PROTECTING HUMAN SUBJECTS

U.S. DEPARTMENT OF ENERGY, OFFICE OF BIOLOGICAL AND ENVIRONMENTAL RESEARCH

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Ethnography & consent 3

News notes 4, 11

Challenging HIV case 5

Compliance vs. ethics 7

Compliance & ethics 9

What subjects hear 10

Investigators & IRBs 12

Web sites 14, 17, 23

Universal ethics? 15

CITI is international 18

Shifting the emphasis 19

Different thinking 21

Sometimes challenging relationships

This edition of *Protecting Human Subjects* focuses on the various and sometimes difficult relationships encompassed by the effort to protect people in research settings. These include the relationships between Institutional Review Boards (IRBs) and investigators, between investigators and other cultures, and between subjects and investigators in challenging situations. Many of these relationships were discussed at the last PRIM&R/ARENA meeting. We have included updated highlights of some of those talks because they raised concerns and suggested ideas that we think deserve further discussion.

In some ways this is a continuation of discussions begun in the last edition, which considered ways that can either assist or impede communication related to the IRBs' effort to protect research subjects.

This time, however, we focus on a different set of issues, beginning with the front page account about the necessity of understanding cultural differences when working in traditional societies. Another article, by **Penelope Eckert** of Stanford University, suggests that in some settings it might be necessary to think about informed consent as an ongoing process that unfolds gradually, over time.

In addition to her account of consent in ethnographic studies, what you will read here includes debates about whether the research community focuses too much on following regulations, and thus fails to fully understand the ethical dimension of its work. Others argue that following regulations is the most certain way to ensure ethical behavior. The back and forth of the discussion in these articles is intended to stir the community toward both reflection and better communication.

A primer: Doing research in traditional cultures

To understand, investigators must listen with their sixth sense

In health care systems, we're dealing with cultural ideas about the origins of disease and the implications of different understandings about those origins. To understand the ideas that another culture has about origins of disease, it is necessary to realize that their ideas may be different from yours.

If you are working in an IRB, this understanding comes about only by recognizing that because of differences in backgrounds and cultures, it is necessary to listen, listen, and listen again, not just with our five senses, but with a sixth sense—listening with your heart.

Nhlanhla Mkhize

This might involve temporarily suspending your own position, even when you think you are right.

As human beings, we cannot act without employing background knowledge, which is that knowledge that informs our decisions. Some call it culture; others refer to it as a world view or our various versions of reality. This is knowledge passed down

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*This article is by **Nhlanhla Mkhize**, who delivered a similar version of it as the keynote address at the last PRIM&R/ARENA meeting. He is a lecturer in the School of Psychology and the Southern African Research Ethics Training Initiative, University of KwaZulu-Natal, in South Africa.*

from generation to generation through which people make sense of themselves and their world. This cultural inherited knowledge includes language, values, and ideas about health and illness.

Cultural knowledge is dynamic
In addition, cultural knowledge is dynamic; we are constantly exposed to new information, which may result in old patterns of understanding being deleted or understood in different ways. In this way our minds shape and reshape the way we think about the world.

Further, some cultures think differently about the world than do others. Some view time as an end; others consider relationships an end. There are additional differences in notions of causality and orientation to nature.

Investigators must understand that traditional conceptions of medicine and disease employ dual understandings.

A health care system is a socially organized response to disease. It includes the culture's social reality, which is how roles are defined and transactions enacted, as well as the culture's beliefs about illness.

In some cultures, for example, people do not question doctors or other people in authority. This can have important implications for the ethical conduct of research. Investigators need to know how people in that culture relate to those in authority, to younger people, to older people, to women.

Two models
The explanatory model the researcher has in mind doesn't necessarily have to correspond with the model the patient or the subject has, but it is important to find out whether the two models are alike or not.

If you are an IRB member, it is important to ask whether the researcher has taken into consideration the various possible models of health care that might be found in a community. Ask, for example, about plans to minimize the effects of differentials in power and authority. These differentials may show up in whether the health care model encourages patients to ask questions or merely to accept the orders of the physician. In the former, differentials in power and authority are minimized. In the latter, differentials are emphasized.

