

SEPTEMBER 2012

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Fewer Copies Needed for Full Committee Submissions

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

Historically, for full committee review, Investigators were asked to provide twenty complete photocopies of their submission for all IRB members, consultant reviewers, and filing. The National Jewish Health Institutional Review Board (IRB) is pleased to announce they have been transitioned to electronic review of full committee submissions! Effective September 4, 2012, researchers need only submit signed original documents plus two (2) complete, collated photocopies.

The IRB does not have an electronic document management system and therefore still requires paper documents for record-keeping and stamping. IRB Staff will scan the submissions for electronic review. Below are some guidelines to ensure success:

Number of copies:

- Submissions requiring full committee review: Original + 2 copies
- Submissions eligible for all other types of review: Original + 1 copy

Original versions:

- All original documents should be hand signed by the Principal Investigator. We cannot yet accept emailed copies and NJH systems do not meet regulatory requirements for electronic signatures.
- All pages should be single-sided so they can be scanned.

Photocopies only:

- It is acceptable for the site to prepare double-sided copies to accompany the original as long as each, discrete document is copied individually. (This process requires manual collation.)
- If a researcher creates a double-sided copy where the first page of one document is copied to the back side of the last page of the previous document, it is not possible for the IRB to stamp the photocopies as individual documents. In such cases, the photocopies will be returned and the researcher must re-copy.
- Photocopy all original versions, including Conflict of Interest forms and clean copies of informed consent and authorization forms.

We are very excited that this transition will lower costs and reduce needs for resources. Please call the IRB office (303-398-1477) with questions.

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Protocol Exceptions (Protocol Waivers)

Wendy Charles

A protocol exception, sometimes referred to as a protocol waiver, is a type of planned change to research. Unlike a protocol amendment, a protocol exception involves a single participant or, less commonly, a few participants and is not a permanent revision to the research protocol. Protocol exceptions are most commonly requested for subjects who do not meet the protocol's eligibility criteria, but may also be requested for subjects unable to complete certain visits or types of procedures.

Historically, IRBs were not notified of protocol exceptions; it was primarily a discussion between the Investigator and the sponsor of the study. However, this practice received intense scrutiny after the death of Jesse Gelsinger, a young man enrolled in a gene therapy study without meeting all eligibility criteria. IRBs are now expected to enforce the requirements of pre-approval for protocol exceptions. And while sponsors may still entertain Investigators' requests for protocol waivers, Investigators are advised that **a sponsor's waiver does not also waive the requirement for prospective IRB approval.**

"From a regulatory standpoint, the act of waiving an inclusion criterion without prior IRB approval is no different than ignoring IRB-approved conditions. Revising inclusion criteria or any other aspect of the protocol, even for a single subject, requires prospective IRB approval." Bankert & Amdur. Institutional Review Board Management and Function 2006;253.

In accordance with 21 CFR 56.108(a) for FDA-regulated research and 45 CFR 46.103(b)(4) for federally-funded research, the IRB must ensure that changes in approved research during the period for which IRB approval has already been given may not be initiated without IRB review and approval except where necessary to eliminate apparent immediate hazards to the human subjects. A planned (non-emergency) protocol exception performed without IRB approval is considered noncompliance and must be processed according to the institution's noncompliance policy. In some cases, the noncompliance must also be reported to federal agencies.

Requesting a prospective protocol exception from the National Jewish Health IRB:

- Submit a *Protocol or Consent Form Changes form* (because the Investigator is seeking an exception to the protocol requirements).
- Submit a memo explaining the basis of the request (including details about the possible subject's eligibility) and how the protocol exception would not impact this individual's safety.
- For commercially- or consortium-sponsored studies, attach the sponsor's/DCC's/Medical Monitor's approval for the protocol exception.
- Note: There should be a separate submission for each subject for whom a protocol exception is requested. If the Investigator requests a particular type of protocol exception for more than two subjects, he or she is encouraged to instead submit a formal amendment to the protocol. For multisite studies where it may be difficult to amend the protocol, the IRB may accept a site-specific protocol addendum prepared by the sponsor or consortium.

Some protocol exceptions can be reviewed by expedited process but must be reviewed by an IRB Chairperson. Investigators are asked to allow sufficient time in the event full committee review is required.

Requesting a retroactive protocol exception from the National Jewish Health IRB:

The IRB cannot retroactively approve any type of submission, including requests for protocol exceptions. If an ineligible subject was inadvertently enrolled, the Investigators must report the deviation using the *Protocol Deviation Report form*. As noted earlier, there are some cases where enrollment of ineligible subjects must be reported to federal agencies.

IRB acknowledgement of a protocol deviation does not grant approval for an ineligible subject to remain in the trial. Specifically, the subject still does not meet the IRB-approved protocol eligibility

requirements. If an Investigator would like an ineligible subject to remain in the study, he or she must also request IRB approval of a protocol exception, protocol amendment, or site-specific protocol addendum, as described above.

IRB Review Considerations:

The IRB will ask the Investigator the following questions when processing a Protocol Exception request:

- If the protocol's eligibility criteria or procedures are based on sound scientific and medical justification, is it indeed appropriate to enroll, allow continuation of, or modify participation for an individual?

