POLICY ON RESEARCH DATABASES, SPECIMEN REPOSITORIES AND CONTACT LISTS
7/9/2010

Introduction

Databases and specimen repositories (sometimes called registries, banks, libraries, or contact lists) are used to store data and/or specimens for future use. When the use is for clinical purposes or quality improvement (QI), IRB approval is not required. However, when the use is for research purposes, the databases/specimen repositories (DSRs) must be approved by the IRB. The DSRs must satisfy the requirements of the Common Rule (45 CFR 46) for protection of human research subjects and the requirements of the Privacy Rule, i.e., the Health Insurance Portability and Accountability Act (HIPAA) (45 CFR 160 and 164), for protection of individually identifiable health information. Further information is available on the National Institutes of Health (NIH) website: http://privacyruleandresearch.nih.gov/pdf/researchrepositories_final.pdf

DSRs require consent and authorization (C/A) by subjects for the storage and potential future research use of their data/specimens, or a waiver of C/A by the IRB. Exemption from IRB review is not an option if the data/specimens retain an identifier or a link that would permit anyone to identify, directly or indirectly, the person whose data/specimens are stored.

RESEARCH DATABASES/SPECIMEN REPOSITORIES (DSRs)

A. When used for a specific research study. When the data/specimens are stored in a DSR for use only in a designated specific research study, a description of the storage and use must be included in the IRB protocol and in the C/A form for the specific study.

B. When used for future unspecified research studies.

1. Maintained at the Duke University Health System (DUHS). When the DSR is maintained partly or completely at DUHS, a separate IRB protocol must be submitted for the DSR itself. The protocol should include the following:

   a. Purpose of the DSR. Describe the research to be done with the data/specimens. Describe the DSR not as a research study itself, but rather as the source of data/specimens for future unspecified research studies. To avoid confusion, do not use the word “study” when referring to the DSR in the protocol narrative or in the C/A form, because no research studies will occur under the sole auspices of this DSR protocol.

   b. Separate protocols for research studies. A statement should be made in the DSR protocol that separate IRB approval will be requested for each specific research study that uses data/specimens from the DSR. Each study is considered to be a research activity that is separate from the activity of the DSR itself.

   c. Data/specimens to be included. Describe the data/specimens to be included, their sources, and the process of acquisition. If some of the data/specimens have been or are to be collected at sites outside of DUHS for storage at DUHS, include a recommended collection plan and C/A document for distribution to data/specimen collectors and possible use by their local IRBs. Confirm that documentation of local IRB approval will be provided to the DUHS IRB for each site contributing data/specimens to the DUHS DSR.

   d. Security and confidentiality. Describe how and where data/specimens will be stored, and how the privacy of subjects and the confidentiality of their data will be protected. A Certificate of Confidentiality is recommended, but not required, as an additional protective measure. If a Certificate of Confidentiality is to be requested, the IRB first could approve the database protocol contingent on receipt of the certificate. The appropriate institute at the National Institutes of Health may then issue the Certificate. The Certificate may relieve the investigator of any obligation to identify a subject in answer to a subpoena from state or federal
court or from local civil or criminal authorities. The federal government need not fund the research for the research to be eligible for a Certificate. Also, subjects must be informed when a Certificate is in effect. The subject must be told that the Certificate does not apply to child abuse reporting, to reportable communicable diseases, or to threats of violence to self or others.

**e. Access to the data/specimens.** Describe who will have access to the data/specimens, what the requirements for access are, and who will control access.

**f. Consent and authorization (C/A).** Describe how C/A will be obtained from subjects, or why waiver of C/A is justified.

(1) **Written C/A.**

(a) **Content:** The C/A form should contain all the elements for C/A required by federal regulations. (See Attachment 1.) Be sure to have a clear statement in the C/A form that the subjects are giving permission for their data/specimens to be stored in the DSR for possible use in future research studies relating to the stated area of investigation. In the future, when an IRB protocol is submitted for each specific study, the IRB will consider a request for waiver of C/A (provided that all criteria for the waivers have been met) given that subjects have expressed their willingness to have their data/specimens stored for possible use in future research.

(b) **Separate C/A Forms** Separate C/A forms are required for each specific study and for the DSR.