Keep in mind, as well, the clinical realities that result from differences in beliefs about the causes of illness. Those in the West are accustomed to certain ideas about causation, but there are other beliefs out there. The traditional African view of illness is holistic; there are both a physical and a psychic component existing simultaneously.

This isn't unique to Africans. In many developing societies, 80% of people rely on this understanding, and, even in industrialized populations, biomedical science acknowledges that some 60% of illness has psychosocial origin. This is why the placebo effect can be so effective.

Socio-spiritual illness persists over a long time because it does not respond well to treatment.

Dual understandings
Investigators, therefore, must understand that traditional conceptions of medicine and disease employ dual understandings. Some things are caused by germs, others by social or spiritual transgressions. People move between these systems all the time. They take illness to the medical healer as well as to a traditional healer, depending upon how the illness is being defined at the time.

Biomedical illness is thought of as normally of short duration and responding to treatment by medical doctors. But socio-spiritual illness persists over a long time and recurs because it does not respond well to treatment.

The implication for ethical conduct of research is that it is necessary to have a plan that takes these conceptions into consideration. How will it influence your research? What will you do if people stop taking your drug and begin moving to a different health care system?

Different conceptions of personhood
Similarly, differing concepts of personhood can influence reality. The Western concept is of a rational, autonomous self that is separate from others, self-contained. The focus is on internal psychological attributes such as thoughts and emotions (e.g., **Descartes'** "I think; therefore I am."

In the event of illness, the individual is treated alone and is relatively free to make autonomous decisions. Thus the ethical decision-making model is guided by abstract, universal principles.

—Continued on page 22

This article is by **Penelope Eckert**, who delivered a version of it during an address at the last PRIM&R/ARENA meeting. She is a professor of linguistics at Stanford University. She is the author of *Language and Gender* (with **Sally McConnell Ginet**), *Linguistic Variation as Social Practice*, and *Jocks and Burnouts: Social Identity in the High School.*

Consent as an ongoing process

Slowing down ethnographic studies to develop a long-term relationship

Consent is a process that unfolds gradually between individuals, but that is also embedded within a community. This should be kept in mind as researchers work out how to maintain healthy relationships with subjects, and IRBs should be keeping it in mind as they help researchers.

I am struck by the constant reminders that IRBs don't take sufficient use of the option to waive signed consent for research in the behavioral sciences. The slavish use of consent forms serves to alienate researchers and to mystify subjects.

Penelope Eckert

Consent as conversations

More importantly, focus on consent forms distracts us from maintaining open relationships with our subjects. We need to think of consent not as a thing but as a process, not as a form but as a series of conversations, actions, and understandings.

The slavish use of consent forms serves to alienate researchers and mystify subjects.

My research is ethnographic, so it isn't a matter of a moment or an hour spent with a subject or a specific task I ask a subject to perform. Rather, it is an ongoing relationship with multiple individuals and embedded within a community.

Research activity will have an effect on people's relationships within the community. The things that get said one-on-one are just the tip of the iceberg. In my work in a small village in the Pyrenees of France, I encountered the belief that the German philologists who had worked there in the 1930s were precursors to the Nazi invasion. This made me a potential spy—particularly since it didn't make sense to many of the inhabitants of the village that I would come just to learn their dialect. As a result, my every research move entered a larger community discourse.

Altered relationships

More importantly, when we work in other cultures, we don't know in advance what subjects will view as the risks of our research. Neither do we know that they will understand or share our objectives. What people do willingly may have unexpected repercussions, affecting not just their relationship with me, but with others.

While one woman enjoyed an interview with me, her husband became angry at her when he learned that we had discussed the war years—a time of considerable conflict in the village. While the woman was confident that what she had said would not go beyond me, her husband, who didn't know me as well, wasn't so sure.

I recently did an ethnographic study of elementary school kids as they moved through to eighth grade. At the beginning of the project, when I told them what I was going to do and how I would do it, that was the beginning of a project-long discussion, a conversation kept alive throughout.

It was a community-embedded consent that required me to slow down and learn what subjects expected from our interactions, including how that squared with what I anticipated.

