

## The Impact of the Privacy Rule on Cancer Research: Variations in Attitudes and Application of Regulatory Standards

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### A B S T R A C T

#### Purpose

The American Society of Clinical Oncology (ASCO) Cancer Research Committee designed a qualitative research project to assess the attitudes of cancer researchers and compliance officials regarding compliance with the US Privacy Rule and to identify potential strategies for eliminating perceived or real barriers to achieving compliance.

#### Methods

A team of three interviewers asked 27 individuals (13 investigators and 14 compliance officials) from 13 institutions to describe the anticipated approach of their institutions to Privacy Rule compliance in three hypothetical research studies.

#### Results

The interviews revealed that although researchers and compliance officials share the view that patients' cancer diagnoses should enjoy a high level of privacy protection, there are significant tensions between the two groups related to the proper standards for compliance necessary to protect patients. The disagreements are seen most clearly with regard to the appropriate definition of a "future research use" of protected health information in biospecimen and data repositories and the standards for a waiver of authorization for disclosure and use of such data.

#### Conclusion

ASCO believes that disagreements related to compliance and the resulting delays in certain projects and abandonment of others might be eased by additional institutional training programs and consultation on Privacy Rule issues during study design. ASCO also proposes the development of best practices documents to guide 1) creation of data repositories, 2) disclosure and use of data from such repositories, and 3) the design of survivorship and genetics studies.

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### INTRODUCTION

During the regulatory process that produced the US Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule<sup>1</sup> and in the years after its April 2003 implementation, members of American Society of Clinical Oncology (ASCO) voiced concerns about its impact on cancer research. Although they applauded the intent of the Privacy Rule to protect the privacy of individuals' health information, ASCO members have experienced situations in which the regulation has slowed or even blocked certain types of studies that would benefit cancer patients and survivors. Research efforts aimed at understanding the long-term impact of cancer treatment on cancer survivors, investigating familial cancer syndromes, or utilizing data stored in repositories present the most significant Privacy

Rule compliance challenges. In its own outcomes research projects, ASCO has experienced obstacles created by the Privacy Rule. For example, ASCO's National Initiative on Quality Cancer Care was significantly delayed by Privacy Rule requirements that were interpreted to require consent of patients and separate review by the institutional review board (IRB) or privacy board of each participating institution. Cancer researchers are also concerned that, without a careful evaluation of the impact of the Privacy Rule on cancer research and consideration of more effective compliance strategies, cancer research will continue to experience significant adverse effects as a result of the Privacy Rule.

To better understand how the Privacy Rule may affect cancer research, ASCO undertook structured interviews with investigators, compliance officers, IRB members, and other key decision makers

who are involved in the design, conduct, review, and approval of cancer research studies. The intent of the interviews was to ascertain divergences of opinion regarding compliance approaches across institutions and between investigators and compliance officials and to identify effective strategies for achieving compliance with the Privacy Rule.

## METHODS

In the interviews, ASCO obtained qualitative data about compliance officials' and investigators' attitudes regarding the Privacy Rule as well as information about the compliance standards followed at their institutions. ASCO selected the institutions and practices on the basis of the membership and recommendations of its Cancer Research Committee and then supplemented that base of interviewees with additional interviewees to ensure a distribution across research sites, including cancer centers, academic health centers, community or regional hospitals, health plans, and community oncology practices. For the most part, the cancer researchers who were interviewed were members of the ASCO Cancer Research Committee. Compliance officials were in turn identified by the participating researchers. The intent in choosing a diverse set of institutions was to investigate whether size and nature of institution or practice influenced HIPAA compliance philosophy.

Thirteen institutions were represented in the interviews: seven National Cancer Institute (NCI)-designated cancer centers; three additional cancer centers; two private oncology practices, each served by the IRB at a community hospital; and one large health plan. The institutions were geographically distributed as follows: five cancer centers on the east coast, from the Mid-Atlantic to New England; two Midwestern institutions, including a cancer center and a large private practice; two cancer centers in the South; and four institutions on the west coast, including two cancer centers, a health plan, and a private practice.

Twenty-seven interviews, with 13 investigators and 14 compliance officials, were completed. A cancer researcher and a compliance official (including IRB members, compliance staff, and privacy officers) were interviewed at each of 13 institutions/practices except one, for which two interviews with compliance officials were conducted. The investigators who were interviewed were actively engaged in research. Most had initiated studies comparable to the scenarios and therefore had interacted with their IRBs and compliance staff on the compliance issues raised by these scenarios. Although there was some diversity in the job responsibilities of the compliance officials, all were senior officials who could speak from experience about their institutions' approach to the compliance issues presented.

All of the investigator interviews were with a single individual. In several cases, the compliance interviews were with a team of officials. In the case of

team interviews, a single answer to each question was recorded. The interviewees sought concrete and specific answers to questions that accompanied the scenarios and were able to obtain a consensus answer when a team of compliance officials was interviewed. The records of the team interviews in some cases reflect observations or information from more than one interviewee, in addition to the consensus answers to specific questions, if those comments provided useful insights about the scenarios or compliance strategies.