(2) **Waiver of C/A.** Waiver of C/A can be granted by the IRB as follows:

(a) For inclusion of data/specimens in the DSR that have been collected in the past from DUHS patients for other research studies or solely for clinical or QI purposes. The federal criteria must be met for waiver of consent [45 CFR 46.116(d)] and waiver of authorization [45 CFR 164.512(i)(1)and(2)]. (See Attachment 2.) The principal requirements for waiver are:
   i. No more than minimum risk, and
   ii. No adverse effect on rights or welfare, and
   iii. Research cannot “practically be carried out” without the waiver. At the present time there is no specific federal guidance for defining “practically,” although informally Office for Human Research Protections (OHRP) representatives interpret "impracticable" to be positioned somewhere between “impossible” and “inconvenient”. The DUHS IRB interprets the regulation to mean that C/A can be waived for use of data/specimens from patients who have been seen at DUHS in the past, but who are not expected to be seen at DUHS on a regular and frequent basis in the future. Patients who are expected to return soon should be asked for written C/A at their next visit. OR

(b) For inclusion of data/specimens in the DSR that will be collected in the future from DUHS patients for other research studies or solely for clinical or QI purposes, provided that the federal criteria for waiver of consent and authorization have been met, as well as all of the requirements of the Policy on IRB Determination of Research Not Involving Human Subjects for Research Using Coded Specimens or Coded Identifiable Private Information. Please note that DSRs cannot be exempted [45 CFR 46.101(b)(4)] under this referenced policy because the policy applies only to specific research studies that use coded data or specimens. OR

(c) For inclusion of data/specimens in the DSR that will be collected in the future, provided that the federal criteria for waiver of consent and authorization have been met, and also that both of the following conditions have been satisfied:
   i. The data/specimens will be collected for purposes other than submission to this DSR, e.g., solely for clinical purposes, QI, or prior IRB-approved research, and
   ii. The data/specimens are entered into the DSR without any identifiable private data or information, i.e., none of the 18 HIPAA identifiers [45 CFR 164.514(b)(2)(i)] and no codes or links of any sort maintained either by the submitter or by the DSR that would permit access to identifiable private information about the individual from whom the data/specimens were obtained.

2. **Maintained outside of DUHS.** When the DSR is maintained outside of DUHS, and also there is no DUHS IRB protocol for a related specific study, then a separate protocol and C/A form are required for the external DSR that follow the guidelines above for DUHS DSR. (See B.1. above.) On the other
hand, when there is a DUHS IRB specific study protocol, then a separate IRB protocol is not required for the DSR. However, the following are required:

**a. Description.** The external DSR must be described within the IRB protocol for the related specific study. Details are required on the purpose of the DSR, the type and source of data/specimens, the process of acquisition, how and where data/specimens will be stored, who will have access to the data/specimens, how access will be managed, how the privacy of subjects and the confidentiality of data will be protected, and whether a Certificate of Confidentiality has been obtained or will be requested.

**b. Assurances.** The DUHS IRB requires either documentation of local IRB approval at the DSR site (such as at an academic institution), or written assurances from the keeper of the outside DSR (such as with an industry sponsor) that the subjects’ privacy will be protected adequately. These assurances can be provided as part of a data use agreement between DUHS and the institution or sponsor maintaining the DSR, or in a separate document. The assurances are those required by HIPAA for data use agreements [45 CFR 164.514(e)(4)], i.e., appropriate safeguards are to be used to ensure that protected health information (PHI) is not used or disclosed inappropriately, and no attempt will be made to identify the individuals to whom the PHI pertains, or to contact such individuals except as otherwise stipulated in the C/A form. The wording of the assurance may vary depending upon the specific characteristics of the DSR and other circumstances.

**c. Consent and Authorization (C/A).** Describe how C/A will be obtained from subjects, or why waiver of C/A is justified.

(1) **Written C/A.**

(a) **Content:** The C/A form should contain all the elements for C/A required by federal regulations. (See Attachment 1.) Be sure to have a clear statement in the C/A form that the subjects are giving permission for their data/specimens to be stored in the DSR for possible use in future research studies relating to the stated area of investigation. In the future, when an IRB protocol is submitted for each specific study, the IRB at the proposed site for the specific study will consider a request for waiver of C/A (provided that all criteria for the waivers have been met), given that subjects have expressed their willingness to have their data/specimens stored for possible use in future research.

(b) **Compound or Separate C/A Form:** C/A for an external DSR may be included within the C/A form for the related specific research study, i.e., a compound C/A form, or in a separate C/A form. When a compound C/A form is used, the requirements are different for external databases than for external specimen repositories, as shown below:

[1] **External databases:** When only data are stored externally, there should be assurances in the C/A form that the subjects’ privacy will be protected adequately, i.e., appropriate safeguards are to be used to ensure that identifiable private information, such as protected health information (PHI), is not used or disclosed inappropriately, and no attempt will be made to identify the individuals to whom the information pertains, or to contact such individuals except as otherwise stipulated in the C/A form.