Continuing renewal of understandings

Further, when the project continues for a long time, it is necessary to renew the understandings as we go along. This creates an ongoing process of continuing informed consent.

For example, when a girl tells me about losing her virginity, we need to have the same understanding of the nature of the interaction. We both need to

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know that I'm not a good friend who will be impressed by her story, or a clinician who can help her work out any issues involved, or that simply listening necessarily signals approval (or disapproval).

Beginning of exploration

The review process should be asking researchers to try to figure out these issues in advance, but it also should incorporate an understanding that this advance understanding should be considered only a beginning of exploration.

How can the IRB help researchers pursue consent as a process of continual discovery? For one thing, don't stress the forms. Instead, ask how the form fits into an overall plan to maintain a consensual relationship.

Stress the open question of how the community views risk as well as how it views the researchers' goals and procedures. Stress the need for time to build this into the project.

In addition, work with investigators in the same way you want them to work with human subjects. The review should be a conversation, not a set of procedures. Help the investigator move away from the view of consent as a ticket to get on with it.Δ

News notes

Most-frequent research "misconduct" aren't the high-profile varieties

The most frequent varieties of research "misconduct" are not the result of fabrication, falsification, and/or plagiarism. Instead, researchers in Minnesota say their survey of 1,500 scientists whose work had been financed by the National Institutes of Health reported that most questionable practices involve behavior such as interpreting data in a questionable way, using inaccurate or inappropriate research designs, and changing study methods to satisfy a sponsor.

The survey results were reported by **Cornelia Dean** in the June 14, 2005, *New York Times*. The researchers said "mundane 'regular' misbehavior" threatens the integrity of science more than the occasional high-profile case.

"Our findings reveal a range of questionable practices that are striking in their breadth and prevalence," say the researchers, **Brian C. Martinson** of Health Partners Research Foundation in Minneapolis, **Melissa S. Anderson** of the University of Minnesota, and **Raymond de Vries** of the University of Minnesota and St. Olaf College. The survey was limited to biomedical research.

The *Times* article reported that 70% of midcareer scientists surveyed said they had applied funds from one research grant to another project. "The federal government frowns on this," **Martinson** said, but "scientists don't think it's wrong. They see it as a way of getting the best and the most research out of the dollars they have available to them."

Martinson, a sociologist, told the *Times* that his work on the issue grew out of his interest in how scientists respond to the pressures of high-level research and the stress of obtaining money to pay for it. "A lot of the behaviors we are looking at fall into that category—the ways you have to behave if you are going to continue to get funding," he said. "Does that make them right? I don't know."

Some of the survey results are ambiguous, he said. For example, one of the issues is inappropriately assigning authorship credit. This may mean that someone who contributed minimally to a report was listed as a coauthor, a common practice among scientists. But it may also mean that scientists allowed themselves to be listed as the authors of a paper ghostwritten by a commercial sponsor.

A challenging case

How should an IRB rule when a protocol calls for using an extremely vulnerable population: the dying?

The following debate was presented at the last PRIM&R/ARENA meeting. **Robert Levine**, professor of medicine at Yale University School of Medicine, moderated the session.


George Agich

He presented the case to be debated as a proposed Phase I protocol to test the efficacy of an AIDS vaccine. It is a highly toxic drug administered to a patient near death. It is hoped that the drug can be used to prevent infection, but the risk is that the subject could be infected with HIV.

The ramifications of this risk can be reduced greatly by selecting subjects unlikely to live long enough to develop AIDS. (Issues related to this are also discussed in **Rebecca Pentz**, et al., [2003], "Revisiting Ethical Guidelines for Research with Terminal Wean and Brain-Dead Participants," *Hastings Center Report* 33.1, 20-26.)

Yes, approve the protocol

George Agich *argued the position in support of the protocol. He is professor of bioethics, Cleveland Clinic, Lerner College of Medicine, Case Western Reserve University, Ohio.*

The goal of protecting human subjects is to protect their welfare and their rights, as well as to think about minimization of harm in light of benefits.

Are these proposed subjects situated in a way that they will be used in a way that is unethical?

An AIDS vaccine has the possibility of benefit, so risk is appropriate. An objection, however, is that the proposed subjects are vulnerable. But are they? Are they situated in a way that they will be used in a way that is unethical?