Cancer Research Committee members and other Privacy Rule experts whom ASCO consulted identified several types of research studies that they considered particularly difficult to design or initiate to achieve compliance with the Privacy Rule. Three hypothetical scenarios were constructed to address the following issues: (1) communication with cancer clinical trial participants' family members to request their participation in genetic studies intended to investigate familial cancer syndromes (Table 1); (2) the establishment and utilization of biospecimen and clinical data repositories containing protected health information (PHI) (Table 2); and (3) the identification, consent, and authorization of cancer survivors to participate in long-term survivorship studies (Table 3).

All interviewees were provided the research scenarios in advance of the interviews. The interviews, conducted by a three-person team including ASCO staff, consultant, and counsel elicited information from interviewees about the likely compliance standards for each scenario at each interviewee's institution, as well as general observations regarding the Privacy Rule and its implementation, benefits, and burdens. Each interview began with the specific questions that were provided along with the research scenarios, but interviewees in almost all circumstances chose to offer additional observations that went beyond the specific questions.

## RESULTS

Almost all investigators initially suggested that they had significant disagreements with their compliance officials and IRBs regarding the interpretation of the Privacy Rule and stated that the regulation was stifling certain kinds of cancer research. When the interviewees turned to the specific scenarios, the situation was more complex. Investigators and research compliance officials shared a strong view that they have a special responsibility to protect the confidential health information of cancer patients. This shared sense of responsibility was seen most clearly with regard to the genetics study, where virtually all interviewees described the special steps that investigators and institutions must take to protect the information related to a cancer diagnosis. There was more substantial divergence of opinion about the appropriate standards for creation of biospecimen and clinical data repositories and

**Table 1.** Genetics Study Scenario

Scenario involving contact with family members regarding participation in genetics study: A researcher is studying the *CG64* gene to determine its role in development of pancreatic cancer. Germline mutations in *CG64* are thought to be associated with a higher risk of pancreatic cancer. A trial protocol for treatment of pancreatic cancer specifies that if a trial participant has the *CG64* gene, the researcher will ask the participant if she/he has any blood relatives whom the researcher can contact to inquire about whether they would be willing to participate in a study of familial pancreatic cancer. The researcher will contact the relatives directly to inquire about their interest in enrolling on the study. The researcher will request the trial participant's authorization to share her/his protected health information with these relatives.

### Compliance officers

What HIPAA Privacy Rule requirements would the investigator in this situation be required to meet? Would modifications of the study described above be necessary before this research could proceed with IRB approval?

### Investigators

If you have been involved in a research project that would analyze germline DNA, what requirements related to HIPAA Privacy Rule did your IRB impose? Did these requirements cause any modification of your protocol or research process? If you have not been involved in this type of study, do you believe that the Privacy Rule would permit a study of this sort, in which you would directly contact family members of clinical trial participants to inquire about their interest in participating in a study?

Abbreviations: HIPAA, Health Insurance Portability and Accountability Act; IRB, institutional review board.

**Table 2.** Anticipated Compliance Standards for the Research Situation Scenario

<p>Scenario involving creation and use of biospecimen and clinical data repositories</p> <p>Tissue storage: to build a database of tumor specimens, a medical oncologist researcher would like to provide her surgical colleagues an authorization form to give to their patients to provide permission to store their tumor specimen. The authorization form includes language allowing the specimen to be used for “future cancer research.”</p> <p>Compliance officers</p> <p>How would your IRB respond to a request to utilize an authorization that referred to future research uses? Would investigators wishing to utilize data in this tissue and data bank be required to seek IRB review?</p> <p>Investigators</p> <p>If you have been engaged with research of this sort, what kind of authorization form has your IRB required? Have you found the process of establishing a tissue and data bank to be onerous?</p> <p>Tissue use: a researcher wants to access tumor specimens from a tissue bank that is maintained according to an IRB-approved protocol. A previous researcher obtained authorization from patients for their samples, accompanied by protected health information, to be used for his specific research study. If the new research study focuses on a different research question, would the researcher need to seek additional authorization from the tumor sample contributors?</p> <p>Compliance officers</p> <p>What requirements would be imposed on researchers who wish to use data in the tissue bank?</p> <p>Investigators</p> <p>Have you sought use of tissue samples, accompanied by protected health information, that are deposited in a tissue/data bank that is maintained by one of your colleagues according to an IRB-approved protocol? What review processes have you or other investigators been required to undergo in order to use data in the tissue bank? What HIPAA compliance standards were you required to meet?</p>
<p>Abbreviations: IRB, institutional review board; HIPAA, Health Insurance Portability and Accountability Act.</p>

the disclosure and use of data maintained in such repositories. Compliance officials and IRB members voiced concerns about the protection of large repositories of data; some have responded to this pressure by avoiding the creation of data repositories and others have set rigorous standards—often, a process that requires patient consent and reauthorization—for the use of the data in repositories. Investigators believe that this cautious attitude is slowing, if not blocking, research endeavors that might use such databases.

A discussion of the interview results for each of the three research scenarios follows, and more detailed accounting of responses is available online (Table A1, online only).

**GENETICS STUDY**

The interviewees agreed that the central Privacy Rule issue raised by the scenario involving recruitment of the family members of trial participants for a genetics study was obtaining authorization from the participants in the original study for release of PHI revealing their cancer diagnosis. However, the interviewees gener-

ally agreed that obtaining authorization for disclosure of PHI did not end their responsibility to protect data, even if it largely addressed Privacy Rule issues.