[2] **External specimen repositories:** When a research study involving therapy includes a provision for specimens to be stored externally for future unspecified research, there should be either a separate C/A form, or a compound C/A form that includes a separate section with Opt Yes/No statements. These statements should allow the subject to give separate C/A for participation in the external DSR, with the option to decline. This is because research-related treatment, payment, or eligibility for benefits must not be conditioned on C/A for storing data/specimens in the DSR for possible future unspecified research. Subjects must be given the right to participate in the study involving treatment even if they decline participation in the DSR.

(c) **Data from a study involving a Food and Drug Administration (FDA) regulated product:** Ordinarily subjects have the right to decide whether their identifiable private research information or specimens may be stored for possible use in future unspecified research. However, the sponsor of a research study involving an FDA regulated product may be required by FDA in the future to analyze the research data for reasons not currently envisioned. Therefore for research involving an FDA regulated product, regardless of where the DSR resides (within or outside of DUHS), Opt In/Out considerations do not apply for data stored for possible future unspecified research use by the sponsor/designee. Opt In/Out considerations do continue to apply for specimens stored for possible future unspecified research use.
(2) **Waiver of C/A.** Waiver of C/A can be granted by the DUHS IRB as follows:

(a) For inclusion in the external DSR of data/specimens that have been collected in the past from DUHS patients for other research studies or solely for clinical or QI purposes. The federal criteria must be met for waiver of consent [45 CFR 46.116(d)] and waiver of authorization [45 CFR 164.512(i)(1)and(2)]. (See Attachment 2.) The principal requirements for waiver are:

i. No more than minimum risk, and

ii. No adverse effect on rights or welfare, and

iii. Research cannot "practically be carried out" without the waiver. At the present time there is no specific federal guidance for defining "practically." The DUHS IRB interprets the regulation to mean that C/A can be waived for use of data/specimens from patients who have been seen at DUHS in the past, but who are not expected to be seen at DUHS on a regular and frequent basis in the future. Patients who are expected to return soon should be asked for written C/A at their next visit. OR

(b) For inclusion of data/specimens that will be collected in the future from DUHS patients for other research studies or solely for clinical or QI purposes, provided that the federal criteria for waiver of consent and authorization have been met, as well as all of the requirements of the *Policy on IRB Determination of Research Not Involving Human Subjects for Research Using Coded Specimens or Coded Identifiable Private Information.* DSRs cannot be exempted under this referenced policy because the policy applies only to specific research studies that use coded data or specimens. OR

(c) For inclusion of data/specimens that will be collected in the future, provided that the federal criteria for waiver of consent and authorization have been met, and also that both of the following conditions have been satisfied:

i. The data/specimens were collected for purposes other than submission to this DSR, e.g., solely for clinical purposes, QI, or prior IRB-approved research, and

ii. The data/specimens are entered into the DSR without any identifiable private data or information, i.e., none of the 18 HIPAA identifiers [45 CFR 164.514(b)(2)(i)] and no codes or links of any sort maintained either by the submitter or by the DSR that would permit access to identifiable private information about the individual from whom the data/specimens were obtained.

**CONTACT LISTS FOR FUTURE RESEARCH**

Contact Lists (e.g., names, telephone numbers, email, addresses) are essentially databases that store information for possible future use. When stored for clinical purposes or quality improvement (QI), IRB approval is not required. However, when containing identifiable private information stored for research purposes, the Contact List database must be approved by the IRB and satisfy the requirements of the Common Rule and, if applicable, HIPAA.

Investigators have the following three options for establishing Contact Lists:

1. **As part of the main study:** In the main study C/A form obtain the subjects’ consent and authorization to store their contact information only for the duration of the main study. This information may be used only as long as the main study remains open and approved by the IRB.

2. **As a separate database:** Obtain the subjects’ C/A to store their contact information in a separate DSR for possible use in future research. If the DSR is maintained at DUHS, a separate IRB DSR protocol and C/A form are required. If the main study closes and the DSR is maintained at DUHS, the contact information in the separate DSR may continue to be used as long as the DSR protocol remains open and approved by the IRB. If the DSR is maintained outside of DUHS, the main study compound C/A form must describe where the DSR will be maintained and include Opt In/Out signature lines for storage of identifiable private information in the external DSR.