Minimization of risk is structured by choosing a population for whom the risk of contracting the virus isn't the most significant risk—it's developing AIDS. So even if the vaccine fails and the patient is infected, he or she expects to die of another disease before AIDS manifests.


David Smith

Is there social benefit? Yes. Thus, the use of this population is justified.

Patient rights?

Many think terminally ill patients are especially vulnerable. But in a way, we think of all subjects as vulnerable. Some populations are incapable of consent. Are there people at the end of life for whom the opportunity to participate in a study that would have tremendous social benefit would give them a sense of satisfaction? Should that be denied because of our squeamishness about exposing them to a virus?

We should preserve the subject's choice to make altruistic choices. I'd like to remind you of **Victor Frankl's** book, *Search for Meaning*, in which he says that even at death, even in the Nazi death camps, people look for meaning. Thus, getting valid consent in these populations isn't unusually problematic. Further, if the subjects are carefully selected, we'll be in a better position with this population than another, for whom we have no reason to think they won't live long enough to develop AIDS.

No, reject the protocol

David Smith *argued against approval. He is Frederick's Distinguished Visiting Professor of Ethics at DePauw University and Nelson Poynter Senior Scholar at Indiana University.*

The case for using these persons as subjects hinges on two claims: First, choosing to make oneself a partner in research is a liberty that competent people should have.

Second, denying people the right to invest their lives in the search for medical progress is patronizing and paternalistic. The fact that someone is dying — or that good guesses can be made about the length of the person's life — is not a good reason to exclude that person from serving as a subject in a

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risky experiment. The desire to do something important may increase at the end of life.

I don't want to argue that no person with less than a year to live could ever be a legitimate subject in a vaccine test.

Fraught with problems

In this case, however, the patients with a short life expectancy are the target subject pool. I argue that they should not constitute or delimit the pool. Their use is fraught with problems that make my moral antennae twitch.

Let's focus on the question of why these particular subjects are chosen. Forty years ago **Hans Jonas** argued that the basic issue experimentation raises is the conflict between the individual and the community.

Society can't survive without people's confidence that they will be treated fairly and with respect.

We can separate these conflicts into two types. In type one, society faces a threat to its existence, such as invasion or epidemic. **Jonas** argued that with stakes this high, society can legitimately coerce people to run a risk on its behalf, to override individual choice or reluctance to live one's own life. This argument justifies a military draft or compulsory vaccination. The stakes transcend individual rights.

If the threat is less grave, we can't coerce and must rely on volunteers. **Jonas** saw medical progress as less than necessary. It's a good, but a "gratuitous good." Society can get along without medical progress, he claimed, but it can't survive without people's confidence that they will be treated fairly and with respect. Moreover, he noticed that all consents aren't created equal.

The more someone understands the point of an experiment and is committed to working on the problem, the more legitimate is the consent. The less one is able to understand the risk, the less valid is the consent. **Jonas** said experimenting on a comatose person in ways not related to his or her disease is forbidden. "Utter helplessness requires utter protection."

So, is this research necessary? Is it in a different category than ordinary medical research? It may be. We refer to the AIDS pandemic. If we think about developing a successful AIDS vaccine as a matter of necessity, how should subjects be chosen? On **Jonas**' terms we should seek the subject pool likely to give us the best results, as we would in time of war.

According to those standards, these subjects as subjects are suboptimal because they are already weakened and not in good health. We fall back on this strategy because we want to have the benefit from the argument from necessity without paying the price. That is, we want the magnitude of threat to justify fudging the guidelines but don't want to be seen as forcing anyone to do anything. That's disingenuous.

Therapeutic misconception

I wouldn't say that none of these subjects could be subjects, but there are additional problems related to the therapeutic misconception. The subjects may blur the difference between their condition and this research.

These are particularly vulnerable subjects from whom securing authentic consent will be very difficult if not impossible.

Moreover, they may think that as research subjects, they may receive better treatment than they would as a regular patient; "I'll go along with them and they'll look out for me down the road."

These are particularly vulnerable subjects from whom securing an authentic consent will be very difficult if not impossible.