Interviewees said that the second issue was determining how the family member would be contacted. There was a split among interviewees regarding the appropriate person or team to approach the family member who has been identified as a potential participant in a familial cancer study. Of 27 total interviewees, 12 (including nine compliance officials and three investigators) said that their institutions would require that the request to participate in a genetics study be extended by the patient/original trial participant to his/her family member. Eight interviewees—evenly divided between compliance officials and investigators—said their institutions sanctioned contact by the study principal investigator to the family member, but only with a script that had been reviewed and approved by the IRB.

Regardless of which party—the patient/original trial participant or principal investigator—is permitted to approach the family member regarding trial participation, several interviewees said that their

**Table 3.** Survivorship Study Compliance Standards Scenario

<p>Scenario involving request for participation in survivorship study: Investigators wish to contact survivors who were treated for leukemia at their institution to seek their participation in a study to evaluate the late effects of treatment. The research team wishes to review the medical records of these leukemia survivors to determine those most appropriate for study participation and to contact them to request their participation in a long-term follow-up study, which may include completion of patient questionnaires at regular intervals. The data from these questionnaires, along with other protected health information, will be maintained in a database that will exist beyond completion of the follow-up study.</p> <p>Compliance officers</p> <p>If a study of this sort were reviewed by your institution’s IRB, what HIPAA requirements would be imposed on the investigator? If such a protocol were presented to your institution’s IRB, do you anticipate that the investigator could meet the HIPAA requirements without extraordinary effort or burden?</p> <p>Investigators</p> <p>If you have undertaken a chart review of this sort, what HIPAA requirements were you required to meet? Did these requirements cause any modification of your research plans? Have you considered and abandoned any survivorship studies because of your research plans? Have you considered and abandoned any survivorship studies because of your perception that the burden imposed by HIPAA would be unmanageable or would force a significant or unacceptable revision of the study? Would your institution/practice allow access to your records by an unaffiliated researcher? Have you tried to obtain access to records for research from another institution/practice?</p>
<p>Abbreviations: IRB, institutional review board; HIPAA, Health Insurance Portability and Accountability Act.</p>

institutions would take steps to avoid coercion to participate in the trial. One of those protections is a consent and authorization form including opt-out provisions that gives the potential trial participant several opportunities to decline to participate.

Although investigators agree with compliance officers and IRBs regarding the sensitive nature of genetics studies that involve family members, they express reservations that IRBs make reviews overly cumbersome and often insist on an opt-out authorization form that has the effect of discouraging study participation. Researchers also note that IRBs can devote significant time—often stretching over several IRB meetings and a period of weeks or even months—reviewing the scripts that will be used to contact family members regarding trial participation. A number of IRB officials and compliance officers defended the caution that they take in managing the contact with the family member of a trial participant, even if it results in consideration at more than one IRB meeting and a delay in the initiation of a study.

### CREATION AND UTILIZATION OF DATABASES

The creation of biospecimen and clinical databanks/databases and the disclosure of PHI from those repositories elicited the greatest level of disagreement between investigators and compliance officials. Investigators generally said that their compliance officials impose consent and authorization requirements that discourage participation in tissue banks and that those compliance officials unreasonably insist on re-consent and reauthorization for disclosure of PHI from repositories. The interview questions focused on Privacy Rule authorization requirements, but these questions were answered with reference to combined consent and authorization forms. Although institutions generally include the elements of authorization in a combined consent and authorization form, they often take special steps to ensure that authorization elements receive adequate attention from research participants and therefore provide them appropriate notice about future uses. A number of interviewees indicate that their institutions reject the use of waiver of authorization, and those institutions as a result insist on “reconsent and reauthorization” for use of data in repositories.

Although there was no single preferred approach to consent and authorization for depositing data in a repository, nine interviewees (six compliance officials and three investigators—identified strategies that were intended to give individuals significant and specific notice regarding the possible future use of their data. Three interviewees (one investigator and two compliance officials) said that their institutions require that the authorization for deposit of data in a tissue bank be separate from the consent form, to ensure that the patient does not overlook or misunderstand it. Four interviewees (two compliance officials and two investigators) said their institutions use authorization forms that have opt-out features to protect patients from feeling pressure to deposit data. Two compliance officials described authorization forms that have language strictly limiting possible future uses of data in a repository. In contrast, two compliance officials said that the forms used at their institutions simply reference the potential for “future research use” of the data in a database, which is intended to facilitate future use without reconsent or reauthorization.

The core concern for both investigators and compliance officials is providing individuals appropriate notice regarding the possible future uses of the data they agree to deposit in a database. However, investigators say that their compliance officials are so concerned about abuses of databases that they unreasonably limit any potential future uses at the time a database is created by using restrictive language regarding future uses or they discourage individuals from depositing their data in a repository by requiring authorization forms that include opt-out check boxes.

In those situations where data repositories are created, investigators often complain that their institutions render the repositories meaningless by requiring reconsent and reauthorization for disclosure and use of data, when waiver of authorization might be appropriate.

Seven interviewees (five compliance officials and two investigators) said their institutions always or almost always require reconsent when a researcher seeks access to data in a repository. Three compliance officials said that they always or almost always release only de-identified information from their databases. Three compliance officials said that a waiver of authorization is likely or possible. Four interviewees (two investigators and two compliance officials) said that the decision of the IRB regarding disclosure of PHI is governed by the language of the original authorization form and whether it gave the patient adequate notice regarding the potential for future research uses of their PHI.

