

# Health Law

## Pharmaceuticals, Medical Devices & Biologics

### Clinical Trials

#### Breach of Privacy Risks for Clinical Research Sponsors

*Contributed by Jill E. Anderson, Moses & Singer LLP*

Although sponsors generally are not considered “covered entities” under the Health Insurance Portability and Accountability Act of 1996 (HIPAA), they are increasingly exposed to privacy liability risks through their use of clinical research data or tissue samples obtained from clinical research subjects as part of the trial.<sup>1</sup> These risks result primarily from the sponsor’s review and approval of the content of the informed consent form (ICF) and from the sponsor’s representations and warranties in the clinical research agreement with an institution.<sup>2</sup> However, there are several steps a sponsor should take to minimize its liability when receiving tissue samples or associated study subject data resulting from clinical research.

In addition to increasing our understanding about the effectiveness of new interventions, clinical research provides researchers with the opportunity to perform additional research. These additional research studies may use data from a databank or samples from a tissue bank for future clinical research uses.<sup>3</sup> For example, the molecular characteristics of tissue samples might be analyzed after the clinical trial is completed to determine if there is a

relationship between the amount of a specific protein in the study subjects’ tissue and how that study’s subjects responded to the study drug they received. Information obtained from these correlative studies could lead to more accurate predictions about how individual patients will respond to certain treatments, improved ways of detecting the disease earlier, new methods of identifying people who have an increased risk of the disease, and new approaches to prevent the disease.<sup>4</sup>

#### Privacy Rule v. Common Rule

The U.S. Department of Health and Human Services (HHS) has interpreted<sup>5</sup> the Privacy Rule under HIPAA to prohibit blanket or broad research Authorizations<sup>6</sup> for “nonspecific research” or “future, unspecified projects” and requires that Authorizations be study-specific for purposes of complying with the Privacy Rule’s requirement that an authorization must include a description of each purpose of the requested use or disclosure.<sup>7</sup> This means that the description cannot be so broad as to encompass future unspecified clinical research. HHS has stated that this interpretation addresses its concern that study subjects lack necessary information about the future research to make an informed decision about whether to participate in such future research. In other words, under HIPAA, researchers and institutions cannot ask study subjects to agree to include their information or tissue samples in databanks or tissue banks that would be used to support future, unspecified research.

The Privacy Rule allows study subject data to be disclosed for future research purposes if the researcher obtains a separate Authorization, an IRB-approved Waiver of Authorization, or uses a limited data set.<sup>8</sup> In addition, institutions and researchers may de-identify PHI according to standards set forth in the Privacy Rule.<sup>9</sup>

The federal Common Rule, however, does permit informed consent for future research activities, so long as the future uses are described in sufficient detail to allow an informed consent.

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<sup>10</sup> As a result of HHS's current interpretation, institutions that agree with HHS's interpretation of the Privacy Rule often limit a sponsor's right to use and disclose study subject data so that it is consistent with the institution's obligations under both the Common Rule and the Privacy Rule. In general, the effect is that institutions often contractually limit a sponsor's use of study subject data to purposes related to the clinical research and compliance with applicable law, thereby prohibiting the sponsor from using tissue samples or associated study subject data for future, unspecified research.

HHS issued a much anticipated Notice of Proposed Rulemaking (NPRM) in July, 2010 soliciting comments on modifications to the Privacy Rule, including whether to modify its existing interpretations of the Privacy Rule that require an Authorization for the use or disclosure of protected health information (PHI) for clinical research to be study-specific.<sup>11</sup> HHS stated that part of its rationale for considering revising its interpretation of this requirement is the fact that, in accordance with the Common Rule, many institutional review boards (IRBs) approve informed consents that allow future research on study subjects' PHI or tissue samples. In addition, HHS noted that the Institute of Medicine and the Secretary's Advisory Committee on Human Research Protections have "have urged the department to allow the HIPAA authorization to permit future research use and disclosure of protected health information or, at a minimum, for the department to modify its interpretation to allow the authorization to encompass certain future use and disclosure of protected health information for research, provided certain parameters are met." As a result, there is conflict if the Authorization does not allow future research. Revising the Privacy Rule to allow an Authorization for future use and disclosure of study subjects' PHI would obviously create consistency between the Privacy Rule and Common Rule. Since the NPRM comment period closed on September 13, 2010, HHS will review the comments received and publish a final rule. There is no formal time frame for the publication of the final rule. The NPRM includes the stated assumption that the final rule will be effective 30 days after its publication, with compliance generally expected 180 days after the rule's finalization.<sup>12</sup>