Furthermore, there is an inevitable uncertainty about the predictions on which the selection is based. What would one say to a patient who lived long enough to develop AIDS?

Conclusion

If this research is necessary, in the rigorous sense of that term, then we should target and draft the best possible subjects, which are those who are robust, healthy, and unlikely to have compromised immune systems—not unlike those we'd want to draft into the army in time of war.

If it is not necessary, the pool should be opened to anyone who may choose to participate. If appropriate safeguards are in place, some persons who are dying may be found to have given authentic consent. Allow them in, yes; target them, no.Δ

Has compliance eclipsed ethics?

Should we expect serious ethical consideration or give up and admit that regulations are the only hope?

This debate pits bioethicist **Nancy Dubler** against attorney **Mark Barnes**. Regulations sometimes are seen as supplanting moral judgment. But are regulations really the best way to ensure at least an adequate consideration of the ethical dimension of protecting human subjects? This is the debate.


Nancy Dubler

***Nancy Dubler** is director of the Division of Bioethics at Montefiore Medical Center and professor of Epidemiology and Population Health at the Albert Einstein College of Medicine, Bronx, New York.*

***Mark Barnes** is a partner in a New York law firm. He has long been involved in troubleshooting for institutions dealing with ethical problems in research settings.*

Ethics: a more generous spirit

Nancy Dubler

There is a clear difference between ethical consideration and mere compliance. Compliance assumes the letter of the law; ethics assumes a more generous spirit.

Notions of appropriate research have evolved over the last three decades as bioethics has grown as a field. The National Research Act, passed in 1974, was the first attempt to articulate national guidelines for research.

At the same time, bioethics was struggling to develop from a nascent idea of how doctors, patients, research centers, and hospitals did relate to each other to decide how they should relate to each other. Bioethics was, too, struggling to move from description to normative behavior.

In this search for rules and principles, certain milestones appeared. One was the publication of **Beauchamp's** and **Childress's** book, *Principles of Biomedical Ethics*, which argued that autonomy, beneficence, nonmaleficence, and justice were the principles that should undergird the relationships.


Mark Barnes

Two philosophical systems

These foundational bioethical scholars argued that if a conflict arose, resolution of the conflict would emerge in the balancing of these values to determine the appropriate order in any particular case. The origins of these principles, they argued, could be found partly in the philosophical system of consequentialism—how do you do the best for the greatest number of people—and also partly in the other great philosophical system of deontology—what are our inherent duties and obligations to each other?

As these analyses were emerging, the legal system became a player in developing rules for caring for patients. In 1976, the New Jersey Supreme Court decided the case of **Karen Ann Quinlan**, which held that a guardian could decide to withdraw or withhold care from a patient who could not make a decision for herself, thereby permitting the patient's death.

> *Enshrining autonomy is an excellent beginning but misses the basic facts of human relationships.*

These two areas, law and philosophical analysis, have traveled as colleagues and disputants ever since as we have sought to identify and protect the interests and rights of subjects and patients.

Feminist scholars

Then, in the late 1980s and early 1990s, feminist bioethics scholars such as **Susan Sherwin, Rosemarie Tong,** and **Jennifer Parks** argued that philosophical and legal principles that enshrine autonomy are excellent beginnings but miss the basic facts of human relationships.

People, if they're lucky, aren't isolated, autonomous beings existing in a bubble of singular decision-making authority. They are persons, related to those who love and interact with them.

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Hence they said the basic notion of medicine isn't only autonomous decision-making but rather relational decision-making. Many feminist scholars also began to talk about race and class and power—issues perhaps more evident to women, who may tend to be more disempowered and marginalized than empowered white males who largely began these discussions.

During the last few years, still another voice has become powerful in the growing discussions. These are mostly physicians, writing about narrative medicine. They argue that conflicts are not resolved solely by principles, but by discussion, engagement, finding options from which to choose, and crafting a consensus based on narrative and relationship.

Adversarial relationship

Problems began to arise, says the physician and philosopher **Rita Charon**, when the doctor-patient dyad came to be conceived as adversarial. Contractual safeguards were crafted to protect one from another, including advance directives, IRB protocols, the informed consent process, and conflict of interest disclosures.

