

October 2015

# Human Subjects Protection Update

## (Special Communication)

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## Notice of Proposed Rulemaking (NPRM)

The U.S. Department of Health and Human Services has issued a Notice of Proposed Rulemaking (NPRM) with the purpose of modernizing, strengthening and making more effective the federal policy for the protection of human subjects. The NPRM is 500 pages long and includes the rationale for changes (the preamble), the actual revised regulation and questions for additional comment. More information about the NPRM may be found at:

<http://www.hhs.gov/ohrp/humansubjects/regulations/nprmhome.html>

This special communication newsletter will provide a very brief overview of the more significant proposed changes pertinent to Boston Children's Hospital (BCH). We are providing this information so that you are aware of the proposed changes being considered. **Please note the changes are not final and the proposed changes may be modified or even eliminated depending on the public comment.** If enacted there would be a proposed period of 1 year for compliance with most of the changes and three years for compliance with changes pertinent to single IRB review and consent requirements for all biospecimen use. BCH will be submitting comments however investigators are encouraged to work with their own professional organizations and submit comments. It is important for HHS to receive comments from the investigator community. Comments may be submitted to:

<http://www.regulations.gov>

Docket ID#: HHS- OPHS-2015-0008

While there are many changes we have elected to summarize those that are most likely to impact BCH investigators and our research community. There are more changes and many more details than provided.

### 1. USE OF BIOSPECIMENS AND DATA

The change in proposed regulations will require informed consent for all secondary use of left over biospecimens that are collected for clinical purposes, even if the investigator is not provided with information that would enable him or her to identify whose biospecimen it is. IRBs will no longer be able to waive informed consent for any use of a biospecimen. The consequence of this modification is that most future uses of biospecimens will require at least a "broad informed consent" for future use that is obtained either at the point of collection or prior to the subsequent use. The NPRM describes the elements to be included in a broad consent to be developed by HHS. The broad consent will allow undefined use of the specimens for future research.

It will no longer be possible to obtain discarded blood or pathology tissues collected for clinical care and use it for research without the consent of the individual. In order to make clinically acquired specimens available to researchers, BCH will potentially need to set up a mechanism to enroll all patients into a consented institutional biobank so that all patients are approached when they visit the hospital and asked for consent to utilize remaining clinical samples for research. Their responses will need to be tracked and their decisions respected as to whether discard clinical sample or tissue may be utilized for research. BCH does have an existing institutional biobank with some of the infrastructure but may require some modifications and has not been expanded to all parts of the hospital and clinics.

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At the time the regulations are enacted, existing or identified collections of biospecimens may continue to be used with a waiver of consent however this will require the development of systems to track samples before and after the date the regulations take effect.

There are a few exceptions that are proposed. One exception is the use of a biospecimen for internal operational monitoring and quality improvement or when secondary use of a non-identified biospecimen is designed only to generate information about an individual that is already known (for example research to develop a diagnostic test for a condition using specimens from individuals known to have the condition and those known not to have the condition).

There are also some changes regarding the use of identifiable data. The proposed regulations are more restrictive for biospecimens. The differences in the NPRM with regards to how data and biospecimens are treated and reviewed is a topic of discussion and controversy. For example, using a sample of de-identified tissue for genome wide sequencing is treated differently than if the sequencing data of the same tissue was available in a medical record for clinical care purposes.

The proposed changes for the use of biospecimens and data are complex and perhaps the most controversial part of the NPRM. Many more details may be found in the NPRM and revised regulation.

## **2. SINGLE IRB REVIEW**

The proposed revised regulation would mandate that only one IRB can act as the IRB of record for U.S. sites participating in a multi-site study. The National Institutes of Health has already distributed a draft policy for comment that promotes the use of a single IRB for multi-site NIH studies. The proposed regulation specifies that the funding department or agency would be responsible for choosing the IRB of record, and for studies with no funding agency the lead institution conducting the research would be responsible. Under the proposed rules, the requirement for a single IRB of record would not apply to: (1) cooperative research for which more than single IRB review is required by law (e.g., FDA-regulated devices); or (2) research for which the Federal department or agency supporting or conducting the research determines and documents that the use of a single IRB is not appropriate for the particular study.

Currently BCH already utilizes single IRB review options on a voluntary basis; however the proposed regulations would mandate this. BCH has already served as a single IRB and also relinquished IRB review to other institutions. We have already established some systems to support single IRB. However, if mandated additional changes in policies, procedures, and staffing will be required to support this mandate.

## **3. ACTIVITIES EXCLUDED FROM IRB REVIEW**

The NRPM creates a new section of the regulations that would exclude certain activities from the requirements of IRB review and oversight. Most pertinent to BCH is the excluded categories of program improvement, if activities are limited to data collection and analysis only, and quality assurance activities that only involve the implementation of practices that are already accepted with a goal of improving delivery or quality of treatments or services. It is also clarified that public health surveillance required by law to assist respective authorities in fulfilling their missions to protect public health does not require IRB review. BCH has already developed policies that specify that QI activities do not fall under the jurisdiction of the IRB, however the proposed regulations have specific wording that may limit the scope of what is not considered research. While we recognize the classification of research versus QI is not always straightforward, we do plan to respond and suggest that the proposed regulatory language is rather restrictive in the definition of what constitutes quality improvement.

Another proposed exclusion category is research with adults involving tests, surveys, interviews or observation, if subjects cannot be identified or disclosure would not put subjects at risk. For children this exclusion only applies for research involving educational tests, or observations of public behavior when the investigator does not participate in the activities being observed and does not include surveys of children. This category was previously an exempt category that has now been moved to exclusion.