- Is there evidence that it would be safe for the person to enroll, continue in the study, or modify participation as proposed?
- How would the data analysis be affected?
- Is it appropriate for the IRB to grant a protocol exception, or should the Principal Investigator amend the protocol? This question is particularly pertinent if the investigator has submitted more than one request for the same type of protocol exception.

For more information, contact:
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Boundaries of Recruitment Activities

Wendy Charles and Steve Leibold, MSHA, Corporate Compliance Manager and Privacy Officer

Where is the boundary between informing patients about research and conducting research recruitment activities?

Recruitment is a regulated research activity, so it is important to distinguish between providing objective information about research opportunities (which could be considered communication as part of the treatment relationship) and participating in protocol-specific recruitment activities. While many healthcare providers are eager to help their colleagues recruit for a study, there is a limit to what providers can and cannot do, or services they can provide, if they are not members of the research team.

While different institutions may provide different guidance, we recommend the following approach:

Talking to Patients/Possible Subjects:

Can: A healthcare provider who is not a member of the research team can share information about a research opportunity. Generally, "information" is limited to: title, purpose of study, basic eligibility criteria, Principal Investigator, study site location, and the researchers' contact information.

Cannot: OHRP guidance states that those who provide information about research opportunities should not act as representatives of the Investigator or of the research team. A provider should not answer questions about procedures, risks, benefits, payment, or offer information that requires protocol-

specific training. Instead, the provider should direct interested patients to obtain answers from a member of the research team.

Contacting Patients by Phone:

Can: A healthcare provider (or designee) may telephone patients who may be eligible to participate in research. The call should first introduce the treatment relationship between the patient and provider, then limit information about the study to the guidance provided in the preceding section. Interested patients should be directed to contact the researchers for more information.

Cannot: As noted earlier, a provider cannot represent himself/herself as acting on behalf of the Investigator or give the impression that he/she is a member of the research team. A provider can inform subjects about basic eligibility criteria but cannot ask screening questions to determine eligibility.

Providing Documentation:

Can: A provider can post flyers, provide brochures about the trial, or can provide the business cards (or other form of written contact information) for the researchers. The interested patient must then initiate contact with the researchers.

Cannot: The provider cannot give the patient's name or other distinguishing information to the researchers.

Can: A healthcare provider can offer a copy of the informed consent document to a patient to review or take home.

Cannot: The provider cannot obtain informed consent or answer questions about the consent form content.

Can: If a patient seems interested in the study, a provider can ask his/her patient to sign the National Jewish Health *Recruitment Authorization to be Contacted about Research* form (HIP-001). [The equivalent authorization form at the University of Colorado, Denver is called HIPAA-A.] The provider can give the signed copy to the researcher, which allows the researcher to call the prospective subject directly. A patient can also mail the form back.

Cannot: The recruitment authorization form can only be used for the study (or recruitment database) that the patient was told about. If a patient signs the form with interest in one study, the authorization form cannot be used to contact this patient for other studies.

Sending Letters:

Can: A healthcare provider can send IRB-approved recruitment letters to his/her own patients to inform them of the research. These letters should list the provider's name and instruct prospective subjects to contact the researchers for more information.

Cannot: A provider cannot give any identifying information about these patients to the researchers (such as a providing a mailing list). The provider must protect the identity of his/her patients.

Tip: It is customary for researchers to give IRB-approved letters (or letter templates), envelopes, and postage to providers. The providers will then add the patients' names and addresses for mailing.

Querying Patient Databases:

Can: A patient database, such the EMR, can be queried for many types of treatment and healthcare operations. It is acceptable under the Privacy Rule for a healthcare provider to query a database with the intent of informing his or her own patients about research opportunities. The National Jewish Health Research Database can also be queried by

providers who are not members of the research team to obtain lists of their own patients.

Cannot: A patient database cannot be queried by a member of the research team (ostensibly for research purposes) without IRB approval. Further, a provider cannot obtain lists of patients where there is not a treatment relationship.

Tip: To query the National Jewish Health Research Database to obtain lists of his or her own patients, a provider (who is not a member of the research team) should contact Pearlanne Zelarney (x2527).

Querying Research Recruitment Databases:

Can: A research recruitment database has different rules than a patient database. If a subject has provided informed consent to be added to a recruitment database, only members of the database research team may perform the query or receive results of the query, regardless of treatment relationships. [For the purposes of this guidance, the National Jewish Health Research Database functions as a patient database—not as a research recruitment database.]

Cannot: The database manager must respect the terms of the database informed consent form and protocol for future uses of the recruitment information. Therefore, a recruitment database cannot be used to query about health conditions or for researchers outside the terms specified in the consent form and protocol.

As a final recommendation, consider this distinction: A provider can talk about the contents of a flyer/brochure, whereas a member of the research team can talk about the protocol.

With any approach, researchers should make sure they have obtained IRB approval for the planned methods and locations of recruitment. A provider does not need IRB approval to inform patients about research if he or she follows this guidance.

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The IRB did not issue a newsletter in August, 2012.