Although most, including investigators and compliance officials, were aware of the federal guidance document on data repositories, they indicated that they did not find the document useful. The general complaint was that it was too “legalistic” and not useful because of the lack of examples or scenarios.

IRBs and compliance officers share the view that individuals must be given adequate notice regarding the possible future uses of PHI that is stored in a repository. The nature of notice given to research participants with regard to the future use of their PHI is weighed heavily by IRBs as they consider whether a future research project using information in a database or biorepository may be conducted under a waiver of authorization or whether reconsent/reauthorization may be necessary.

Investigators and compliance officials have substantial differences of opinion regarding what constitutes adequate notice. Some believe that sufficient notice of future uses requires significant specificity about the possible future research use, whereas others hold the view that informing the patient that his or her data might be used for a “future research use” constitutes adequate notice. Investigators take the view that they cannot describe all possible future research uses with specificity at the time of creation of a database and that “future research use” should be considered sufficient notice to a research participant. Moreover, investigators advance the view that notice about future uses that is not specific is nonetheless generally acceptable to research participants.

### SURVIVORSHIP STUDY

Most interviewees identified two issues that would be raised by the survivorship study. First is the matter of how the IRB would evaluate

the proposed records review to identify potential participants in the survivorship study.

Eight respondents (seven compliance officials and one investigator) said that the records review would be allowed to move forward without IRB review until it became a recruitment effort. At that point, IRB review would be necessary. Six (three investigators and three compliance officials) said that compliance personnel at their institutions evaluate all proposed records reviews to determine if they are reviews preparatory to research or recruitment, but they do not necessarily refer all studies to the IRB. Six investigators said that their institutions refuse to make a determination that a records review meets the Privacy Rule standards for review preparatory to research and insist on IRB review in all cases.

Almost half of interviewees, representing roughly half of the institutions and evenly divided between investigators and compliance officials, say that they now routinely include consent and authorization for participation in a survivorship study as part of a treatment trial consent and authorization. Even if the survivorship study is not incorporated in the treatment trial, by obtaining authorization and consent in advance the investigator and institution will know the identity of possible participants in a future survivorship study.

Whether the possible participants are identified by records review or by the investigator, institutions then confront a second challenge related to the appropriate means for contacting those possible participants. The analysis by the interviewees was similar to the analysis of the genetics study.

Three interviewees (two investigators and one compliance official) said that their institutions use research coordinators or some other “honest broker” to talk to the possible survivorship study participant to avoid any possibility of coercion that would exist if the treating physician requested participation. Two compliance officials said they send written invitations, including opt-out provisions, to possible survivorship study enrollees, with a goal of avoiding coercion to participate. Four interviewees (two investigators and two compliance officials) said that the contact with survivors should be undertaken by the treating physician. Several interviewees—both compliance officials and investigators—said they are eliminating the need for such follow-up contact by incorporating consent and authorization for participation in survivorship studies as elements of the consent process for treatment trials.

The obstacles that were identified by investigators and compliance officials in developing an appropriate authorization form for database development were also encountered in survivorship studies. There is a range of opinion among compliance officials regarding the requisite specificity of the “future research use” language in an authorization form, whereas investigators expressed a strong preference for more general language in the authorization form so they will have maximum flexibility for use of the data from survivors.

Those investigators engaged in survivorship research offered unprompted observations about the overall consent process. They encouraged consideration of Privacy Rule authorization burdens as part of ongoing reviews of the consent process that are focused not only on Privacy Rule authorization requirements but all elements of the consent process and that are intended to minimize the overall burden of the consent process on survivors and their families.

## LIMITATIONS OF THE STUDY

Three issues related to the design of this study may affect the ability to generalize its findings. These design issues are: (1) the limited number of institutions (13) represented by 27 data sets from 27 interviews; (2) the fact that the compliance officials who were interviewed include IRB members as well as compliance staff at the institutions, officials who may have slightly different perspectives on compliance; and (3) convenience sampling of institutions conducting cancer research studies.

Despite these limitations, data from the interviews were strong and revealed consistent themes. Although participants were a convenience sample of institutions represented in large part by members of the ASCO Cancer Research Committee, interviewees were from the full spectrum of practice settings where ASCO members engage in cancer research, with the exception of intramural research conducted by the federal government. There were obvious differences in approach between investigators and compliance officials, but differences seemed to be tempered by implementation of training programs and well-established means of routine communication about Privacy Rule matters. The diversity of job titles among the interviewees described as “compliance officials” was not reflected in their responses; instead, the interviews revealed a consistency of approach among compliance staff and IRB members.

## DISCUSSION AND RECOMMENDATIONS

The impetus for this study was the perception among members of the ASCO Cancer Research Committee that the differences of interpretation among institutions and the divisions between compliance officials and investigators on matters of HIPAA Privacy Rule compliance were substantial and impose a negative impact on cancer research. Identifying and describing these differences might lead to strategies to bridge this gulf and streamline Privacy Rule compliance strategies. The committee members also believed that potential reforms and revisions of the Privacy Rule, additional federal guidance, or identification of successful approaches might be identified through this project. Although the anticipated differences of opinion were confirmed, the interviews also revealed a strongly shared view that the protected health information of the cancer survivor and the survivor’s family members deserves special protection. During the process of defining and designing the interview scenarios and questions, ASCO Cancer Research Committee members suggested that studies were abandoned as a result of HIPAA burdens. The interviews, in contrast, suggested that delays—as opposed to abandonment—were more likely and occurred both in studies initiated at the individual institution and in multi-institutional studies. The circumstance in which a project might be described as abandoned was the creation of databases. Researchers at a limited number of institutions suggested that they discontinued efforts to create databases in the face of HIPAA obstacles. The key to enhancing Privacy Rule compliance for cancer studies may relate to finding ways to build from the widely shared view about the special sensitivity of data about cancer diagnosis and treatment and the desire to facilitate research to identify new detection, treatment, and supportive care methods.

