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IRB ADVISOR

Your Practical Guide To Institutional Review Board Management

INSIDE

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Privacy rules, advancing technology raise tissue procurement questions

IRBs have responsibility over use, study

Investigators have a variety of options available with regard to using human tissue in research, and each new possibility raises additional questions and ethical concerns that should be considered by IRBs.

IRBs will need to establish policies that address whether patient consent is necessary and specify how long tissue samples can be stored and by whom. Also, IRBs should consider how to handle situations in which research using a patient's tissue inadvertently uncovers health problems, such as HIV disease, and how disclosure to the patient will be handled.

The U.S. Food and Drug Administration (FDA) and the Office for Human Research Protections (OHRP) offer little guidance, but for the most part, IRBs are on their own in developing policies regarding the handling of human tissues. **(See story on FDA and OHRP statements, p. 27.)**

Always or occasionally necessary

Many IRB coordinators would argue that informed consent is necessary whenever tissue is procured during a trial.

"It is important to inform the subject of all the risks and benefits involved in tissue procurement and the methods employed to ensure privacy and confidentiality of data," says **Mary Barnhart**, CIM, IRB coordinator of Oakwood Healthcare System in Dearborn, MI.

The OHRP offers guidelines stating that human subjects would not be involved and tissue procurement would not be considered human research if the following conditions apply:

- The material in its entirety was collected simply for unrelated clinical purposes.
- The material was collected for legitimate but unrelated research purposes, and the material was submitted without identifiable private

data or information.

Only in these cases would informed consent not be required, Barnhart says.

"The present guidance from the regulatory bodies is that consent should be obtained for all specimens that are prospectively collected," Barnhart adds. "However, we must remember that guidance is not a regulation; it's the FDA's or OHRP's current thinking on how to meet the requirements of the regulation."

Federal guidance often changes and is modified as new issues arise, including the relatively new practice of genetic testing.

"For many types of research with tissue, such as genetic testing, it should be mentioned in the consent form that blood will be drawn and the test done on it," says **David Forster**, JD, MA, CIP, director of regulatory and legal affairs for the Western Institutional Review Board in Olympia, WA.

"If it's low-risk testing, then generally a statement in the regular consent form is sufficient," Forster says. "If they plan to do genetic testing with the sample, then we usually require a separate consent form or a consent form addendum."

Forster recommends that consent forms incorporate all of the elements required by regulations, including a discussion of why the sponsor wants to do genetic testing, what will be done, and what the confidentiality risks are, including the possible effect on insurance and employment.

"Then you go on to list steps of how the genetic information will be identified and whether a link will be maintained with the subject's identity, or whether a link is permanently broken so they are truly anonymous," Forster explains. "It's a case-by-case situation, and generally if the link is maintained, then the standards are higher, and the board expects more in terms of confidentiality and information given to subjects."

Also, there are controversial issues raised by each new technology or medical/scientific trend.

For example, should an IRB be concerned about whether institutions collecting cord blood are exploiting parental fears about very low-risk disease dangers to their children?

"One of the concerns I had about cord blood was that I was fearful people out there were trying to sell its storage to mothers and parents to buy as additional insurance for their kids," says **Frank L. Gold**, MD, CIP, associate dean for organizational ethics and co-chair of the Peoria Community IRB at the University of Illinois College of Medicine in Peoria.

"The benefits of storing a child's cord blood are unforeseeable," Gold adds.

Officials with a cord storage bank company recently met with the Peoria Community IRB to discuss establishing a contractual relationship. Company officials had alleviated Gold's concern by saying that the company's primary goal was to establish a public cord bank, rather than a private one.

"The public bank would be able to provide stem cells, cord blood samples, or collections as transplant material in a large registry," Gold says. "So, someone in Idaho could call with typing data and see if there was one on the shelf that would match."

Still, these concerns will arise as private companies become involved in the business of storing and selling human tissue.

Who owns the tissue?

Storage and ownership are another hot issue involving specimen collection and study.

"We have taken the stance that subjects cannot be made to waive property rights in tissues, and this derives from federal regulations," Forster says. "However, in California, there is a case that concluded people don't have property rights in products developed from tissues."

Colorado gives people property rights over their own DNA information, but most states have no laws.