### The Havasupai Case

Several court cases demonstrate the potential liabilities researchers and institutions may face for conducting future research on tissue samples where the Authorization failed to specifically state such research purposes. While these cases did not involve sponsors' use of tissue samples or data, liability could be imputed to sponsors in similar situations where the sponsor is responsible for developing and approving the content of the ICF. In one well-publicized case, members of the Havasupai tribe donated blood samples to researchers at Arizona State University (ASU) for research related to the tribe's diabetes epidemic.<sup>13</sup> The researchers then used the blood samples and associated data for additional research. In addition to research on schizophrenia and inbreeding, the researchers used the samples and data to demonstrate that the tribe's ancestors crossed the frozen

Bering Straits into North America, a concept contradictory to the Havasupai belief that the retreat of waters from a global flood carved the Grand Canyon, and that the Grand Canyon is the birthplace of the human race. The Havasupai donors contend they would not have consented to the use of their samples for the additional research. The parties entered into a settlement agreement, which included a requirement that ASU pay \$700,000 to members of the Havasupai tribe, return all blood samples in its possession, and return documents such as lab books and genealogy materials containing research derived from the blood samples.

The Havasupai case brings to light the importance of respecting personal, religious, and culturally held beliefs and traditions in conducting research involving tissue samples. Sponsors should consider the religious, cultural and personal beliefs and traditions of the study subjects and the study subjects' community when planning future research that will include collection of tissue samples. In addition, the ICF should state whether research participation could benefit or potentially negatively impact study subjects' families and communities. For example, the ICF should indicate if there is a risk of stigmatization and discrimination based on research results.

### Recommendations for Sponsors

There are several steps sponsors can take to keep study subjects appropriately informed, including making sure the ICF describes what types of data will be collected and how the data will be used and stored. Where applicable, the ICF should state whether identifiable or coded information will be maintained in the tissue bank or databank and if research results will be linked to other data about the human research participant, such as clinical data obtained from anatomic pathology and clinical pathology laboratory information systems and cancer registries. If longitudinal data will be collected by accessing the participant's medical records, the ICF should clearly state so.<sup>14</sup> The ICF also should describe whether the tissue samples and/or the data associated with or derived from tissue samples will be shared with other researchers and, if so, the oversight mechanisms for such sharing.<sup>15</sup>

The ICF may include an option that allows study subjects to select whether they would be willing to be re-contacted about the use of their tissue samples and/or data for future research studies. If possible, the ICF should specify how the study subjects' contributed tissue samples will be used and provide study subjects with greater specificity about secondary research.<sup>16</sup> If the purpose of the tissue bank is to provide tissue samples for a broad range of research, generalizing the type of research that will be conducted may be burdensome and uninformative to the research subjects.

Examples of language related to specific future research in an Authorization include:<sup>17</sup>

- *My tissue may be kept for use in research to learn about, prevent, or treat cancer.*

•My tissue may be kept for use in secondary research to learn about, prevent, or treat other health problems; e.g., diabetes, Alzheimer's disease, or heart disease.

•My tissue may be associated with my medical record and history.

•I am willing to be contacted about future research studies.

Sponsors should work together with institutions and researchers to develop the ICF to ensure all parties have the same understanding about how tissue samples and associated data will be used. The individuals responsible for negotiating the clinical research agreement and consent on behalf of the sponsor should freely communicate with researchers at both the sponsor and institution to ensure all parties are on the same page regarding use of the data. Contractually, the sponsor and institution should agree on how the data may be used and include in the clinical research agreement specific terms regarding such use. Sponsors should be particularly cautious about agreeing to language that limits use of tissue samples and associated data or specifies that the sponsor will comply with HIPAA. Sponsors are well advised to work with their legal counsel to develop alternative language.

Study subjects deciding whether to contribute tissue samples for research should understand how their tissue may be used in the future, including any potential anonymous use. The ICF should disclose whether tissue samples may, at some point, be anonymized and subsequently used for secondary research purposes beyond those described in the original ICF.

The benefit of stored tissue samples and associated data for future testing is invaluable. As new research questions arise, it cannot be predicted which tests will need to be conducted on the stored data or tissue samples in the future. However, sponsors, researchers, and institutions will need to work closely together to determine all possible future research that may be conducted on tissue samples or associated data. An ICF should specify the types of testing that may be performed, such as testing for infectious diseases, testing for biomarkers of disease, and performing genetic studies, in order to provide a guide to study subjects of the types of research issues that their tissue samples and associated data may help to address.

*Jill E. Anderson is Counsel to Moses & Singer LLP's Healthcare practice, where she counsels a variety of entities in the healthcare industry, including sponsors, on issues relevant to clinical research. For more information on this topic, please contact Jill at janderson@mosessinger.com or 212-554-7836. To learn more about Moses & Singer, please visit [www.mosessinger.com](http://www.mosessinger.com).*

<sup>1</sup> For purposes of this article, the term "sponsor" means any entity which coordinates or funds clinical research and receives data resulting from the research.