The interviewees did confirm the general observation that there are differences of philosophy and analysis of compliance standards

between investigators and compliance officials. Investigators believe that the approach of their IRBs and compliance officials results in delay of some studies while IRBs attempt to perfect consent and authorization forms, develop scripts for discussions with patients or family members regarding a cancer diagnosis, and review letters that may be sent to potential study participants. This is particularly frustrating to investigators involved in multicenter, federally-sponsored trials that have already undergone multiple levels of review. Moreover, investigators convey frustration that their compliance officials are significantly concerned about warning individuals of potential uses of their protected health information—whether sharing a diagnosis with a family member, permitting data to be used in future research projects, or storing and analyzing survivorship data—and that as a result they unreasonably frighten individuals and unintentionally persuade them not to share data or participate in a trial. Although investigators concede that these efforts are stimulated by a concern about protection of highly sensitive information, they note that compliance officials have not achieved the right balance between individual patient protection and future patient benefit that might be realized through completion of clinical studies.

Because cancer patients and potential trial subjects were not among those interviewed, no reliable conclusions can be offered about the level of concern among patients about the risk of inappropriate disclosure of their protected health information and the impact of that concern on their willingness to participate in cancer research studies such as those described in the scenarios. This is an area for future study.

The interviews confirmed that officials at some institutions harbor a strong concern about the risks associated with the storage of protected health information in databases or repositories. Thus, these officials will not allow release of data from repositories unless it can be de-identified or they can obtain a specific consent for the disclosure and use of data in a repository. These officials reject the possibility that the original consent and authorization for deposit of data might provide appropriate notice to the patient about future research uses of data and that an IRB might grant a waiver of authorization after evaluating the consent and authorization as well as the risks of inappropriate disclosure and use. This compliance approach creates significant tension between compliance officials and investigators, as investigators believe it may be an over-interpretation of Privacy Rule requirements that effectively blocks access to useful research data and that is at odds with the wishes of patients who want to see their data used for research, if used appropriately.

Several institutions can be distinguished for the relative ease and speed of review of the types of scenarios presented and for the limited disagreements about these difficult research situations among investigators, IRB officials, and other compliance officials. A key to the success of these institutions seems to be clear communication about compliance standards, accompanied by the establishment of venues for resolving differences of opinion about the HIPAA Privacy Rule. Three institutions (an academic health center, a community hospital, and a community practice) have routine Privacy Rule training sessions with required attendance. All reported that these sessions are important not solely or even primarily for the formal training that is provided but for the opportunity for a diverse group to address HIPAA issues outside an IRB meeting. Other institutions report training on a more intermittent basis. It seems that the regularity of opportunities

for interactions is important because they ensure that new issues can be discussed and addressed without significant delay.

Among the institutions interviewed that impose onerous requirements for the release of data from a repository for future research uses are a cancer center and a community hospital. Despite setting a rigorous standard that requires re-consent and reauthorization for the disclosure and use of data in repositories, these institutions have not in fact blocked release and use of data from repositories. Instead, they have fairly strong history of being able to obtain re-consent and reauthorization, an achievement related to collaboration between the compliance teams and investigators. Although most investigators would not endorse a standard of re-consent and reauthorization for future research use of database information, the institutions described above have demonstrated their ability to foster research, even while imposing a rigorous compliance standard. It seems that communication and collaboration may be the keys to foster research, even where the compliance standard is a stringent one that investigators may oppose philosophically.

The creation of data repositories and the disclosure and utilization of data from those repositories created substantial conflict between investigators and compliance officials. Interviewees veered significantly from the simple questions posed to them and offered advice about database creation and use. Their recommendations point toward the creation of a document, developed and endorsed by cancer research organizations, individual investigators, and compliance officials, that uses a descriptive case-based methodology. Some interviewees noted that the National Cancer Institute informs investigators of general Privacy Rule requirements in a June 2007 document entitled *National Cancer Institute Best Practices for Biospecimen Resources*. However, interviewees did not indicate that they rely significantly on this document for guidance regarding Privacy Rule compliance. Another guidance document from the Department of Health and Human Services (HHS), *Research Repositories, Databases, and the HIPAA Privacy Rule*, was also cited by some interviewees as a resource for compliance. Interviewees expressed an interest in having access to case-based guidance documents that would supplement the existing documents developed by HHS.<sup>2,3</sup> The interviewees suggested that a situation-specific document describing the successes of other institutions in the area of database creation and use would be superior to another federal guidance document.

There was significant agreement about the challenges associated with contacting family members to invite them to participate in a familial cancer study, but there were nonetheless substantial delays created by repetitive review of phone call scripts, letters, and consent and authorization forms. This is thus another area where a descriptive guidance document, including sample forms, letters, scripts, and standard procedures that have been used successfully in previous research efforts, would be useful.

