AMERICAN HEALTH CONSULTANTS®

IRB ADVISOR

*Your Practical Guide To Institutional Review Board Management*

## INSIDE



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# CMS proposes changes to privacy rules, but critics say more still are needed

*Identifiers remain an issue for researchers*

The federal government wants to add some flexibility to privacy regulations, including eliminating the need for researchers to use multiple consent forms. But even with these changes, the privacy regulation may have a chilling effect on research, some industry experts say.

This spring, the Department for Health and Human Services (HHS) proposed various changes to the Standards for Privacy of Individually Identifiable Health Information, which is part of the Health Insurance Portability and Accountability Act (HIPAA) that covers health plans, health care providers, and health care clearinghouses. The privacy rule, effective April 14, 2001, will require most covered entities to comply by April 14, 2003.

Among the modifications proposed to the privacy rule is a change to the uses and disclosures for research purposes.

HHS proposes to require researchers to use only one combined informed consent/privacy form for research purposes, rather than to add an additional consent form related to information privacy rights. HHS also proposes to simplify other provisions to make the privacy rule more closely follow the requirements of the common rule governing federally funded research.

"I think they've certainly made a step in the right direction, with the acknowledgement that one can combine HIPAA privacy with authorization," says **Lisa Murtha**, JD, chief audit and compliance officer at The Children's Hospital of Philadelphia.

"The less paperwork required for subjects to sign, the easier it is to recruit them," she adds.

However, IRBs and researchers still have some concerns about the privacy rule's identifier requirements, which still could have a chilling effect on certain types of research even under the proposed changes, Murtha notes.

"Sometimes, the identifiers are the very things you need in order to do the research you want to do," she says. "So you can't do anything short of getting full authorization from the patient, and that may be absolutely fine, but it may also be an additional task people have to go through to do their job in the research area."

A separate and more reasonable standard is needed for the de-identification of protected health information for research purposes, wrote **Jordan J. Cohen**, MD, of the Association of American Medical Colleges (AAMC) of Washington, DC, in an April 11, 2002, letter to HHS that comments on the proposed modifications.

"The single most important thing is the identification," says **Jennifer Kulynych**, JD, PhD, director of the division of Biomedical and Health Sciences Research at AAMC.

"HHS discussed a proposal for a limited data set that is somewhat similar to what we had suggested in our comment letter on the final rule," Kulynych says. "It would remove direct identifiers rather than the entire list of identifiers."

Under this suggestion the researcher would agree to use the information solely for research purposes and the information could be released to research without authorization or waiver, Kulynych explains.

"HHS discussed that and asked for more comments, but they do not propose it yet, and we think that's critically important," Kulynych adds.

In a March 21, 2002, memorandum, HHS notes that the department is aware of the research community's concerns about the rule's approach to de-identification, but that it believes that identifiable information should have strong protections.

"My own bias is that it's rare for an investigator to say they don't need an identifier," says **Robert M. Nelson**, MD, PhD, associate professor of anesthesia and pediatrics at The Children's Hospital of Philadelphia.

"At the very least, if you're looking at medical records you need to be able to go back and look at missing data points," Nelson says. "So by definition, it is therefore linked."

The HHS memorandum states, "Therefore, HHS is seeking comments on establishing a limited data set that does not include directly identifiable information, but in which certain identifiers remain.

"In addition, to further protect privacy, the department proposes to condition the disclosure of the limited data set on a covered entity's obtaining from the recipient a data use or similar agreement, in which the recipient would agree to limit the use of the data set for the purposes for which it was given, as well as not to re-identify the information or use it to contact any individual," HHS wrote.

It's that kind of language that makes it difficult for IRBs and research institutions to decide how to prepare for the implementation of the privacy rule, Nelson suggests.

"One of the challenges in this whole area is taking the arcane language of HIPAA and translating it into a language where researchers will have a clue of what you're talking about," Nelson says.

"I tell attorneys to tell me what it really says, but at this point it's in a state of flux," Nelson adds. **(See story on the need for IRBs to prepare for privacy rule, p. 63.)**

The AAMC, in the April letter, offers several suggestions for how the privacy rule could be improved and still protect patients. Here are a few of the association's ideas:

• **Clarify the requirement regarding authorizations to obtain permission for disclosure of private health information to a database maintained for research purposes.** HHS now asks that researchers disclose on the authorization form the potential for information to be disclosed by those who have access to the information.

