the National Jewish Health IRB has also chosen to use this term. The IRB is cognizant that this term might be perceived as inelegant to those outside the research community, but the term has very specific meaning.

"Experiment" vs. "Experimental component"

Many, if not most, researchers mistakenly describe the "experiment" in the sections of the application form and consent form that request an explanation of the "experimental component."

To explain the experimental component, the Investigator should provide written consideration of the investigational, unapproved, non-validated, or novel features of the research. For example, while a blood draw might be performed only for research purposes, the experimental component is not the blood draw but the exploratory search for biomarkers in the blood.

"Consented," "Enrolled" and "Randomized"

Each institution, sponsor, or consortium might define these terms differently. To accommodate the broad spectrum of research at National Jewish Health that may not involve randomization, the IRB uses the following definitions:

Consented: This term applies to subjects who provide informed consent to participate in the research. After providing informed consent, subjects may participate in a number of screening procedures to determine if they meet eligibility criteria. Because subjects face risks from screening procedures, the IRB asks researchers to keep track of the number of subjects who provide consent.

Enrolled: Subjects are considered "enrolled" after they complete all screening procedures and are determined to meet the eligibility criteria to participate in the research. The enrollment estimate is very important because enrolled subjects could receive all procedures (and risks) described in the protocol.

Randomized: The research may be designed to assign subjects to a treatment or group by chance.

Randomization can occur at the same time as enrollment, but can also occur much later in the research. As an example of late randomization, a study of an investigational drug may first administer the drug to all enrolled subjects to assess tolerability and then randomly assign dosing regimens.

While consortia or commercial sponsors may focus on the number of subjects who "randomize," the NJH IRB is more concerned about the number of subjects who "enroll." As noted earlier, subjects may be exposed to risk much earlier than the point of "randomization."

"Screen failure" vs. "Pre-Screening Failure"

Screen Failure: The term, "screen failure," is applied to a person who *provides informed consent* to be in the study and completes some or all of the screening procedures, but does not meet the protocol's eligibility criteria to continue in the study. Because these individuals might be exposed to risk as part of the screening process—sometimes even significant physical risk—the IRB asks researchers to track the number of people who provide informed consent and initiate screening.

Pre-Screening Failure: Researchers often perform a number of activities to find individuals who might be interested in study participation. As examples, researchers may query the National Jewish Health Research Database or telephone the Investigator's clinic patients to find suitable candidates. Unless these prospective subjects have provided consent to participate in the actual research, the IRB considers these exploratory searches or conversations to constitute "pre-screening." The IRB needs to know which activities are planned for pre-screening but does not request the number of subjects approached or the number of records examined for pre-screening.

"Dropout" vs. "Withdrawal"

As with the terms "enrolled" and "randomized" above, there are varying definitions regarding "dropout" and "withdrawal." At National Jewish Health, the distinction is based on the person who initiates study discontinuation.
Dropout: This term is defined exactly as it sounds; a subject "drops out" of the study. More broadly, this term encompasses any type of discontinuation *initiated by the subject.* A subject may passively drop out of a study by failing to return for follow-up visits or may actively drop out by discussing his or her desired discontinuation with the Investigator.

Withdrawal: This term is applied when a member of the research team initiates a subject's discontinuation. As an example, an Investigator may withdraw a subject from ongoing participation because continued involvement may cause harm.

"Informed consent" vs. "Informed Consent Document"

Informed consent: "Informed consent" is *not a document* but a critical, ongoing process of communication between the subject and research team. While subjects may provide written informed consent at the beginning of their involvement, the research team must keep them informed about the study and continue to discuss their willingness to remain in the study.

Informed consent form/document (ICF): This is the IRB-approved form or document that describes the research study and details all procedures, risks, and benefits. Subjects are asked to review the consent document and, if they are willing to participate in the research, are asked to initial the bottom of each then sign the last page of the document. As noted earlier, subjects cannot sign an "informed consent;" they can only sign documentation of informed consent.

"Exemption" vs. "Non-human subject research"

Exemption: An "exemption" is a classification of human subject research that falls within narrowly-defined criteria specified by the federal Office for Human Research Protections (OHRP) or the Food and Drug Administration (FDA). The research may be exempt from ongoing oversight by an IRB but is not exempt from the requirements of the institution's human research protections program. Researchers must maintain current training in human research protections, provide conflict of interest disclosures, and implement privacy/security protections under HIPAA, if applicable.

Under a Federalwide Assurance to receive federal funding, the recipient institution is required to

appoint an individual or organization to determine whether a study may qualify for exempt status. At our institution, the IRB has been designated to make this determination.

Non-human subject research: Data or specimens must be identifiable (at some point in the study) to meet the federal definition of "human subject." Even though data or specimens may originate from humans, if the identity of the human source cannot be ascertained by anyone on the research team—directly or indirectly through coding systems—the nature of research may be classified as "non-human subject research." [Exception: Specimens used in FDA-regulated *in vitro* diagnostic research are not identifiable, but the research is still classified as "human subject research."]

Non-human subject research cannot receive an "exemption" from the IRB. As noted above, only human subject research that meets the federal criteria for an exemption can receive an exemption. Research that does not meet the federal definition of "human subject research" receives a "non-human subject research" determination.

"Expedited Review" vs. "Faster Review"

Expedited Review: "Expedited review" or "review by expedited process" are phrases in both OHRP and FDA regulations that describe a method of reviewing human subject research where the research is determined to be minimal risk and falls within narrowly-defined categories. Not all minimal risk research procedures fall within these categories. Research eligible for expedited review does not require review by the convened IRB and can be reviewed by an IRB Chairperson or experienced IRB member. The IRB staff or the convened IRB makes the determination as to whether initial or continuing review can be performed by expedited process.

Faster review: "Expedited review" does not mean "faster review." While expedited review often occurs sooner than review by the convened IRB, the phrase "expedited review" is type of review procedure defined in the federal regulations.

If a researcher needs a review determination by a particular date, he or she is asked to communicate the deadline to the IRB rather than request "expedited review."

It should also be noted that "expedited review" does not involve less stringent review or fewer criteria for IRB approval. Expedited review is not "review-lite."

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More Guidance Documents Posted on IRB Website

Wendy Charles

Within the past few weeks, the IRB posted two new guidance documents on the IRB website.

Guidance on Informed Consent and Authorization Elements:
This document explains each informed consent and authorization element individually to help researchers understand how to write or edit consent and authorization forms.

Guidance on Waiver of Informed consent and Authorization elements:
This guidance document explains the differences between waivers of informed consent, waivers of documentation of informed consent, and waivers of authorization. Practical examples are offered that may assist researchers with completing submission forms for these waivers.

Both guidance documents are found on the Informed Consent page of the IRB website: http://www.nationaljewish.org/professionals/research/support/compliance/irb/submissions/informed-consent/.

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