The interviewees not only identified case-based documents and educational programs that would be useful to them and their colleagues but also signaled an interest in researchers and compliance officials collaborating on these initiatives. Interviewees also cited two other documents—*The Privacy Rule and Public Health* and *The Privacy Rule and Research*—as generally useful while at the same time recommending the development of additional documents that would be specific to cancer research and that would discuss specific cases.<sup>4</sup> ASCO can partner with other organizations and professional societies to bring representatives of these stakeholder groups together to

develop these tools to enable institutions to engage in the following activities.

One, those institutions that update investigators regularly through Privacy Rule educational efforts report fewer compliance issues and less confusion around these matters, and their model might productively be replicated.

Two, those institutions that encourage discussion between compliance officials and investigators during trial design report that Privacy Rule issues can be anticipated and addressed before IRB review, a practice that might be encouraged at other institutions.

Three, because interviewees generally report that they do not consult the HHS guidance document related to creation and use of data repositories, efforts to develop new, case-based resources and cancer research-specific documents should be considered.

Finally, a guidance document on studies related to familial cancer syndromes would be particularly useful if it is descriptive and developed by investigators and compliance officials who can capitalize on their significant experience in reviewing and approving such studies.

The results from this study also point to a larger need for cancer research stakeholders to continue to participate in ongoing efforts to review and improve the research consent process as a way to explain the burden that can be imposed by the HIPAA Privacy Rule authori-

zation process and the problems that this can cause in hampering research that would benefit our future patients and their families.

#### AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The author(s) indicated no potential conflicts of interest.

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## Appendix

Table A1. Study Scenario Summaries

## Genetics study scenario

## Summary of interviews on familial cancer syndrome scenario

- Require that trial participant contact family member. Twelve interviewees—nine compliance officials or IRB members and three investigators—reported that the request to participate in a genetics study must be offered by the patient/original trial participant.
- Allow investigator contact, according to script. Eight interviewees—four investigators and four compliance officials—said the principal investigator may contact the potential genetics trial participant if done according to IRB-approved script.
- Permit contact by genetics counselor only. Two investigators stated that a genetics counselor would be responsible for contact.
- Other responses. Others said contact could be made in collaboration between treating physician and investigator or that the IRB would analyze on case-by-case basis.
- No experience with this sort of study. Three investigators had no experience with these studies.

## Protocol for requesting assistance of patient/trial participants

The 12 respondents (nine compliance officials or IRB members and three investigators) who said contact by the original patient/trial participant was preferred also agreed substantially about the sequential protocol for engaging the participant: (1) the treating physician would contact the patient directly to ask his or her involvement in contacting a family member, or (2) a letter would be sent to the patient with a request that he or she contact the family member. Some interviewees said that in extraordinary circumstances their IRB would allow the investigator of the follow-on study to contact the patient to ask him or her to contact the family member.

## Opportunities to opt out of study

The 12 interviewees (nine compliance officials or IRB members and three investigators) who said that contact would be required by the original trial participant also said that their institutions require that consent and authorization forms be drafted in such a manner to provide individuals multiple opportunities to opt out of study participation.

## Standards for direct contact between institutions and family members

Interviewees (eight—four investigators and four compliance officials) who said that institutions permitting direct contact by the investigator also specifically set the standards for contact, which might include (1) a phone contact from the research team to the family member, according to a script reviewed and approved by the IRB; (2) a phone or letter contact to the family member, only if made by a member of the team that cared for the initial trial participant; or (3) an approach that includes several opportunities for the family member to opt-out of study participation.

## Standards for obtaining authorization to share PHI

Interviewees said that they would not necessarily accept inclusion of the authorization to share PHI with a family member as an element of the consent and authorization for the initial research study but would instead prefer that the research team obtain a separate authorization from the patient—perhaps at the end of the original study—for release of PHI to a family member.

## Review and approval of script or letter for contacting family member

Interviewees (eight—four investigators and four compliance officials) from those institutions that would permit the investigator to contact the family member said that the script of the call or the text of a letter would be reviewed by the IRB to ensure that it takes into account the impact of the revelation of a cancer diagnosis on the family member.

## Summary of investigator interviews

- Three investigators reported that the request to participate in a genetics study must be offered by the original trial participant.
- Four investigators said it was permissible for the principal investigator to contact the family member regarding participation in the study.
- Two investigators stated that contact by a genetics counselor would be necessary.
- Three investigators had no experience with such studies.

## Summary of compliance interviews

- Nine compliance officials said that the request to participate in a genetics study must be posed by the original trial participant.
- Four compliance officials said that the principal investigator may approach possible genetics study participants.

## Concern regarding low ascertainment in study

Two investigators suggested that, regardless of the means of communicating the diagnosis and request to participate in a trial, there would be very low ascertainment in a study of this sort, as family members would be reluctant to participate.

## Creation and use of databases scenario

## Summary of interviews related to creation of tissue banks

- Standards for ensuring patients have adequate notice about potential future uses of data. Institutions employ a wide range of strategies for ensuring patient notice about future uses of data at the time that they seek to create repositories.
- Three respondents—one investigator and two compliance officials—stated that their institutions would require that authorization and consent be secured through separate forms to ensure adequate notice.
- Four interviewees—two investigators and two compliance officials—said that their institutions use forms with opt-out provisions to avoid pressure on patients to participate in data banks.
- Two compliance officials stated that their institutions routinely use authorization forms that strictly limit future research uses of data.
- Two compliance officials stated that their institutions' authorization forms simply reference the potential for "future research use" of the data in the database.
- Three interviewees—two investigators and one compliance official—said their institutions are still developing compliance plans for data repositories. In these institutions, the establishment of databases and release of data from repositories have not been absolutely blocked, but both activities are approved with great caution. Interviewees expressed optimism that clear guidance will streamline approval of both activities.