Since tissue samples can be stored indefinitely and often requires the use of a tissue repository, the custom is for the repository to become the

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FDA, OHRP have little to say on tissue protection

Here's their guidance in brief

IRBs that are addressing policy regarding informed consent in cases where research uses human tissue should take note of the small amount of guidance offered by the U.S. Food and Drug Administration and the Office for Human Research Protections (OHRP). Here's what the agencies say:

• The FDA, in an IRB information sheet that can be found on-line (www.fda.gov/oc/ohrt/irbs/faqs.html#Informed) mentions the topic of specimens only once, and that is question 52:

Q: *Is it acceptable for the consent document to say specimens are "donated"?*

A: What about a separate donation statement? It would be acceptable for the consent to say that specimens are to be used for research purposes. However, the word "donation" implies abandonment of rights to the "property." 21 CFR 50.20 prohibits requiring subjects to waive or appear to waive any rights as a condition for participation in the study. Whether or not the wording is contained in "the actual consent form" is immaterial. All study-related documents must be submitted to the IRB for review. Any separate "donation" agreement is regarded to be part of the informed consent documentation, and must be in compliance with 21 CFR 50.

• The OHRP at a Cooperative Oncology Group Chairpersons Meeting on Nov. 15, 1996, wrote this about "Exculpatory Language" in Informed Consent:

No informed consent, whether oral or written, may include any exculpatory language through which the subject is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, the institution, or its agents from liability for negligence — 45 CFR 46.116.

Examples of exculpatory language:

• By agreeing to this use, you should understand that you will give up claim to personal benefit from commercial or other use of these substances.

• I voluntarily and freely donate any and all blood, urine, and tissue samples to the U.S. government and hereby relinquish all right, title, and interest to said items.

• By consent to participate in this research, I give up any property rights I may have in bodily fluids or tissue samples obtained in the course of the research.

• I waive any possibility of compensation for injuries that I may receive as a result of participation in this research.

Examples of acceptable language:

• Tissue obtained from you in this research may be used to establish a cell line that could be patented and licensed. There are no plans to provide financial compensation to you should this occur.

• By consenting to participate, you authorize the use of your bodily fluids and tissue samples for the research described above.

• This hospital is not able to offer financial compensation nor to absorb the costs of medical treatment should you be injured as a result of participating in this research.

• This hospital makes no commitment to provide free medical care or payment for any unfavorable outcomes resulting from participation in this research. Medical services will be offered at the usual charge. ■

owner of the tissue, provided an informed consent has been signed by the subject, Barnhart says.

"Where a repository is not used, then the tissue samples are the property of the primary investigator of the protocol or study," Barnhart adds. "Again, informed consent should be obtained, and all possible methods should be employed to ensure the privacy and confidentiality of the subject."

At hospitals and university medical centers that collect tissues for universal tissue banks, the collection process, study, and/or use of the specimens is seen as a public service. Just as blood and skin grafts can be stored for lifesaving purposes, so might umbilical cord stem cells.

For instance, if the medical center affiliated with the University of Illinois College of Medicine in Peoria agrees to collect umbilical cords for the public good, it could provide a boon for people in need of stem cell-related medical services of various

ethnic backgrounds, Gold says.

"We'd see it as a public service locally, [because] we have 5,600 baby deliveries a year here in our community and we have a large minority population in Peoria," he reports. "It's an area where there's a dearth of donations, and it's very crucial when you think about some of the treatable diseases like sickle cell anemia."

Plan for the future

Maintaining some link to the tissue donor might benefit the donor in the event some undiagnosed medical problem arises.

"For obvious reasons, there are some confidential links still there; so if there is something discovered about the mother or child that's relevant to health care, it's possible that this could be tracked back," Gold says.

At least one umbilical cord bank company plans to handle such situations by using a code to link donors to the tissue, and only key people would be able to track the code to the donors' names, he explains.

The same cord bank would separate stem cells that are available for transplantation from those that are unsuitable, and the unsuitable tissue would be available for research, Gold says.

"So the primary issues the IRB would have would be confidentiality and boilerplate concerns that are the same concerns as when tissues are banked for other purposes, such as cancer tissue that is banked for unforeseeable research," Gold says.

"The other issue that's important is that these samples are screened for HIV and hepatitis, and those are public health issues that require a mechanism for notifying the patient if these are discovered, and that's built into the consent as well," he adds.

Would the IRB be involved in the event that some disease or infection is discovered in the stored tissue sample?