Problems began to arise when the doctor-patient dyad came to be conceived as adversarial.

Bioethicists joined licensing boards, insurance companies, and hospital overseers in building tort-based law furthering the project of controlling doctors and protecting patients.

Many of these protections were needed to control the abuse of power and deviations from quality care, and medicine, as a whole, is safer than it otherwise would be. Nonetheless, thinking of medicine as an adversarial enterprise has hurt the enterprise deeply.

Substantial conflicts of interest

I understand that there are more substantial conflicts of interest now in research than there were in the 1970s. These conflicts affect the behavior of institutions, sponsors, and principal investigators. Because of these critical issues, we must have clear regulations to protect human subjects.

However, as **Charon** points out, the adversarial nature of the relationships has constrained the vision we bring and the form we assume for our obligations to research subjects. This is not always productive. It does not ground the most robust discussion of the ethics of research with human subjects.

Members of IRBs should consider it a privilege and an honor to be part of committees whose goal is to protect human subjects. But that's not how most IRB members conceive of their task. Most IRB members are not compensated for the enormous amount of work that committee membership entails. They are underappreciated. And, most importantly, they work in a milieu that too often values compliant practice rather than best practice.

Some consent processes are barriers

These two, *compliant* and *best* practice, conflict especially in approaching the review of informed consent documents, which are supposed to assist subjects in understanding.

But a 16-page, single-spaced, lawyer-driven document is not an assist; it is a barrier. Its purpose should not be to protect the sponsor or the institution, and yet too often the process of consent has been captured by those two groups.

The regulations do not shape the end of the discussion, but they outline the beginning analysis without which a hardy contemplation of the ethics of research would not be possible.

Regulations are the best hope

Mark Barnes

Nancy has said regulations are the floor and that there is something above the floor: ethics. In the real world of research, however, ethics are not always apparent. So let there at least be compliance.

The bad cases

I see the real world because I'm the one who gets called in for the bad cases, when researchers do bad things: having conflicts of interest, ignoring regulations, doing research solely to make money, delegating consent to graduate students, failing to report serious adverse events such as death, and using informed consent only to protect the investigator, not to give choices to patients and subjects.

I'm the one who gets called in for the bad cases, when researchers do bad things.

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This leaves me at a loss to know what we're talking about when we think there's going to be an ethics discussion. That's too often the last thing on the mind of some hospitals, research centers, and researchers. So if they're not going to do ethics, then let them at least embrace the rules. Where there are no ethics, let there at least be compliance.

Regulations force ethical behavior

Consider the Health Insurance Portability and Accountability Act (HIPAA) regulations, for example. They're a mess, especially when applied to research. The Common Rule says we're supposed to look at how the privacy of patients will be protected.

But how many truly did that before HIPPA came along? The regulations are faulty, but they have forced us to address something we should have been addressing a long time ago, partly because the Common Rule says we should have addressed it, and partly because addressing privacy is an obvious concern of basic research ethics. The HIPAA rules, however, have forced us to comply with standards of ethical behavior.

So, instead of denigrating the various rules, instead of thinking they're our enemy, we should embrace them. In most cases the rules at least state clear standards. There are experts at the agencies who know what they're talking about. Remember, the alternative is to let nonexpert courts make the decisions.

This doesn't mean we should not take a critical eye to the regulations. We should look at them very carefully. But I believe the people in the federal agencies are willing to listen.

Sleep at night

Let me tell you why compliance and embracing regulations are important: they allow us to sleep at night because we have a sense of legal safety. At least the regulations have clearly articulated standards for what researchers and IRBs are expected to do.

The alternative—to rely entirely on ethics and vague standards—is more likely to end us up in court, where we would not be able to point to clear standards for our behaviors toward research subjects. Subjects, along with everyone else, have access to the regulations. If we have compliance and respect for legal standards, at least the agencies will be there to back us up.

The regulations we follow are those that the agencies have said are appropriate. Research regulations have predictability and transparency, express social consensus, and are an aid to those of us who want things to be better. They help us promote best practices. Investigators too often view these regulations as mere "make-work," as rules too difficult to follow.

