HIPAA and human tissues

A framework for applying the new privacy regulations

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In April 2003, almost seven years after enactment of the Health Insurance Portability and Accountability Act of 1996, commonly referred to as HIPAA, the U.S. Department of Health and Human Services (HHS) under authority granted by the Act announced the effectiveness of "the first-ever federal privacy standards to protect patients' medical records and other health information provided to health plans, doctors, hospitals and other health care providers" (*1*). Much attention has focused on the application of these regulations in the expansive downriver delta of health care—the provision of care to patients, from pharmacy to surgery. Less discussed has been HIPAA's reach upriver to preclinical development of drugs and beyond to the sources of drug discovery, particularly those sources that derive from human tissues.

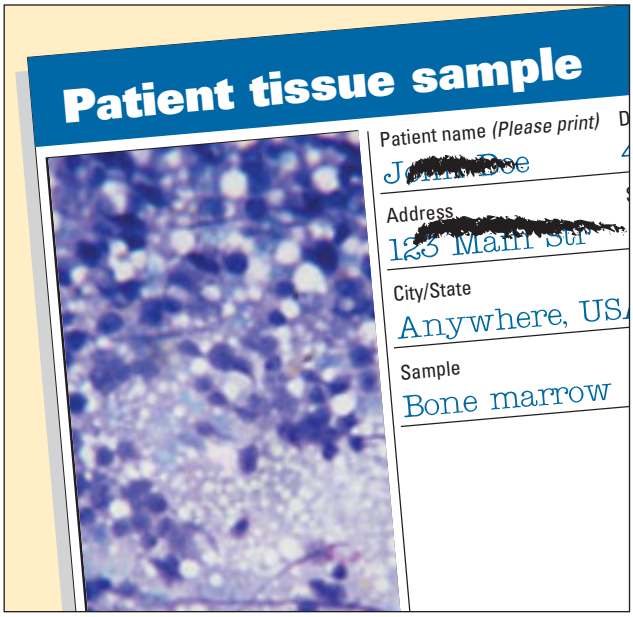
Assays derived from human tissues can potentially foster the generation of safer and more effective lead candidates for clinical trials in less time and at lower cost than would otherwise be the case. The impact of these assays may thus be to help control not only the cost of traversing the path from discovery through preclinical studies, but also the cost of clinical trials (*2*).

HIPAA extends the legally protected penumbra of personal sanctity beyond the patient's body and physical health to the patient's "individually identifiable health information", which includes everything from name and address to biometric identifiers such as fingerprints.

It is clear that human tissues will have a growing role in the hunt for new drugs. The privacy issues that human-tissue-based assay or biomarker development present require these activities to be probed for compliance to the new regulations.

Tissue hypotheticals

In the December 2003 issue of *Modern Drug Discovery*, Cullen Vogelson discussed the general applicability of HIPAA to clinical research and generically defined compliance measures that might be taken by a scientist (*3*). Here, the law is put into the context of real-world situations involving the use of human tissues in biomedical research.



Consider a simple hypothetical: A medical professional extracts tissue from a patient. The tissue is then used to create an assay useful in drug discovery, preclinical and clinical development, and/or medical care.

This simple hypothetical generates a range of questions:

- Does extraction of the tissue sample require an invasive medical procedure?
- Is the sample composed of the patient's tissue or material foreign to the patient, such as a virus, bacterium, or other pathogen?
- Will the assay be used for diagnosing or treating the patient or for uses beyond the patient, such as creating diagnostic tests for other patients or for drug discovery and development?
- Will the assay be used for non-profit-bearing medical research or for commercial gain? If for commercial gain, who will derive such gain? Will the attending physicians or other health care professionals derive any financial gain from development and commercialization of the assay?
- Will the assay be used today or several years in the future, possibly after the patient is long cured or deceased?
- Will the patient's "protected health information" be collected and/or saved as part of the procedure?
- Will the patient's protected health information run with the tissue sample or assay?
- Will any activity related to the tissue sample or the assay implicate any issues of national or municipal security?

The range of potential answers to these questions gives rise to a policy-making framework that can be illustrated with a radar graph. Each axis in the graph represents a policy question, the answer to which can be bipolar or continuous and is plotted on the axis. Most of the axes are important to judging what steps need to be taken in terms of HIPAA requirements. Within this graphic framework, wide polygons with one or more points in the "red" zone out near the tips of the axes indicate a significant interest in regulation by government and/or oversight by Institutional Review Boards (IRBs) or other health care oversight organizations. The opposite is true for narrow polygons with most, if not all, points in the "green" zone near the central origin of the axes. By assessing a set of specific circumstances on each of these axes, one

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should gain insight into what steps will need to be taken to maintain HIPAA compliance.

For example, a specific situation might be the following: The patient is undergoing percutaneous transluminal angioplasty and stenting for treating a closed coronary artery. During the procedure, the surgeon snips and removes a small glob of atherosclerotic plaque. In the hospital lab, a rare human vascular cell is found in the plaque, and the hospital begins to develop a gene expression profiling assay for predicting the degree of heart disease in other patients. The gene expression profile comprising the assay can be used to identify the patient.