Gold says that the IRB's involvement primarily would be to make certain the storage bank has a mechanism in place to handle that sort of situation.

"We can say, 'Do you have a mechanism in place if the patient tests positive to HIV, so that there is counseling to the patient and the appropriate referral for that problem?'" he explains. "If the answer is 'Yes,' then we don't need to see all the paperwork because the investigator will have that mechanism as standard operating procedure."

Typically, it would work like this: The bank would obtain the specimen and do infectious disease testing. If the sample is HIV-positive, then a whole procedural system would begin, and the bank would call the investigator to discuss the findings. The investigator would notify the subject's doctor, who would be listed on the research documents, Gold says.

Forster says that disclosing health problems to subjects should not be the IRB's responsibility. "Someone with a clinical relationship to the subject should provide that data when possible," Forster says.

Barnhart agrees.

"However, if there is a good chance that research will yield results that could affect the subject's medical care, it may be appropriate for the investigator to ask them if they wish to be contacted and informed," she says.

"The decision about whether to provide results to subjects depends upon the ethical implications of each protocol," Barnhart adds. "There are cases in which it would be ethical to provide results to subjects, such as when the research is in the early stages and the clinical significance has not been determined." ■

Vaccine, drug development link IRBs and researchers

Key is to not repeat past mistakes

Depending on a person's level of confidence in the current human research protections, the answer is either: "It will never happen again" or "We need to be careful or it's possible."

The question is: "Could the United States trample human subjects' rights in the push to produce a vaccine for a bioterrorism threat?"

IRBs and researchers may be loathe to be reminded of past research transgressions, such as the World War II outbreak of jaundice that was connected to a yellow fever vaccine administered to soldiers and civilians. To find out what was wrong with the vaccine, government health officials intentionally inoculated healthy people at a Lynchburg, VA, facility for the mentally disabled and studied what happened, says **Paul Lombardo**, PhD, JD, director of the program of law and medicine for the Center for Biomedical Ethics at the University of

Virginia in Charlottesville. Lombardo also is an associate professor in the School of Law and is a member of an IRB. He has studied and written about the eugenics movement.

"Several hundred people were enrolled as volunteers in this study with knowledge that they were legally unable to volunteer, the capability of many of the people to understand what was going on was limited, and protections were limited," Lombardo says.

It turned out that the vaccine was contaminated with hepatitis, which caused the jaundice and eventually also infected the institutionalized Lynchburg population.

Lombardo and other experts on vaccine policy and prevention spoke about this topic at the Bioethics and Bioterrorism Conference, presented by the Center for Bioethics at the University of Pennsylvania and the Center for Biomedical Ethics at the University of Virginia, held in February at the National Press Club in Washington, DC.

". . . If we had a national emergency that was somehow equivalent to World War II, would we feel free to dispense with rules we've had in the last 50 years to protect human subjects?"

Things different today

The Lynchburg incident is irrelevant to today's discussion about producing a vaccine to prevent widespread bioterrorism of anthrax, smallpox, or other agents, says **David Weiner**, PhD, an associate professor of pathology and laboratory medicine at the University of Pennsylvania School of Medicine in Philadelphia. Weiner also spoke at the bioterrorism conference, and has been involved extensively with HIV vaccine and West Nile virus vaccine research.

Today's situation is entirely different because there is no pressure to pull out all stops in producing a vaccine, Weiner says. "We have so many more options than we used to have, and vaccine is only one option."

For example, the recent anthrax scare was frightening, but not dire because of the availability of powerful antibiotics that can be used to successfully treat the infection, Weiner says.

Even with a smallpox threat, there are about 20 drugs that might inhibit the growth of smallpox, Weiner says.

"And actually inhibiting it may be enough to prevent death, and so this is a different time," Weiner adds. "This country and the world are much more sophisticated now; and we have a lot of resources, and we have to put them all to use."

Also there is a stockpile of smallpox vaccine that could be diluted to where it could be supplied to 75 million people, Weiner says.

These resources include vaccine trials, which should be conducted under the same stringent human subjects' protections that are accorded every other human subject, Weiner says.

For instance, the government is working on developing vaccines for the Ebola virus and other subtropical viruses that could be used in a bioterrorism threat.

However, there still remains a concern that during a time of national emergency, just as the Lynchburg incident occurred during a time of national emergency, that a vaccine trial or new drug development could be rushed, Lombardo says.