"The AAMC requests that this criterion be modified as it is not possible for a covered entity even to estimate the risks of disclosure in any particular instance because these risks will be largely unknown to the entity and often outside its control," Cohen wrote.

• **Develop a separate, more reasonable standard for the de-identification of protected health information for research purposes.**

## COMING IN FUTURE MONTHS

- Develop a risk-benefit matrix that clarifies the decision-making process
- Set policies for conducting expedited reviews
- iMedRIS computer application integrates all aspects to research
- IRB shopping

"Covered entities should be permitted to release information that has been de-identified under this research standard if the recipient researcher agrees in writing not to attempt to re-identify or contact the subjects of the information, and not to further disclose the information except as required by law," Cohen wrote.

• **Revisit the requirement that health systems provide a specific accounting for all research disclosures made before a waiver of authorization, which will impose an administrative burden upon providers.**

"We fear in particular that community providers and hospitals that do not view research as their primary mission will be reluctant to assume this burden and thus unwilling to make patient records available to researchers," the letter says. "This unfortunate result would impede or even prevent much valuable epidemiological and health services research to the great detriment of patients whose care is enhanced by new medical knowledge."

• **Permit covered entities to disclose public health information to sponsor-initiated registries, provided these are created for quality and safety purposes.** The regulations do not permit covered entities to make the same disclosures to registries run by academic investigators and institutions or other nonprofit organizations, even when these are operated under IRB supervision and do not disclose direct patient identifiers to researchers accessing the data, the letter states.

"These registries are vitally important to researchers who study epidemiological patterns of disease or track the success of health interventions across broadly dispersed populations," the letter says. ■

# Hospital system and IRBs: Get started on HIPAA regs

*It's time to take first steps*

Although the privacy regulations still are being changed and may be significantly altered by 2003, it's not too early for an IRB and health care/research institution to begin to prepare for implementing the rules.

The Department of Health and Human Services (HHS) has proposed some modifications to the Standards for Privacy of Individually Identifiable Health Information under the Health Insurance Portability and Accountability Act (HIPAA).

For example, The Children's Hospital of Philadelphia has hired a consultant to examine all processes involved in the areas of data security and data transactions, says **Robert M. Nelson**, MD, PhD, an associate professor of anesthesia and pediatrics.

"Part of the difficulty is we won't know until next fall what the regulations will be, and if you wait until next fall, you'll be way behind the curve," Nelson says.

For this reason, The Children's Hospital already has begun the process of developing guidelines and monitoring processes that clinicians, investigators, IRBs, and all other health care personnel will be required to follow. The institution has a HIPAA oversight committee and 14 working groups that each has chairs, co-chairs, and multiple members.

One of the working groups oversees the privacy rule as it applies to research and another working group will develop training guidelines. Nelson is on the oversight and research committees.

With about 20 members, the research-working group consists of the chair of the IRB, the vice president of research, administrators, the deputy director of an affiliated research institute, and representatives from a clinical trials office, finance, investigators, and others.

The groups meet monthly and divide the tasks to develop policies and procedures.

"Our plan is to get everything in place by the time the final regulations come out," Nelson says. "We should have a work plan developed within the next couple of months, and I would hope that in the fall we're looking at training and implementation."

The institution's IRB will serve as the privacy board, and there may be the addition of another full-time position to help with the extra workload, Nelson says.

While it may be optimistic to expect that every single investigator and protocol will be brought up to full compliance with privacy regulations by next April, there at least will be a process put into place that will help identify problem areas.

"We will have a survey tool we'll use to sample a range of research with respect to how they're handling data," Nelson adds.

The tool will ask questions about these topics:

• How is storage and security of databases being handled?

• What are the different types of electronic transactions that are being conducted?

• Who has access to electronic transactions and databases?

• Are people sharing information external to the institution?

"We plan to use that survey response to make an assessment and to begin to guide [policy]," Nelson says.

The survey method will be modeled after the hospital's continuous quality improvement process, focusing primarily on high-volume, low-risk data and low-volume, high-risk data. Surveyors will select studies in sensitive areas and sample them, probably looking at 40-50 investigators/protocols out of the institution's 800-900 total number of open protocols, Nelson explains.