3. **As a database with no identifiable private information, such as no PHI:** Investigators may establish and maintain a Contact List of subjects without obtaining or maintaining IRB approval when the information associated with the list does not contain identifiable private information, such as PHI. Such identifiable private information includes the diagnoses, disease states or medical conditions by which individuals on the Contact List are categorized. While such a contact database without private information may exist for
CONVERSION OF A CLINICAL DSR TO A RESEARCH DSR

Data/specimens that have been stored in a DSR solely for clinical or QI purposes in the past can be moved into a research DSR under an IRB waiver of C/A. Ordinarily, this would occur only once per research use because care must be taken to ensure that the continued collection of such data/specimens occurs solely for non-research purposes.

Some currently approved IRB protocols include not only a specific research study, but also a DSR to store data/specimens for possible future research studies. When the DSR is maintained at DUHS, the protocol should be split into a separate protocol for the specific study and a separate protocol for the DSR, with separate C/A forms. This is primarily a paperwork activity to reword the protocol summaries and C/A forms to meet the requirements outlined above. Subjects who are currently enrolled under the combined protocol usually will not have to be re-consented because they have already given C/A for both the specific study and the DSR. Future subjects in the research study must sign separate C/A forms for the specific study and the DSR.

ATTACHMENT 1: Elements of Consent and Authorization

COMMON RULE ELEMENTS OF CONSENT
[Excerpts quoted from 45 CFR 46.116(a) and (b)]

“(1) …statement that the study involves research…purposes of the research…expected duration…procedures to be followed…and identification of any procedures which are experimental,
(2) …risks or discomforts,
(3) …benefits,
(4) …alternative procedures or…treatment, [Not applicable for minimum risk studies.]
(5) …extent to which…confidentiality of records…will be maintained,
(6) …compensation…and…available medical treatments if injury occurs, [Not applicable for minimum risk studies.]
(7) …whom to contact…for questions about the research and research subject’ rights,
(8) …participation is voluntary…refusal…will involve no penalty…and the subject may discontinue participation at any time.

When appropriate, one or more of the following elements of information shall also be provided to each subject:
(1) …statement that the particular …procedure may involve risks to the subject …which are currently unforeseeable;
(2) …circumstances under which the subject's participation may be terminated by the investigator without …the subject's consent;
(3) …additional costs …;
(4) …consequences of a subject's decision to withdraw …;
(5) …statement that significant new findings …will be provided to the subject; and
(6) …approximate number of subjects involved in the study.”

PRIVACY RULE (HIPAA) CORE ELEMENTS AND REQUIRED STATEMENTS FOR USE OR DISCLOSURE OF PHI [Excerpts quoted from 45 CFR 164.508(c)]

“(a) Core Elements…
i …information to be used or disclosed,
ii …identification of the person(s)…authorized to make the requested use or disclosure,
iii …identification of the person(s)…to whom [DUHS] may make the requested use or disclosure,
iv …each purpose of the requested use or disclosure,
v …an expiration date…of the use or disclosure,
vi …signature of the individual and date.
(b) Required Statements…
i …individual's right to revoke the authorization in writing,
ii …condition treatment…on the authorization,
iii …potential for information…to be subject to redisclosure…and no longer protected.
(c) Plain Language Requirement…”
ATTACHMENT 2: Requirements for Waiver of Consent and Authorization

COMMON RULE WAIVER OF CONSENT [45 CFR 46.116(d)]

“An IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth in this section, or waive the requirements to obtain informed consent provided the IRB finds and documents that:

1. The research involves no more than minimal risk to the subjects;
2. The waiver or alteration will not adversely affect the rights and welfare of the subjects;
3. The research could not practically be carried out without the waiver or alteration; and
4. Whenever appropriate, the subjects will be provided with additional pertinent information after participation.”

PRIVACY RULE (HIPAA) WAIVER OF AUTHORIZATION [45 CFR 164.512(i)(2)(ii)]

“Waiver criteria. A statement that the IRB or privacy board has determined that the alteration or waiver, in whole or in part, of authorization satisfies the following criteria:

A. The use or disclosure of protected health information involves no more than a minimal risk to the privacy of individuals, based on, at least, the presence of the following elements:
   (1) An adequate plan to protect the identifiers from improper use and disclosure;
   (2) An adequate plan to destroy the identifiers at the earliest opportunity consistent with conduct of the research, unless there is a health or research justification for retaining the identifiers or such retention is otherwise required by law; and
   (3) Adequate written assurances that the protected health information will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research study, or for other research for which the use of disclosure of protected health information would be permitted by this subpart;

B. The research could not practically be conducted without the waiver or alteration; and

C. The research could not practically be conducted without access to and use of the protected health information.”

A "Request for Waiver or Alteration of Consent and HIPAA Authorization" form may be found on the IRB website.

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