"What is the impact of that kind of emergency on the usual rules of research?" Lombardo asks. "And if we had a national emergency that was somehow equivalent to World War II, would we feel free to dispense with rules we've had in the last 50 years to protect human subjects?"

IRBs should consider this question, Lombardo suggests: "What kind of national emergency might justify relaxation in the rules and whether or not these relaxations would be appropriate?"

Lombardo and Weiner offer these ethical and practical considerations that IRBs may encounter should a significant bioterrorism threat occur:

- **How much risk is acceptable with a vaccine?**

The smallpox vaccine had a risk rate of one in 10,000 serious adverse events in the 1960s and 1970s, Weiner says.

"And it's likely that due to AIDS and immune deficiency that risk would go up," Weiner adds. "So we need newer vaccines that are safer."

Science leaps forward

Most current vaccine technologies use recombinant vectors that are considered safe in the lab.

"So in theory, depending on the experiment, one could work with these vectors with genes from pathogens that are separated from the whole pathogenic organism in a relatively safe way," Weiner explains. "And they permit a lot of experimentation of vaccine testing and development in absence of pathogen challenge."

Side effects from recombinant approaches

would be due to the protein use, and research testing of these vaccines would go through a relatively similar toxicology and safety evaluation as any other vaccine, Weiner says.

Human subjects research would use surrogate markers in a comparison of antibodies produced by the newer and the older-style vaccine in cases such as smallpox where there already have been vaccines that work, Weiner adds.

"We know the newer vaccines are intrinsically safe because they don't replicate and don't spread infection," Weiner says.

Still, there probably will be small human trials and not be widespread testing of many of these vaccines once they are researched in animal models, and the resulting product will be produced in a large enough quantity to be deployed if needed, Weiner adds.

• How might IRB members insulate themselves from being swayed by public alarm?

"IRBs should try real hard to not be swayed by events that are occurring because those public emergencies tend to make us all leapfrog over the kind of logic that is in place to make sure the science is done well and to make sure that no one is unduly harmed," Lombardo says.

"You don't want to let the fear of further disease blind you to the quality or effectiveness of therapy you have in hand," Lombardo says. "But there still is a line to be drawn in research to discovering its effectiveness."

Also, a bioterrorism threat needs to be put into perspective with other significant health concerns and the sense of urgency some will feel about getting a product quickly to the market.

"This is the whole story of IRBs as far as I'm concerned," Lombardo says. "It isn't even a hard question because if a medicine is being tried out that doesn't provide much hope, then no one rushes to get it on the market."

Alternatively, when there's a particularly vicious disease and the potential of very hopeful medication, people will ask why researchers or the government are waiting, Lombardo notes.

"The very people whose lives are at stake often are unfortunately talked into a hope which may not be justified by the data, and that's the whole therapeutic misconception," Lombardo says. "It's 'I'm sick and you've got the pill, so give it to me.'"

• Which research groups and IRBs are likely to be involved in bioterrorism vaccine research?

The research typically would begin in significant federal containment facilities in partnership with the Centers for Disease Control and Prevention (CDC) in Atlanta. Animal challenges would be an important part of the development.

The most likely scenario would be for these bioterrorism vaccines to be studied at military hospitals and facilities, although universities and academic centers may be involved in small-scale trials of safety, Weiner says.

"I think you might have some sort of surrogate analysis, which may be a small stage 3 trial that is looking for the antibody level or for an elevated spot as an indication of cellular immunity levels in an individual, as well as safety research," he says.

The U.S. Food and Drug Administration, the CDC, and the Department of Defense would provide the oversight of vaccine research, so a single IRB probably would not be alone in deciding ethical considerations.

"I believe this is a different situation," Weiner explains. "We're not going for a commercial license."

Rather, the goal would be to develop something that needs to be stored and used in the case of a national emergency.

The decision about licensure would be based on a committee agreement that whatever the material is after the studies are complete would be worth stockpiling, Weiner says.

Anthrax scare was a learning opportunity

• How can the risks of new vaccines be adequately communicated to subjects and to the public?

"You have a separate concern about application of new therapies and vaccines to populations that are infected or might be," Lombardo says. "So the public health issues of how do you prevent further spread of some infectious agent is really a different issue than how do you protect people from research."

The recent anthrax scare is a good example of how the public might be warned of potential vaccine problems.