"This is just meant to be a guide for us in getting an action plan formulated," Nelson says. "We have a consultant helping with that, and we have a set of external attorneys helping to guide the entire process within the facility."

Most of the education will be for investigators who, unlike IRB members, may not give data security and access much thought, Nelson says. "There will be a significant cultural change that takes place."

For instance, when the IRB reviews research data sheets, there already is a policy of not allowing identifiers, Nelson says.

"If we see anything on the sheet that is identifiable piece of information, we tell them to remove it and place it on a separate data sheet so it will be all collected in one area," Nelson says.

This way no individual can be identified from the data sheet.

The next step is to educate investigators about how to de-identify these data sheets and how to store them securely in their offices.

"Education of investigators will be crucial, and they'll need specific guidelines on how to handle data, confidentiality, security, exemptions, and how that data [are] shared," Nelson says.

Researchers will need to learn to be more attentive to what information is displayed on their Excel spreadsheets, which are electronically transmitted.

"I would envision we'll have concrete guidance about the different ways one could secure the data so that unauthorized access is not permitted, and that ranges from the simple 'Keep your door locked' to a way to protect data all day," Nelson says. ■

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# New rules proposed for IND exemptions

*HHS guidance issued in April*

The rules soon may change for investigational new drug (IND) studies that involve lawfully marketed cancer drugs or biological products.

"It will have a significant impact," says **Francis LeVeque**, DDS, chairman of the Human Investigation Committee at Wayne State University in Detroit.

Under regulations 21 CFR 312, sponsors who plan to study a drug or biological product in humans must submit an IND application to the Food and Drug Administration (FDA). The regulations provide for some exemptions under certain criteria. Now in a draft report, the FDA offers further explanations for how those exemptions might apply.

"Guidance for Industry: IND Exemptions for Studies of Lawfully Marketed Cancer Drugs or Biological Products" was issued in April 2002 by the Department of Health and Human Services (HHS). It was prepared by the Division of Oncology Drug Products in the Center for Drug Evaluation and Research and the Center for Biologics Evaluation and Research at the FDA.

"I believe that the general understanding of use of INDs is not good among investigators in this country," LeVeque says.

While most investigators generally know that if they are using an investigational drug or device that needs an IND, most fail to realize that there are many other situations that require INDs, LeVeque explains.

"The problem is with the lack of knowledge or overall misunderstanding that approved drugs, if they are going to be used in other applications in different dosing ranges and conjointly with other drugs, etc., may also require an IND," LeVeque says. "They'll need either a reference IND or manufacturer's IND for each drug that is approved."

The guidance may clarify some of the misunderstandings, but it also may put more responsibility on the shoulders of IRBs to decide whether an investigator has correctly interpreted the FDA exemptions, LeVeque says.

Previously, the policy at some IRBs, including the committee LeVeque chairs, has been to require investigators to obtain IND numbers for

all investigational drugs and products. And if they are unable to obtain such a number, they will need to provide documentation and justification for not having it. **(See sample of protocol summary form questions, p. 63.)**

Now IRBs will need to have a clear understanding of the FDA exemptions for INDs.

"The FDA is clever and uses the phrase, 'It may be exempt,'" LeVeque says. "But there is an old saw in research that nobody can exempt themselves."

So while there may be exempt research at Wayne State, those exemptions need to be granted by some authority, LeVeque says.

"Once they're granted there is no further interface with the IRB except for changes, chart reviews, etc.," he adds.

## Five criteria for exemption

The FDA regulations state that some studies may be exempted from IND regulations if they meet the following five criteria, as stated verbatim:

1. The study is not intended to support FDA approval of a new indication or a significant change in the product labeling.
2. The study is not intended to support a significant change in advertising for the product.
3. The investigation does not involve a route of administration or dosage level or use in a patient population or other factor that *significantly increases the risks* (or decreases the acceptability of the risks) associated with the use of the drug product.
4. The study is conducted in compliance with IRB and informed consent regulations set forth in 21 CFR parts 56 and 50.
5. The study is conducted in compliance with 21 CFR 312.7 (promotion and charging for investigational drugs).

In the new FDA guidance, the FDA acknowledges that these rules require a considerable amount of professional judgment in determining whether the condition significantly increases the risk associated with using the drug.