## Summary of interviews related to research use of data in repositories

- Standards for future research use of data stored in repositories. Institutions report a wide range of standards for permitting future research use of data in repositories. The interviewees identified the following.
- Seven interviewees—five compliance officials and two investigators—said their institutions always or almost always require re-consent when a researcher seeks access to data in a repository.

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**Table A1.** Study Scenario Summaries (continued)

- Three compliance officials said that their institutions always or almost always release only de-identified information from their databases.
- Three compliance officers said that their institutions might grant a waiver that would permit use of data in repositories without re-consent or reauthorization.
- Four interviewees—two investigators and two compliance officials—said that the analysis of the IRB regarding the standard for release of PHI for future research use would depend on the extent to which the original authorization form informed patients regarding the possible future uses.

#### General observations about creation of databases and future research use of stored data

The responses to this scenario—related to both the creation of databases and the future research use of stored data—revealed a significant divergence of opinion among interviewees. In general, there was a difference of philosophy between investigators and compliance officials about the language and structure of the authorization form required for deposit of PHI in repositories. Compliance officials advised greater specificity in the “future research use” references in authorization forms than was preferred by investigators, and many compliance officials preferred an opt-out mechanism in the form, a standard resisted by investigators. Compliance officials conceded that forms with opt-out features might discourage participation in databases but concluded that these requirements were in keep with the spirit of the Privacy Rule.

#### Creating a database of PHI

Interviewees across the board agreed that authorization would need to be included as part of the consent process for deposit of data or samples in a repository. They generally analyzed the purpose of the authorization form as giving subjects appropriate and adequate notice about the manner in which their samples and PHI would be used in the future. However, there was significant disagreement about the language and structure of the authorization form.

#### Patient skepticism about deposit of data in repositories

Five investigators expressed concerns about the willingness of individuals to participate in tissue bank or database initiatives. Two investigators complained that the HIPAA Privacy Rule, by implying that data might be breached or misused, has contributed to cynicism about researchers and a reluctance to share data. Two additional investigators suggested instead that the HIPAA problem is one of form overload, with the authorization form or language serving to overwhelm individuals and discourage them from research participation. A fifth investigator suggested that asking for a tissue sample is perceived by a patient as asking for more tissue than would be required for treatment purposes, which serves as a discouragement for participation.

#### Implications for future treatment

Two investigators suggested that the consent and authorization form should also include notice to the patients that depositing a biospecimen with PHI in a research database might mean the sample would not be available in the future for a treatment purpose; these investigators conceded that this level of notice about future uses might well discourage database participation but they contend that this notice is necessary for ethical reasons.

#### Future research use language

Three investigators said that it is virtually impossible to anticipate a future research need with any specificity and that authorization forms should have no more specific reference than “future research use.”

#### Burden of re-consent/reauthorization

Several investigators expressed the view that imposition of a requirement of re-consent and reauthorization was tantamount to derailing a research study. In contrast, some compliance officers and IRB officials suggested that their institutions had developed a means of obtaining new consent, including through a process that begins with a contact by letter. Because these officials do not consider re-consent impracticable, they are willing to impose the requirement without a fear that a project relying on use of data in a database will be threatened.

#### Strategies to increase participation in data collection/banking efforts

Three interviewees said their experience with databases and biorepositories has been very positive and the level of participation at their institutions very high. These interviewees—two investigators and a compliance official—said that willingness to participate in databases relates to the research culture and culture of trust that is created at an institution and that a positive culture can balance any concerns created by HIPAA requirements. Two institutions have developed mechanisms for reporting back to research participants regarding the uses of databases and repositories. The individuals representing these institutions caution that the reports are not intended to tell an individual patient how his or her data might have been used but instead to report on the institutional effort. Representatives of both institutions report very positive feedback from patients regarding this practice.

#### Summary of investigator interviews

- One investigator noted that his institution would require separate consent and authorization forms for deposit of data in repositories, in order to protect against coercion.
- Two investigators stated that their institutions require authorization forms with opt-out provisions in order to avoid coercion to participate in databases.
- Two investigators state that their institutions always or almost always require re-consent when a researcher seeks access to data in a repository.
- Two investigators said that the standard for release of PHI for future research use would depend on the nature of the database authorization form and whether it gave patients adequate notice regarding possible future research uses.

#### Summary of compliance official interviews

- Two officials said their institutions would require separate forms for consent and authorization in an attempt to provide adequate notice to the patient regarding data deposit.
- Two compliance officials said that opt-out language would be required in authorization forms to guard against coercion to participate in the database.
- Two compliance officials said that their institutions’ authorization forms significantly limit possible future uses of data in repositories, while two said that their forms reference only “future research use” in an effort to ensure broad access to data in the future.
- Five compliance officials stated that their institutions require re-consent for release of data in a repository, whereas three said that they almost always release only de-identified data.
- Three compliance officials said that their institutions would likely grant a waiver of authorization, thereby permitting release and use of data without re-consent and reauthorization.