National Institutes of Health researchers made it clear that the vaccine is not really well understood, so it was offered to people with the hope that some of them would look at the data and make an informed decision about whether or not to take it, Lombardo says.

"Most people didn't take it because the data were unclear of whether or not it would be a benefit to them since they already were on

Ciprofloxacin and other antibiotics and since there wasn't any apparent renewed threat of exposure," Lombardo adds.

"This is a case where you could have had much worse results and the government might have had to coercively vaccinate people," he says.

Educate about the risks

On the other side of the coin, the AIDS vaccine research presents an example of how subjects might be fully informed of an investigational vaccine's risks.

Weiner has been involved with developing an AIDS vaccine that presents no risk of HIV transmission but also may not inoculate subjects against the virus. There is the desire on the part of researchers and IRBs to make certain subjects know that they must continue to take as many precautions as previously or they will place themselves at risk of infection.

"In our HIV vaccine trials, we tell subjects that we assume the vaccine doesn't work," Weiner says. "And actually, they're counseled to think that as far as we know we have no efficacy in this vaccine at all; that we have no knowledge that the vaccine works at all. So, to really do the study, what they're really doing is volunteering." ■

SPOTLIGHT ON COMPLIANCE

Key finance question: Is relationship covered?

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

As you already are aware, last December, the Washington, DC-based Association of American Medical Colleges (AAMC) issued the first of its two-part model addressing policies and guidelines to be used as *baseline standards* for the oversight of financial interests in research. The first installment addresses the interests of faculty, employees, students, and staff. The second, due later in 2002, will address constitutional financial interests.

The AAMC guidelines target relationships where covered individuals have a significant financial interest. A covered individual is one who conducts research involving human subjects. This includes any faculty, whether or not salaried, or faculty agent. Faculty agents can be further defined to include staff, students, fellows, trainees, or administrators. Conducting research is defined broadly to encompass not only the direct process of research as defined in an approved protocol, but also enrolling subjects in research, or even submitting manuscripts concerning the research for publication.

Know the key definitions

Significant financial interests generally mean any "entitlements to payments in connection with the research not directly related to the reasonable costs of the research [as specified in the research agreement between the sponsor and the institution]." This includes service as an officer, director, or any other fiduciary role for a commercial entity which itself has a financial interest in the research, whether that position is paid or not.

In defining these interests, a series of specific categories are set forth as examples of relationships that are and are not covered.

Among the covered relationships are:

• **Consulting fees.**

Fees include honoraria, either directly or indirectly from an interested commercial interest, gifts or "in-kind compensation." The definition encompasses a wide variety of activities which are within the scope of this example — lectures, service or an advisory board, or consulting. A specific limitation is that to be considered significant or purposes of the AAMC, the *"de minimus"* threshold established in existing law (U.S. Public Health Service regulations currently establish $10,000) must be exceeded within a calendar year or are expected to exceed that amount in the next 12 months. (Why the guidelines did not make the exception threshold applicable to any 12-month period is unknown).

• **Private equity interests.**

This includes the right to such an interest whether by stock option or otherwise of any

amount in a nonpublicly traded interested company.

• **Public equity interests.**

Included is the right to such an interest in a publicly traded company. As in the private interests, it must exceed a *de minimus* amount. Whether this is to be an aggregate number that once crossed forever meets the standard or can be later mitigated or eliminated does not appear to be addressed.

• **Royalty issues.**

Royalties also include future royalty rights where the research is directly related to the licensed technology or work. There does not appear to be any *de minimus* threshold that must be exceeded. Similarly included would be any bonus or milestone payments in excess of costs incurred either from an interested company or from the institution.

A number of reasonable exceptions also have been created. Reminiscent of the fraud and abuse type exceptions in federal law, they include interests in publicly traded companies that meet the *de minimus* criteria of the federal law. Also included is any interest in a mutual fund, payments directly related to the reasonable costs of the research, and salary or other payments for services from the institution. Stock options in public companies are to be valued and treated in the same fashion as stocks themselves.

The core policies

The core policies consist of a series of guidelines designed to be "baseline standards and practices" — minimums for institutions to adopt with such additional restrictions as they deem appropriate. The goal of these policies is to ensure protection of human subjects (the "foremost concern") and foster an environment where scientific integrity is maintained. As a result, the guiding principle is that a presumption exists to reject any significant financial interest in human subjects research absent "compelling circumstances."