This is where oncology drugs and biological products are different from other types. Unlike other uses for drugs/biological products, it is a common practice to modify labeled dosing recommendations, and cancer drug treatment typically is associated with significant risk from known toxicity. Also, off-label therapy with cancer drugs is common practice, according to the FDA guidance.

Although the FDA does not require submissions to determine an exempt status, the agency will perform an initial limited review of such applications to determine whether the study is exempt. Then if the review determines that the study protocol is exempt, the FDA will send a letter to the study's sponsor.

However, the FDA's new guidance makes it clear that it's preferable for the study sponsor to determine that a protocol is exempt and therefore reduce the number of unnecessary IND applications to the FDA.

"If the drugs have been used and published, then there probably is a good chance for an exemption," LeVeque notes.

"I think IRBs need to get some guidance as to how to manage these exemptions, particularly in investigator new use studies," LeVeque says. "Industry often doesn't do these studies — why would they want to do studies with approved drugs?"

So the primary researchers doing studies of this nature will be oncology cooperative groups that are either investigator-initiated studies or that are sponsored by the National Cancer Institute, LeVeque says.

This still leaves open the question of who should have the final say over whether a study is exempt from an IND application, if that final say is not going to be from the FDA.

Since the FDA says the decision about exemptions should be based on a risk-benefit ratio, then it would appear that IRBs need to be involved in the decision-making process.

"If you have a situation where there is a significant risk to using a drug combination and the benefit is marginal, then that weighs into the decision," LeVeque explains. "And as far as IRBs are concerned, they do look at that combination of risk vs. benefit."

The FDA notes that planned studies may be considered exempt from the requirements of an IND if the studies involve a new use, dosage, schedule, route of administration, or new combination of marketed cancer products in a patient population with cancer when the five criteria apply.

Some examples of studies that generally are exempt, according to the FDA, are as follows:

- **"Single-arm, phase 2 trials using marketed drugs to treat a cancer different from that indicated in the approved labeling and using doses and schedules similar to those in the marketed drug labeling are usually exempt.** An exception may exist when standard therapy in the population to be studied is very effective (e.g., is associated with a survival benefit); in that case, use of

## IRB's protocol summary form queries INDs, IDEs

The Human Investigation Committee (HIC) at Wayne State University in Detroit uses a nine-page protocol summary form that asks investigators detailed questions about investigational new drugs (INDs) and investigational device exemptions (IDEs).

Although the Food and Drug Administration (FDA) has recently proposed new guidance about IND exemptions, it's still a good idea for IRBs to require thorough explanations from investigators about when they claim an exemption to obtaining an IND number, says **Francis LeVeque**, DDS, chairman of the Human Investigation Committee at Wayne State.

"It's incumbent upon IRBs and organizations such as human investigation committees, before they review protocols, to make sure an indication for an IND is either there or not there," LeVeque says. "In our institution, we've reworked our protocol summary form, an application for research, and we're asking specific questions about INDs that will help us determine whether an exception is required."

Here are the institution's protocol summary form questions that are within the section on "Interventions/Measurements Solely for Research Purposes:"

- **Is this a therapeutic/treatment study?** If yes, go to next question.
- **Does it involve a placebo?**
- **Is an experimental agent(s)/device(s)/use involved in this project?**
- **Is this a new indication of the study agent/device/use (new use, altered dose, new route of administration, new participant population, etc.)?**
- **Provide the IND (Investigational New Drug) number or IDE (Investigational Device Exemption) number.**

**Note:** Approval cannot be granted until the required IND/IDE number is provided.

If the FDA has provided no IND/IDE number for the above indications, please justify why this number is not required. Include a copy of any documents supporting this justification or the name, date, and the essence of verbal communiqué from the FDA. Refer to the HIC web site (www.hic.wayne.edu) Helpful Links for FDA requirements.

- **Will non-FDA approved drugs/chemicals without IND numbers be given to research participants?** If yes, describe the safety/pharmacology profile of the drug/chemical and provide a copy of the literature search that determined this dose/use.
- **Has a copy of the Investigational Drug Brochure/package insert been included?**
- **Will research participants be exposed to imaging or diagnostic radiation (e.g., X-rays, CT scans, etc.) over and above that given for clinical purposes?** If yes,

— Specify the facility where radiation will be given.

— Describe the additional imaging or diagnostic procedures.

— Describe the total amount of the additional radiation exposure in rads/millirads.