#### Recommendation regarding harmonization of Privacy Rule and Common Rule

Two compliance teams offered a strong recommendation that Common Rule and HIPAA Privacy Rule standards related to biospecimen and clinical data banking be harmonized. Both groups believe that HIPAA has added a layer of review—with accompanying paperwork and compliance concerns—without offering research participants any additional protection.

#### Survivorship studies

##### Summary of responses related to standards for records review to identify study participants

- Standards for records review. There was a lack of agreement among interviewees regarding the standards for review of records to identify participants in a survivorship study.
- Eight respondents—seven compliance officials and one investigator—said that the records review would be allowed to move forward without IRB review until it became a recruitment effort, which would trigger IRB review.

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Table A1. Study Scenario Summaries (continued)

- Six—three investigators and three compliance officials—said that their institutions evaluate all reviews of records to determine if they are review preparatory to research or recruitment, but they do not necessarily refer all studies to the IRB.
- Six investigators say that their institutions refuse to make a determination that a records review meets the Privacy Rule standards for review preparatory to research and insist on IRB reviews in all cases.

#### Summary of responses related to appropriate standards for contacting potential participants in survivorship study

- Standards for contacting potential participants in survivorship study. In determining the standards for contacting the potential participants in a survivorship trial, the interviewees analyzed the research scenario in a manner comparable to the genetics study.
- Three—two investigators and one compliance official—said that their institutions utilize a research coordinator or other “honest broker” to eliminate pressure that would exist if the treating physician asked a patient to participate in a trial.
- Two compliance officials said that their institutions would send written invitations to potential participants to minimize pressure to participate.
- Four—two investigators and two compliance officials—said that contact with survivors should only be undertaken by the treating physician.
- Several interviewees at multiple institutions said they are eliminating the need for follow-up contact by incorporating survivorship studies as elements of treatment trials.

#### Concerns about the affect of authorization process on survivors' willingness to participate in studies

Investigators generally expressed concerns that the language and structure of authorization forms for survivorship studies may discourage participation in studies by unnecessarily raising alarms about the security and future use of data. Compliance officials generally held to the view that authorization forms must be specific and clear in alerting research participants regarding the parameters of data use in survivorship studies, and investigators expressed concerns that this level of specificity may hinder participation. Possible tensions between investigators and compliance officials around these issues are being alleviated by efforts by investigators to obtain consent and authorization for survivorship studies as part of the consent and authorization process for treatment trials.

#### Summary of investigator interviews

- On the issue of review of records preparatory to research, one investigator said that such reviews would be permitted to move forward without IRB review, three said their institutions evaluate all records reviews for possible referral to the IRB, and six said their institutions would insist on IRB review of all records reviews preparatory to research.
- On the matter of the standards for contacting possible survivorship study participants, two investigators said that their institutions would utilize a research coordinator to request participation in a survivorship study and two said that contact could only be undertaken by the treatment physicians. Several said they were attempting to address the issue by incorporating survivorship study consent in treatment trial consent and authorization forms.

#### Summary of compliance official interviews

- On the issue of records review preparatory to research, seven compliance officials said that records review would be allowed without IRB review until it became a recruitment effort, and three said their institutions evaluate all such efforts for possible referral to the IRB.
- One compliance official said that a research coordinator would serve as the honest broker to inquire about survivorship study participation; two said that written invitations would be required; two said that only the treatment physician could request survivorship study participation; and several said they have long-term plans to eliminate this issue by incorporating survivorship study consent and authorization in the treatment study consent and authorization.

#### Inclusion of survivorship follow-up as element of treatment trial

Five interviewees—three investigators and two compliance officials—emphasized that their institutions attempt to prepare for long-term survivorship studies by including a consent and authorization for such study as part of the consent process for treatment trials. All five interviewees noted that the language of the survivorship study authorization can be the topic of extended discussion within the IRB as it reviews the treatment trial. According to these interviewees, there is a concern among IRBs that survivors understand the possible future research uses of their PHI.

#### Patient interest in participating in survivorship study

Interviewees offered a range of opinions regarding survivor interest in participating in long-term survivorship studies. It was suggested that (1) children (and their parents) have a keen interest in participating in survivorship studies if they believe that such studies will provide information about strategies to improve the quality of survivorship; (2) patients enrolled in treatment trials for early stage cancer are interested in survivorship studies; (3) patients enrolled in treatment trials for late stage cancer have limited interest in survivorship studies; and (4) breast cancer patients show a keen interest in survivorship studies.

#### Script for approaching survivors

Several interviewees, including both compliance officials and investigators, said that their institutions would likely want to approve the script of a phone call or the text of a letter that would be used to ask a survivor to participate in a long-term survivorship study.

#### Difficulties associated with multi-institutional survivorship studies

Three investigators described their participation in multi-institutional survivorship studies and the difficulty of achieving agreement among participating institutions on the authorization language referencing future research uses.

#### Difficulties created by review of studies as protocol amendments

An investigator and a compliance official identified obstacles to review of survivorship studies that were follow-on studies to treatment trials. These studies were considered amendments to the original protocol. Although at some institutions protocol amendments are promptly reviewed, at other institutions all protocol amendments are given the lowest priority for IRB review, which can result in significant delays.

Abbreviations: IRB, institutional review board; PHI, protected health information; HIPAA, Health Insurance Portability and Accountability Act.