What might be compelling circumstances is not defined by a "bright line" test. Instead, there should be a facts-and-circumstances balancing of relevant factors measuring the risks and benefits of involvement. The factors to be considered are:

• the nature of the science;

• how closely the interest is related to the research;

• the degree to which the interest may be affected by the research.

Two extremes are given as illustrative examples. If there is a direct relationship between value and affect — equity is a start-up company developing an investigational drug — the presumption against involvement will be at its strongest. If the research is so unique and the value or potential benefits to patient welfare are such that the benefits would not be achieved as safely and effectively without the individual in question, the presumption may be more capable of being overcome with appropriate independent controls.

In any event, to operate under the presumption and meaningfully adjudicate the issues will require full and complete disclosure and reporting. As a result, the report mandates prior and continuing reporting prior to final IRB approval of research and as and when the relevant facts may change.

The conflict-of-interest committee

To effectively implement the policies, the report recommends a standing conflict-of-interest committee (COI) be created. The COI members can then ensure the policies are documented and properly implemented. The COI also would be responsible for establishing its terms and conditions, independent of the IRB, under which parties with significant financial interests would be permitted to conduct human subject research. It would be responsible for creating and educating all the relevant constituencies about the COI policies that should be in writing and widely disseminated.

Hopes for collaboration

The task force concluded that its guidelines "recommend policies that will strengthen the protection of human subjects while enabling the robust, productive collaboration between industry and academic medicine" successful in the past. It is of note, however, that one industry member representative on the task force declined to endorse the report because of her concern that it would actually stifle research innovation.

Whether the guidelines will in fact be widely adopted remains to be seen. If they are not, and the views of academic institutions on this subject vary widely, the work of the task force will not have the broad effect it has targeted. Perhaps after the second installment, we will have a better feel for the overall scope of the changes to be considered. ■

NEWS BRIEFS

Third-party status gets further revision

The National Human Research Protections Advisory Committee (NHRPAC) clarified the status of third parties as human subjects at its January meeting.

Statement published

The committee agreed to a consensus statement, which was sent to Secretary of Health and Human Services Secretary Tommy Thompson, the assistant secretary for Health, and the Office for Human Research Protections for consideration. **(See box below.)**

However, the statement does not represent official policies of either organization. ▼

Clarification of the Status of Third Parties When Referenced by Human Subjects in Research

These recommendations are meant to clarify issues specifically dealing with information provided by a human subject about someone else, such as a third party. It is not meant to readdress situations where information about a research subject is gathered through indirect means, such as a chart review, as these situations are already covered in the existing regulation (45 CFR part 46).

In regard to considering third parties in research, parties whose roles and interests must be considered include:

- investigators or their agents;
- human subjects who interact personally with investigators;
- third parties, about whom researchers obtain information from human subjects but who themselves have no interaction with research investigators or their agents.

The determination of who is and is not a human subject rests with the IRB. The requirement of informed consent, or waiver of consent, pertains only to those deemed to be human subjects by IRBs.

In most instances, the identity of human subjects of research is clear. Whether through interaction, intervention, or identifiable private information, persons are human subjects when they provide personal or contextual information about their own lives, circumstances, perceptions, or histories even when they make reference to others.

Simply because reference to a third party is contemplated in a research design or a third party's information is recorded in research records does not necessarily suggest that a third party must be registered as a research subject.

Nevertheless, investigators, in designing and proposing research projects, and IRBs, in considering and reviewing research projects and in conducting continuing review, should consider how the research design might focus not only on the identified human subjects but on other persons as well. In cases in which a research project's design collects a significant amount of private information in identified form on third parties, the investigator and IRB should consider whether any of these third parties should be regarded and treated as research subjects themselves.

In making this determination, IRBs should consider the following factors, among others:

- the quantity of information collected about the third party;
- the nature of the information collected, including the sensitivity of the information collected and the possibility that such information might cause harm to the third party;
- the ability of investigators to record information on third parties in a manner that protects the identity of those parties;
- the possibility that classification of a third party as a human subject may have an impact on the rights or welfare of the originally designated human subject and requires the IRB to deal with this issue to protect the interests of both the original human subject and the third parties.

Source: National Human Research Protections Advisory Committee, Washington, DC.

Group advocates HIV-positive fertility assistance

A person's HIV status should not necessarily preclude them from receiving assisted reproductive technologies to have children, according to new ethical guidelines developed by the Birmingham, AL-based American Society for Reproductive Medicine (ASRM).