**Note:** In the consent form, the amount of additional radiation and subsequent risk must be described in lay terms. For example, "the amount of radiation from participation in this research study is the same amount that would be received by flying from New York to Los Angeles." ■

another regimen may expose patients to the risk of receiving an ineffective therapy."

- **"The study of new combinations of drugs would not ordinarily constitute a significant risk if these combinations have been described in the literature.** Even when the regimen described in the literature does not use exactly the doses planned for study, incremental differences in doses from those described in the literature would not normally pose a significant risk and would not require an IND.

"Because of the danger of synergistic toxicity occurring with a new drug combination, if there are no data from the literature on its safety, the initial study of a new drug combination should ordinarily be performed under an IND. Synergistic toxicity may be anticipated when one agent interferes with the metabolism or elimination of the other agent; when both agents target the same metabolic pathway or cellular function; or when one agent targets signaling pathways that are reasonably expected to modulate sensitivity to the other agent. If it is determined that synergistic toxicity is likely, animal studies should be considered for determining a safe starting dose for the drug

combination in humans."

• **"Many studies of high-dose therapy in patients with cancer are exempt.** Studies involving adequately evaluated regimens that appear to have an acceptable therapeutic ratio for the population being studied may be considered exempt. Similarly, phase 1 studies involving incremental changes from such well-described regimens are generally exempt." ■

# Human subject protections ed goes on-line at UM

*Consortium joins web-based training program*

When members of the Human Subjects Forum at State University of New York (SUNY) campuses went looking for a better way to train investigators involved in human subjects research, they found the University of Miami's Collaborative IRB Training Initiative (CITI).

Launched September 2000, CITI is a web-based course consisting of 14 modules covering all aspects of human research protections mandated by federal guidelines. The program was developed in response to the June 2000 U.S. Public Health Service (PHS) announcement that anyone engaged in PHS-funded research involving human subjects must have training in the protection of subjects by Oct. 1, 2000.

"When the federal training mandate came to pass, we crunched ideas about how best to satisfy the requirement," says **Judy Matuk**, MS, associate director of the Office of Research Compliance at Stony Brook (NY) University, a SUNY member school. "After a demonstration of the web site and review of the material contained within the modules, it was immediately clear that CITI would be an excellent method of training investigators in the protection of human subjects."

Content for the various modules comes from content experts at institutions from around the country, including Dartmouth College in Hanover, NH, the University of Nebraska Medical Center in Omaha, The Department of Veterans Affairs (VA) headquartered in Washington, DC, and Children's Hospital of Boston.

"From the beginning, it was clear that the only cost effective approach to meet the Oct. 1 deadline was to organize a multi-institutional collaboration for content development," says **Paul Braunschweiger**, PhD, professor of radiation oncology at the University of Miami and director of the university's office of research education.

Though housed and maintained at the University of Miami, CITI is a collaboration between the university and Fred Hutchinson Cancer Research Center in Seattle. In two years, CITI has grown from 10 participating institutions to more than 200 and designed an exclusive site for SUNY, and currently is developing a custom site for the Department of Energy.

Initially, Karen Hansen, director of the institutional review office at the Fred Hutchinson Cancer Research Center and co-founder with Braunschweiger of CITI, recruited the contributing content experts and their institutions, but now word of mouth or an Internet search is bringing in more participants.

"We heard about the program from doing a basic Internet search," says **Ken Capps**, PhD, CPT, MS, clinical research associate in the department of clinical investigation, Walter Reed Army Medical Center in Washington, DC. "Our department compared the CITI course to other web-based courses and found it by far to be the best. Most of the other web-based courses were too specific to the institution that it was created by."

The core CITI modules include:

• history and ethical principles;
• basic institutional review board regulations and review process;
• informed consent;
• social and behavioral research;
• research involving records;
• genetic research in human populations;
• research with protected populations;
• research involving prisoners;
• research involving minors;
• research involving pregnant women and fetuses in utero;
• population risks, group harms, community consultation, and IRB review — research with American Indian and Alaska Native, and other socially vulnerable populations;
• FDA-regulated research;
• research protections in the VA;
• hot topics.