The radar graph developed from this scenario is shown in Figure 1A. Given that the expression profile is not clearly among the individual identifiers that HHS has set forth, one could ask whether HHS would consider the profile to be "any other unique identifying number, . . . characteristic, or code," as the law states, and hence identifiable. If so, the next question is whether it is decipherable only to persons with the "code" to identify it and thus may be considered de-identified with respect to all other potential recipients of the profile.

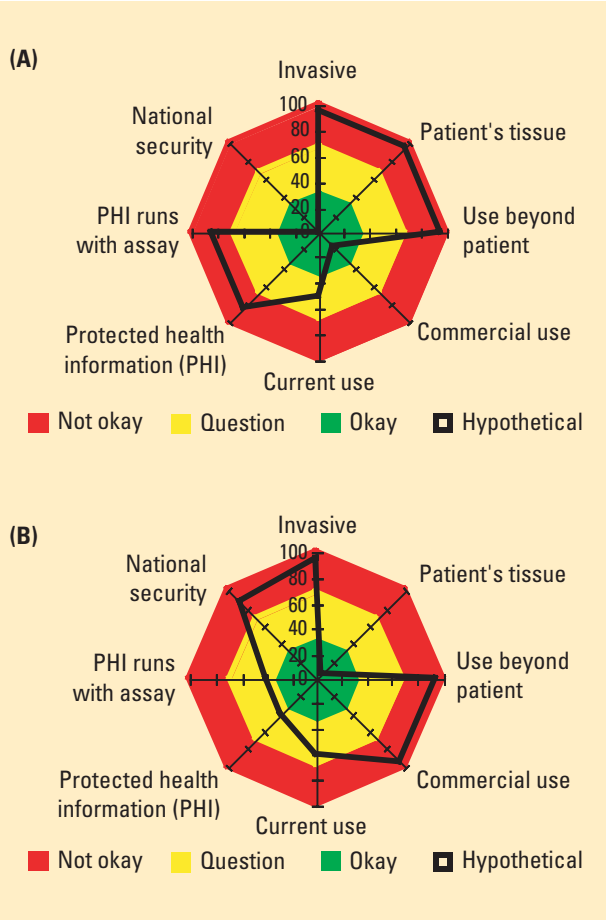

Figure 1. Compliance picture. Radar graphs provide a framework for judging correct HIPAA Privacy Regulations compliance measures. A and B represent two scenarios cited in the text.

Because HHS has not yet provided detailed guidance on these points, particularly as they relate to genomic and genetic data, it appears most appropriate to err on the side of caution and to consider the profile identifiable to all. Thus, where possible, one should obtain the patient's (HIPAA-compliant) authorization to use and disclose the information for research and commercial development purposes. Where that is not possible, researchers may instead pursue a waiver of the authorization requirement from the IRB or privacy board, or they might consider a data use agreement, which heavily restricts the identifiable elements that may be used (see Refs. 3 and 4 for specifics on these options).

Another set of circumstances might be the following: Same as the prior situation, but a previously unknown bacterium is found in the plaque instead of a rare human vascular cell. The hospital lab characterizes the genome of this bacterium and licenses the information to a life sciences company in order to develop a vaccine against the bacterium. The bacterium has unique infectious qualities that pose a public health threat if it is not handled with the highest level of containment. In addition, the pathological impact of the bacterium is limited to a class of patients who share certain genetic markers with the patient in whose tissue sample the bacterium was found. These markers are to be included as part of a diagnostic assay that will be administered before the vaccine is administered.

Here (see Figure 1B), although the sample in question is a bacterium, we arrive at the same basic questions. First, does it identify a person or allow us to identify a person? The answer here appears to be no. Although only persons with certain genetic markets may experience the pathological impact of this bacterium, the bacterium itself does not identify any person.

Conclusion

Compliance with the HIPAA Privacy Regulations for human tissue assay development is complex and provides several alternative compliance mechanisms. The use of these mechanisms will have a dynamic impact on the way human tissue samples and related information are collected, stored, transported, and used and, in turn, on drug discovery and development.

Conversely, the efforts needed to fully exploit human tissue assays for drug development could have a reverse kinetic effect on the regulations. For instance, assays currently suffer from irreproducible test results because of the use of antibodies with differing specificities and binding affinities, as well as variations in sample processing and reference materials (*5*). Overcoming these obstacles may require standardization of materials, implementation of quality control/quality assurance procedures, and, generally, free interaction between expert laboratories, which could conflict with HIPAA.

To ensure the success of these regulations, regulators and drug developers will need to observe and respond to not only the dynamic effects but also the kinetic effects on the regulations of using human tissue samples in drug discovery and development.

References

(1) Protecting the Privacy of Patients' Health Information. Fact Sheet. U.S. Department of Health and Human Services; April 14, 2003; www.hhs.gov/news/facts/privacy.html.
(2) See, for example, Sauter, G.; et al. *Nat. Rev. Drug Discov.* **2003,** *2* (12), 962–972.
(3) Vogelson, C. *Modern Drug Discov.*, Dec 2003, pp 47–48.
(4) Clinical Research and the HIPAA Privacy Rule; February 5, 2004; http://privacyruleandresearch.nih.gov/clin_research.asp.
(5) Sweep, F. C.; et al. *Int. J. Oncol.* **2003,** *23,* 1715–1726.

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