## **4. EXEMPT RESEARCH**

Exempt research consists of activities that are considered human subject research but present so little risk that the requirement for IRB review and written informed consent do not apply. Exempt categories currently exist however the proposed revised regulations seek to expand them. HHS anticipates the development of a software “tool” which investigators could use for determining if an activity is exempt. Institutions could utilize this tool or an individual knowledgeable about exemption criteria (e.g., IRB person) could make this determination. The exemption tool would be developed by HHS and resents a “safe harbor” when the tool is used. The proposed rule modifies a number of the existing exemption categories and introduces several new exemption categories. New categories include:

1. Certain research involving benign interventions with adult subjects (primarily limited to social and behavioral research);

2. Research involving educational tests, surveys, interviews or observations of public behavior when sensitive information may be collected, identifiers or links may be recorded, provided that *data security and information privacy protections policies*\* are followed and subjects are given enough information to make a decision whether to participate
3. Secondary research use of **identifiable private information (data)** originally collected as part of a non-research activity,
4. Storing or maintaining biospecimens and identifiable private information for future, unspecified secondary research studies, or conducting such studies, when a broad consent template to be promulgated by the Secretary of HHS is used, information and biospecimen privacy safeguards are followed, and limited IRB approval of the consent process used is obtained. It should also be noted that this exemption cannot be used if an investigator anticipates individual research results may be returned to subjects.

\*note *data security and information privacy protections* policies and safeguards that will need to be applied will be defined by HHS at a later date. At this time we have no further information on what they might be.

## 5. CONTINUING REVIEW

The NPRM proposes eliminating IRB continuing review of research protocols in at least three situations:

1. For minimal risk studies that qualify for expedited review, unless an IRB reviewer provides a rationale why continuing review should occur.
2. For studies that were reviewed by a the full IRB but have reached a stage of only (1) analyzing data (even if it is identifiable private information); (2) accessing follow-up clinical data from standard care procedures; or (3) doing both.
3. for certain secondary research using information and biospecimens, under new limited IRB review provisions.

The IRB will still need to receive annual confirmation that such research is ongoing and that no changes have been made that would require continuing review. This could be an automated electronic communication in which the investigator types "Yes" to indicate that the study is ongoing without change. The NPRM does not change investigators' reporting obligations including changes to the protocol and unanticipated problems.

## 6. INFORMED CONSENT

The proposal calls for a requirement of the final version of the consent form to be posted on a public federal website. In addition, consent forms could no longer be unduly long documents and the important information must be easier to find; with more appropriate details provided about the research that is most relevant to a person's decision to participate. The consent will need to be organized to provide sufficient detail and facilitate understanding. It would also need to present core information first, including only required regulatory elements and including all other information in appendices.

The NPRM proposes that all consents include a statement about whether or not the subject's data will be used for future research studies if the identifiers are removed. Additional new elements as applicable would include

- Discussion of commercial profit and whether the subject will share in such profit
- Whether clinically relevant results will be returned to the subject
- Options for consenting or refusing to consent to be contacted for more information/biospecimens or another research study

Further, informed consent would be required for secondary research with a biospecimen even if the investigator is not given information that would enable identification of whose biospecimen it is. Such consent would not need to be obtained for each research use of the biospecimen, but rather could be obtained using a "broad" consent form to future unspecified research uses.

## 7. EXTEND APPLICATION OF FEDERAL COMMON RULE

The NPRM would extend the HHS Common Rule regulations and protections to any clinical trial conducted at an institution that receives federal support for human subject research. At BCH, in practice, we already extended the HHS common rule regulations to all research activities so this change would have little impact in how we operationally review human subject research at BCH

We will continue to keep the research community advised about the NPRM and any additional rulemaking activities. The IRB office welcomes your thoughts and will consider them as part of the institutional comments. Please email Susan Kornetsky directly if you have comments for consideration. You are also encouraged to submit your comments directly to HHS and they are due December 7, 2015. If you have any questions you may contact Susan Kornetsky by email [Susan.Kornetsky@childrens.harvard.edu](mailto:Susan.Kornetsky@childrens.harvard.edu) or at 5-7053.

## Important Changes to Staff Amendment Activity in CHeRP

An amendment is no longer required to add/remove BCH personnel from research protocols in CHeRP. Rather than submitting a separate amendment to do so, the PI or an editor on a protocol can now select the new “Manage BCH research team” activity located at the bottom, left-hand menu within the protocol workspace to make BCH staff changes. As with amendments, the activity will still check that **appropriate human subjects training** has been completed before adding new personnel.

However, an amendment is still required to modify study documentation (i.e. recruitment materials, consent forms, protocol documents, that list staff), add and/or remove non-BCH personnel, or change the study’s Principle Investigator.

Of note, the “Manage BCH research team” activity is unavailable while an amendment remains open. If an amendment will be/has been submitted for other modifications to the study, staff changes may be made at that time as usual.



### Boston Children’s Hospital

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*The [Institutional Review Board \(IRB\)](#) has been established to oversee the protection of human research subjects at Boston Children's Hospital. Children's is committed to safeguard the rights and welfare of all children, adolescents, adults and family members who volunteer to participate in research. To this end, the Office of Clinical Investigation upholds the principles of the Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects in Research, as the cornerstone of our mission, organization and daily activities.*

- Have questions or comments about any of the articles in this newsletter?
- Need advice about your research?
- Want to know more about human subjects protection at BCH?

Please don't hesitate to contact the CCI and one of our staff will be happy to assist you.