Institutions are free to choose the appropriate modules for participants, and each user may complete the modules at his or her own pace. That's one of the features that really drew SUNY, says Matuk. "CITI has done exactly what we hoped it would do in this regard — it serves as a valuable alternative to the lecture series, enabling investigators to cover

required material in a manner that fits their schedule, at their own pace, in the privacy and comfort of their office or home," she explains.

"Another feature of the CITI program of which Stony Brook has taken advantage is the ability to require completion of a variable number of modules based on investigator type," she continues. "For example, someone who is only involved in analysis of data has to complete four modules. Alternatively, an investigator who is involved in research regulated by the FDA must complete 12 modules."

"The institutions pretty much determine what modules their people are going to view," echoes Braunschweiger. "Some are not affiliated with a VA facility, so they excuse their people from doing the VA module. Some institutions don't conduct research with prisoners, so they excuse their people from that module."

CITI is subscriber-based. The cost for each institution is $1,000 per year. An unlimited number of learners can access the system for the one fee, and institutions may create institutional pages that contain policy and procedure documents, as well as forms or training materials and quizzes pertinent to that institution. Content for the custom pages is developed by the institution. CITI administrators will upload materials once they are ready.

"Miami provides templates for the institutional pages. [The institution] has to provide content, questions, if desired, and feedback regarding answers," says Braunschweiger.

The university does not assess participants' scores. Instead, institutions are sent weekly reports on their learners' test scores. "We send out reports on each learner so training coordinators can tell whether people have successfully passed the course. Each participating institution decides what a passing score will be," he says.

The CITI course has undergone three revisions since its launch, and user feedback has provided insight for improvements. "We rely on that quite heavily," says Braunschweiger. "One of the major comments was 'the course is too long,' so we've been able to edit it and merge a couple of modules to make it shorter. Also, learners wanted more in the way of case studies, so we've endeavored to add more scenario-based quiz questions."

If you'd like more information on CITI, you may visit the web site at www.miami.edu/UMH/CDA/UMH_Main/1,1770,6460-3,00.html. ■

# QA self-assessment tool now on-line

*Questionnaire asks for detailed info*

In last month's issue of *IRB Advisor*, we discussed the Office for Human Research Protections' (OHRP) new quality initiative. A major part of that program is the Quality Assurance Self-Assessment Tool. That tool, developed by OHRP, is now on-line and can be accessed at http://ohrp.osophs.dhhs.gov/ humansubjects/qip/qatoold.htm.

The tool is a 19-page questionnaire covering all aspects of IRB management and responsibilities, including workload and staffing resources, IRB record keeping, the committee-review process, and written operating procedures and forms. **(See the list of forms that should be in the project packet submitted for initial IRB review on p. 69.)**

Participants will be asked questions, such as:

- Who oversees the day-to-day operations of the human subjects protection program?
- Who selects and appoints IRB members?
- Does your institution/IRB have a separate committee for review of noncompliance incidents?
- Does your institution/IRB have established policies and procedures for disclosure and management of potential conflicts of interest?

Other areas covered by the questionnaire are workload and staffing resources; educational training; and IRB chair, member, and staff functions.

"The OHRP QA/QI Self-Assessment Tool is a good starting point for self-assessment of a human research protection program" says **Erica Heath**, MBA, CIP, president of IRC, an independent IRB in San Anselmo, CA. "Its target is a far more achievable goal than the incredible documentation required for the two accreditation programs — the Association for Accreditation of Human Research Protection Programs and the Joint Commission on Accreditation of Healthcare Organizations. This tool seems quite rational and provides a good starting point for program assessment."

Though generally complimentary, Heath does point out what she perceives to be a shortcoming — the reliance on IRB minutes. "It's too bad that OHRP continues to put so much reliance on documentation in the minutes while effectively ignoring study file documentation," she explains.