The standards issued in February by ASRM say therapies now exist that can greatly reduce the risk of passing HIV, the virus that causes AIDS, to the baby.

However, they do not encourage HIV-infected couples to have children and caution that physicians should ensure that parents understand their baby could be infected, regardless of what precautions are taken.

Since 1994, the group's ethics guidelines have discouraged fertility treatment if a potential parent has HIV. The risks of infecting the unborn child were too great.

Special care can reduce risks

Today's therapies allow many HIV patients to live longer, healthier lives, and most patients are in their prime childbearing years. Special prenatal care can greatly reduce — although not eliminate — the risk of infecting a baby, the society's ethics committee concluded.

According to the Centers for Disease Control and Prevention, an estimated 200-300 infants are born with HIV each year, most thought to have been born to mothers improperly tested or treated for HIV.

The fertility society's new guidelines, available on-line (www.asrm.org) state:

- Appropriate drug therapy, a cesarean, and no breast-feeding drops an HIV-positive pregnant woman's chances of infecting her baby from 20% down to about 2% — but the risk isn't zero.
- If only the potential father has HIV, both mother and fetus could be infected. Unprotected intercourse is not safe. Special sperm washing and testing before artificial insemination appears to greatly reduce risk, but more proof is needed. Couples should be counseled about considering donor sperm, adoption, or not having children.
- If both potential parents have HIV, they must be counseled about the risk of infecting and/or orphaning a baby.

Many couples at risk for genetic diseases, such as cystic fibrosis, attempt conception despite a 25% chance of having an ill child, the guidelines note. Fertility specialists who treat those couples also "should find it ethically acceptable to treat HIV-positive individuals or couples who are willing to take reasonable steps to minimize the risks of transmission." ▼

DA in hockey dad case blocked heart donation

The family of Michael Costin, the Massachusetts man who died after being knocked unconscious in a fight at a hockey rink in July 2000, had wanted to donate his heart, but was prevented from doing so by the district attorney prosecuting the man accused of causing Costin's death.

According to a report in the Jan. 25, 2002, *Boston Globe,* Middlesex District Attorney Martha Cloakley blocked the donation of Costin's heart after he was declared brain dead because she wanted to prevent the possibility for allegations that Costin could have died from a pre-existing heart condition rather than the beating.

Surgeons express dismay

Transplant surgeons have expressed dismay that the organ was withheld, saying that doctors would not have accepted an organ that was not healthy and that there was ample evidence to indicate that Costin's death was caused by brain swelling brought on by internal bleeding.

"With heart transplants, it's literally a life-or-death situation," **Lachlan Furrow**, MD, a general internist and director of the ethics program at Boston-based Beth Israel Deaconess Medical Center, told the newspaper. "It's very, very likely that, because of this decision, someone with heart disease died. I think it's tragic."

But some ethicists said the interests of justice should hold equal value with that of saving lives.

"There's an obvious value in saving lives using donated organs," argues **Ronald Munson**, PhD, professor of philosophy and science and medicine at the University of Missouri-St. Louis. "But there is also the interest in making sure we have all the evidence necessary so that justice is served. As useful as it is to have these organs for donation, indeed to save lives, we may have to make an

exception here to let justice be done, realizing the price we are paying." ▼

Prisoner heart transplant renews scarcity debate

A California prison inmate serving 14 years for robbery received a heart transplant in January, turning up the heat in the debate over who should get desperately needed, but scarce, human organs. And whether patients who have committed crimes against society "deserve" to receive transplants paid for with taxpayer funds.

The transplant, paid for by the California Department of Corrections, is expected to cost $1 million with follow-up care, and occurred as 500 Californians waited for hearts, according to the *Associated Press.*

The operation saved the 31-year-old inmate from dying of a viral heart condition, says **Russ Heimerich**, spokesman for the California Department of Corrections.

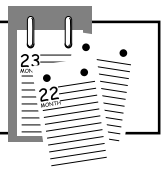
Citing two court rulings in favor of inmate care, Heimerich said, "Our hands are pretty much tied. It's not a question for this department to decide."

A 1976 U.S. Supreme Court ruling held that it is "cruel and unusual punishment" to withhold necessary medical care from inmates. And in 1995, a federal court ordered prison officials to give a kidney transplant to an inmate whose request had been denied.