<sup>2</sup> For purposes of this article the term "institution" refers to an academic medical center, research institute or hospital which conducts clinical research.

<sup>3</sup> National Cancer Institute, *Cancer Clinical Trials*, <http://www.cancer.gov/cancer-topics/factsheet/information/clinical-trials>.

<sup>4</sup> *Id.*

<sup>5</sup> See *Standards for Privacy of Individually Identifiable Health Information*, 67 Fed. Reg. 53182, 53226 (Aug. 14, 2002); National Institutes of Health, *Protecting Personal Health Information in Research: Understanding the HIPAA Privacy Rule*, published Apr. 14, 2003, revised Sept. 25, 2003, [http://privacyruleandresearch.nih.gov/pdf/HIPAA\\_Booklet\\_4-14-2003.pdf](http://privacyruleandresearch.nih.gov/pdf/HIPAA_Booklet_4-14-2003.pdf).

<sup>6</sup> An Authorization under the Privacy Rule is an individual's signed permission to allow a covered entity to use or disclose the individual's protected health information that is described in the Authorization for the purpose(s) and to the recipient(s) stated in the Authorization. 45 C.F.R. § 164.508(c). In contrast, an informed consent document is an individual's agreement to participate in the research study and includes a description of the study, anticipated risks and/or benefits, and how the confidentiality of records will be protected, among other things. National Institutes of Health, *HIPAA Authorization for Research* (2004), <http://privacyruleandresearch.nih.gov/pdf/authorization.pdf>. An Authorization can be combined with an informed consent document or other permission to participate in research. *Id.* If a covered entity obtains or receives a valid Authorization for its use or disclosure of protected health information for research, it may use or disclose the protected health information for the research, but the use or disclosure must be consistent with the Authorization. *Id.*

<sup>7</sup> 45 C.F.R. § 164.508.

<sup>8</sup> See 45 C.F.R. § 164.512(i)(1)(i).

<sup>9</sup> The Privacy Rule designates two ways through which a covered entity can determine that health information is de-identified. The first is the "Safe Harbor" approach, which permits a covered entity to consider data to be de-identified if it removes 18 types of identifiers, as listed in the Privacy Rule, and has no actual knowledge that the remaining information could be used to identify an individual, either alone or in combination with other information. 45 C.F.R. § 164.514(b)(1). The second way is the statistical approach, which permits covered entities to disclose health information in any form provided that a qualified statistical or scientific expert concludes, through the use of accepted analytic techniques, that the risk the information could be used alone, or in combination with other reasonably available information, to identify the subject is very small. 45 C.F.R. § 164.514(b)(2).

<sup>10</sup> 45 C.F.R. pt. 46.

<sup>11</sup> *Modifications to the HIPAA Privacy, Security, and Enforcement Rules Under the Health Information Technology for Economic and Clinical Health Act*, 75 Fed. Reg. 40868 (July 14, 2010) [hereinafter NPRM].

<sup>12</sup> NPRM.

<sup>13</sup> *Tilousi v. Arizona State University Board of Regents, Havasupai Tribe v. Arizona State University Board of Regents*, 204 P.3d 1063 (9th Cir. 2008); Amy Harmon, *Indian Tribe Wins Fight to Limit Research of Its DNA*, N.Y. Times, Apr. 21, 2010, at A1, available at <http://www.nytimes.com/2010/04/22/us/22dna.html?pagewanted=all>.

<sup>14</sup> "Longitudinal data" comprise outcome measures or responses from the same subjects across multiple time points along with study subject characteristic measures. The data may be used to answer questions regarding the change or progression of the disease over time and/or potential risk factors for the disease. The existing data could be used to identify subgroups with different background characteristics or traits. Li, H.-I., *Longitudinal Data*, in Wiley Encyclopedia of Clinical Trials (2008).

<sup>15</sup> Office of Biorepositories and Biospecimen Research, National Cancer Institute, *National Cancer Institute Best Practices for Biospecimen Resources* (June 2007), [http://biospecimens.cancer.gov/global/pdfs/NCI\\_Best\\_Practices\\_060507.pdf](http://biospecimens.cancer.gov/global/pdfs/NCI_Best_Practices_060507.pdf) [hereinafter Biospecimen Best Practices].

<sup>16</sup> Zhen Lin, Art B. Owen, and Russ B. Altman, *Genomic Research and Human Subject Privacy*, Science, July 9, 2004, at 183.

<sup>17</sup> Biospecimen Best Practices.

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