Heath also references the Food and Drug

*(Continued on page 70)*

# OHRP QA Self-Assessment Tool

16. What items are requested and distributed to each designated IRB member(s) for review? *Check all that apply.*

| **Items Collected for IRB Review** | | Distributed for Full Committee Review | | | |
|---|---|---|---|---|---|
| Item | Requested by IRB | IRB Chair | Primary Reviewer | Other IRB Members | Alternate Members |
| a) IRB submission form | | | | | |
| b) Full protocol | | | | | |
| c) Full grant or contract application (if federally funded) | | | | | |
| d) Protocol summary | | | | | |
| e) Informed consent form | | | | | |
| f) Scientific review | | | | | |
| g) Recruitment material (e.g., advertisements, recruitment letters, scripts for telephone conversation or focus groups, etc.) | | | | | |
| h) Investigator's qualifications [e.g., CV, medical license(s), etc.] | | | | | |
| i) Conflict of interests disclosure | | | | | |
| j) List of all investigators | | | | | |
| k) Questionnaires | | | | | |
| l) Other *(Describe)* | | | | | |
| **Additional elements that may apply for biomedical research.** *Check all that apply.* | | | | | |
| m) Investigator Brochure | | | | | |
| n) Package insert providing drug information | | | | | |
| o) Device manual | | | | | |
| p) IND/IDE number | | | | | |
| q) Copy of FDA 1572 form or Investigator Agreement (for device studies) | | | | | |
| r) Copy of case report forms | | | | | |

*Source:* Office for Human Research Protections, Rockville, MD.

Administration tool, "A Self-Evaluation Checklist for IRBs," which has been available since the mid-1970's. "In my opinion," Heath says, "the two tools target different aspects of a program and compliment each other nicely."

Institutions wanting to participate in Phase I of the quality assurance program should contact the Office for Human Research Protections, Division of Assurances and Quality Improvement, The Tower Building, 1101 Wootton Parkway, Suite 200, Rockville, MD 20852, attn: George Gasparis. ■

**SPOTLIGHT ON COMPLIANCE**

# PHS works with biotech comp on stem-cell use regs

*For-profit use generally prohibited*

By **J. Mark Waxman**, JD
General Counsel
CareGroup Healthcare System
Boston

Although the availability of stem-cell lines remains in the news, decisions about how they will be distributed has been slowly moving forward. Through a Memorandum of Understanding (MOU) between the U.S. Public Health Service (PHS) and BresaGen Inc., a Georgia-based subsidiary of Australian biotechnology company BresaGen Limited, provision has been made for distribution of human embryonic stem-cell line materials to PHS and academic researchers.

This MOU, which went into effect April 24, follows a comparable MOU agreement with WiCell, the entity associated with the University of Wisconsin-Madison that has patented technologies and materials concerning primate embryonic stem cells and their cultivation. Because the goal of both MOUs is to make stem cell materials and know-how available, the terms to implement that goal are important.

The structure of the arrangement is in two parts: 1) An agreement between BresaGen and PHS setting forth the terms and conditions under which the materials will be made available; and 2) A Simple Letter Agreement (SLA) for the actual transfer of the materials to PHS contractors and scientists to be executed by recipients.

Availability of the BresaGen materials under the MOU is based on the following conditions:

a) Materials are made available in only specified PHS biomedical research programs.

b) Materials may not be used for any diagnostic or therapeutic purposes.

c) Materials may not be used for commercial purposes — this would include research funded by a for-profit entity where the sponsor could claim rights to the results of the research. What is or is not a commercial purpose is not defined.

d) Materials may not be used for the direct benefit of a research sponsor without a separate direct written agreement. What is actually a direct benefit is not defined.

e) Materials may not be transferred to third parties of any kind without written consent.

f) If using materials results in the discovery of different materials that could be developed for commercial use, rights to the materials will require a separate agreement with BresaGen. PHS appears to have bargained for the availability of such rights, provided that the terms of such agreements will be comparable to other BresaGen licensing agreements.

g) The materials provided come with no warranties, including any warranty that their use will not violate any existing proprietary rights.

h) A transmittal fee, not to exceed $5,000 per sample, may be charged. A separate fee may be negotiated to cover training required to learn to grow or use the materials.

i) The agreement does not supercede any rights available to PHS by statute.

The term of the agreement is three years. Parties are not required to negotiate an extension. There are no provisions that specifically address rights or obligations in the event of a termination.

The SLA is designed to provide a simple process to implement the MOU on a recipient-by-recipient basis. To receive the materials, the receiving scientist and the related organization must both agree to the general conditions set forth in the MOU. A decision to receive materials also is an agreement to:

a) recognize that the materials are and remain BresaGen's property;

b) restrict the use of the material to diagnostic or therapeutic, but not commercial, purposes;

c) not use the material in any PHS research program where rights have already been granted

to a research sponsor without a direct agreement between the sponsor and BresaGen, regardless of whether the sponsor is a for-profit or nonprofit entity;

d) not further distribute the material, even to other nonprofit research institutions, without written consent;

e) acknowledge the source of the material in any publication reporting on its use;

f) acknowledge that the material is "experimental and may have hazardous properties";

g) handle the materials in compliance with all applicable rules and regulations regarding its use or disposal, including a prohibition on use in humans or in contact with other cells or materials to be transferred into humans. This, of course, is a bar to any preparation of somatic cell therapy or gene therapy products;

h) not seek to engage in any human cloning activities using the material.