In addition, the ethics policy of the United Network for Organ Sharing, the organization that oversees the national transplant organ network, outs prison inmates on equal footing with all other patients.

The patient is currently in satisfactory condition at a prison medical facility near San Francisco. ■

CALENDAR



• **Human Research Protections Workshop — May 5, 2002.** Renaissance Stanford Court Hotel, San Francisco. Sponsored by Friends Research Institute. For more information, contact: Friends Research Institute, 505 Baltimore Ave., P.O. Box 10676, Baltimore, MD 21285. Telephone: (410) 823-5116. Fax: (410) 823-5131.

• **Ethics of Research with Children — May 5-7, 2002.** Renaissance Stanford Court Hotel, San Francisco. Sponsored by Friends Research Institute. For more information, contact: Friends Research Institute, 505 Baltimore Ave., P.O. Box 10676, Baltimore, MD 21285. Telephone: (410) 823-5116. Fax: (410) 823-5131.

• **Certification examination for IRB professionals — Oct. 19, 2002.** Sponsored by the Council for Certification of IRB Professionals, a division of Public Responsibility in Medicine and Research (PRIM&R) and Applied Research Ethics National Association (ARENA). Examinations are administered through Professional Testing Centers in New

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Vice President/Group Publisher: **Brenda Mooney**, (404) 262-5403, (brenda.mooney@ahcpub.com).
Editorial Group Head: **Coles McKagen**, (404) 262- 5420, (coles.mckagen@ahcpub.com).
Managing Editor: **Kevin New**, (404) 262-5467, (kevin.new@ahcpub.com).
Production Editor: **Nancy McCreary**.

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Editorial Questions

Questions or comments?
Call **Kevin New** at (404) 262-5467.

York City. Fees are $300 for ARENA members and $400 for non-ARENA members. Regional testing centers will be available in 17 states, including the District of Columbia and Canada. Application deadline for the Oct. 19 examination date is Sept. 1, 2002. For more information, contact: Professional Testing Corp., 1350 Broadway, 17th Floor, New York, NY 10018. Telephone: (212) 356-0660. E-mail: ptcny@ptcny.com. ■

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. ■

CE/CME*questions*

9. The Office for Human Research Protections (OHRP) states that no informed consent, whether oral or written, may include any exculpatory language through which the subject is made to waive or appear to waive any of the subject's legal rights. Which is an example?

A. By agreeing to this use, you should understand that you will give up claim to personal benefit from commercial or other use of these substances.
B. Tissue obtained from you in this research may be used to establish a cell line that could be patented and licensed. There are no plans to provide financial compensation to you should this occur.
C. I voluntarily and freely donate any and all blood, urine, and tissue samples to the U.S. government and hereby relinquish all right, title, and interest to said items.
D. By consenting to participate in this research, I give up any property rights I may have in bodily fluids or tissue samples obtained in the course of the research.

10. As the nation prepares for possible bioterrorism threats, what are some of the ethical considerations that IRBs will need to consider during a push for new vaccines?

A. It would be unacceptable for the government or researchers to use volunteers who are institutionalized for mental disability as happened during World War II when the yellow fever vaccine caused jaundice among servicemen.
B. Participants in small clinical safety trials will need to be fully informed that the vaccine may cause an adverse effect and that it may not provide them with adequate protection against infection.
C. IRB members will need to insulate themselves against public opinion pushes to get a vaccine on the market faster than might be done when all human subjects protections are employed.
D. All of the above

11. Which of the following is not one of the OHRP's guidelines about tissue procurement?

A. Procurement would not be considered human research if the material in its entirety was simply collected for unrelated clinical purposes.
B. Procurement would not be considered human research if the material has been stored for more than 10 years.
C. Procurement would not be considered human research if the material is collected for legitimate but unrelated research purposes, and the material is submitted without identifiable private data or information.
D. All of the above

12. What human subjects transgressions occurred with the "Lynchburg" (VA) incident?

A. A tainted antibiotic was given to members of a Lynchburg mental institution in the 1940s.
B. To find out what was wrong with a World War II yellow fever vaccine, government health officials intentionally inoculated healthy people at a Lynchburg facility for the mentally disabled.
C. Lynchburg was the site of a recent Ebola outbreak among primates, and employees of a research facility were given an untested vaccine that resulted in serious illness among 25 people and one death.
D. None of the above