There are no particular remedies for a breach of the SLA as would normally be found in the typical Materials Transfer Agreement (MTA). Presumably, this omission was part of an attempt to make the process appear less onerous by leaving out possible legal ramifications if the agreement is breached.

Those receiving materials under the MOU, either with BresaGen or other PHS contractors, will need to be quite careful with respect to its provisions. While the terms are actually fewer in number than might be provided in a typical MTA and for the same types of diligent educational effort, record keeping and segregation of materials will be required. It is likely that a failure to abide by the terms of the agreement will be a relatively high-profile event and would be dealt with rather aggressively. ■

## CE/CME objectives

The CE/CME objectives for *IRB Advisor* are to help physicians and nurses be able to:

- establish clinical trial programs using accepted ethical principles for human subject protection;
- understand the regulatory qualifications regarding human subject research;
- comply with the necessary educational requirements regarding informed consent and human subject research;
- apply the necessary safeguards for patient recruitment, follow-up, and reporting of findings for human subject research;
- have an understanding of the potential for conflict of financial interests involving human subject research;
- understand reporting adverse events during research. ■

# NIH nominee supports stem-cell research funding

Noted medical researcher Elias Zerhouni, MD, President George W. Bush's nominee to lead the National Institutes of Health (NIH), indicated

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### Editorial Questions

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Call **Alison Allen** at (404) 262-5431.

strong support for federal funding of embryonic stem-cell research at his initial Senate confirmation hearing, the Associated Press reported on May 1.

Without federal funding, researchers would shy away from a field of study that promises to hold many major new advances in medicine, Zerhouni told reporters outside of the meeting.

In a hotly debated move last year, the Department of Health and Human Services (DHHS), which oversees the NIH, decided that only stem-cell lines already in existence could be used in federally funded research, and federal funds could not be used to fund efforts to derive stem cells from embryos or fund research involving cells obtained from embryos destroyed after the DHHS directive went into effect.

Many scientists believe that although the policy is sufficient to allow current research to continue, more stem-cell lines will be needed in the future.

Zerhouni seemed to echo this belief in remarks to the Senate committee, the report indicated.

He said that the administration's decision was an "important advance" because it allowed some federal funding to go forward. However, he said that, if the current stem-cell lines proved inadequate later, he would "be the first one to assemble that information." ■

# CME*questions*

***CME subscribers:*** *Please use the enclosed Scantron to submit your answers for the January-June 2002 CME test and return it and the survey in the enclosed envelope.*

21. In response to the research and health care industries' concerns about the new privacy rule, the Department of Health and Human Services (HHS) has proposed changes to the final regulations. These include:
A. HHS has proposed eliminating five of the original de-identifiers from the list.
B. HHS has proposed giving IRBs the authority to waive consent when certain de-identifiers are included in research databases.
C. HHS has proposed to require researchers to use only one combined informed consent/privacy form for research purposes, rather than to add an additional consent form related to information privacy rights.
D. All of the above

22. Which of the following is not one of the criteria the Food and Drug Administration (FDA) requires protocols to meet if they qualify for an Investigational New Drug (IND) exemption from application?
A. The study is not intended to support FDA approval of a new indication or a significant change in the product labeling.
B. The study is not intended to support a significant change in advertising for the product.
C. The investigation does not involve a route of administration or dosage level or use in a patient population or other factor that *significantly increases the risks* (or decreases the acceptability of the risks) associated with the use of the drug product.
D. All of the above

23. The OHRP Self-Assessment Tool will evaluate:
A. workload and staffing resources
B. written operating procedures and forms
C. the committee review process
D. All of the above

24. Availability of the BresaGen materials under the MOU is based on the following conditions:
A. Materials may not be used for any diagnostic or therapeutic purposes.
B. Materials may not be used for commercial purposes.
C. A & B
D. None of the above