Researchers who feel that way should check their premises. The rules are there to express and to assist in the implementing of the first ethical principles, those articulated by **Beauchamp** and **Childress** in the book **Nancy** cited. If we follow them, they can be our salvation and our safety.Δ

Neither ethics nor regulations alone

In the following discussion, ***Bernard Schwetz****, director of the Office for Human Research Protections in the U.S. Department of Health and Human Services, provides a response to the positions taken in the debate about whether regulations have eclipsed ethics.*

Neither ethics alone nor regulations alone are sufficient to allow the research enterprise to do what is expected of it.

The regulations we now have are based on principles spelled out in the Belmont report, and so they are an attempt to combine both elements: ethics and regulations. However, the question we are beginning to ask is whether we have begun focusing too much on the regulations and forgotten the importance of the principles spelled out in the Belmont report?

Outdated regulations

One example of the difficulty we face is that we are using regulations that are now 20 to 30 years old. Yet the world is a very different place today. It is more complex.

We face new problems and new circumstances. Informed consent, for example, should be a critical process for safeguarding research subjects. Too often, it is now being employed primarily as a vehicle for protecting institutions against lawsuits.

Many years ago we had informed consent documents that were just one to two pages long, which made them easier to read and thus more likely to be read completely. They were short and were concerned almost entirely with

—Continued on page 20

What do researchers say?

What do subjects hear? Not what they would like to hear. What do subjects need? More information.

By Gigi McMillan, director and cofounder, We Can, Pediatric Brain Tumor Network of Southern California

As director of *We Can, Pediatric Brain Tumor Network,* I have spoken with hundreds of families over the last eight years. Most of these parents were considering enrolling their children in a clinical trial or had already done so.

Their stories are remarkably the same. I can tell you from my personal experience as the parent of a child with cancer and on behalf of scores of other parents that we desperately want to hear and understand what the researcher is telling us, but sometimes we cannot. I suggest three reasons for this difficulty:

Gigi McMillan

The first area of difficulty lies in the fact that subjects (and their caregivers) are emotional, at times desperate. If they have only recently learned of a serious medical problem, they may be in shock, angry, depressed, or frantic.

Desperate for cure

If they have been living with their disease for some time and previous treatment has not worked well for them, they may be desperate for a cure. These emotions are persistent background noise and can short-circuit the ability to absorb information and make rational decisions.

Use lay language and allow for multiple, even repetitious explanations.

We Can parents describe leaving a long consultation with a team of doctors and not remembering a word that was said. In many cases, each parent assumed the other would take the lead on asking questions and recording answers, when in fact, neither was in any condition to do so.

One mother said, "I watched his [the doctor's] mouth move, but in my head all I could hear was my own voice repeating, 'Omygod, omygod, omygod.'"

Potential subjects and their caregivers need to process their emotions in a way that is appropriate to their circumstances. They may simply need time to absorb information and impending changes in their lives. They may need the help of family or other people in their immediate social circle.

They also may need professional counseling. Sometimes a referral to a support group would be of great help. The primary investigator or a member of the research staff should make the referrals accordingly.

Medically uninformed

The second area of difficulty is that potential subjects are medically uninformed; they may not have had time to learn the basic medical facts about their condition.

We Can families express frustration at their inability to have a productive discussions about standard-of-care treatment in comparison to research scenarios. Keeping track of new vocabulary, unfamiliar medical procedures, and treatment schedules while trying to grasp prognosis and quality of life issues is nearly impossible.

We Can members report being able to absorb information only in small pieces. Sometimes it takes several contacts with the doctor or the research staff before a common foundation of knowledge is in place to facilitate a meaningful conversation.

One parent recalls, "When we first met the physician, we called the cancer by the first letter of its official name because we couldn't pronounce it or even spell it out in our notes. By the third visit, we not only could call it by its proper name, we were discussing various combinations of chemotherapy with relative ease."

A researcher must take care to use lay language and allow for multiple, even repetitious explanations. Visual aids should be offered. In addition, the potential subject should clearly understand who to contact if they have questions about their medical condition. By giving the subject command over the

vocabulary of their disease and introducing them to the larger perspective of their medical situation, the subject will be better able to participate in the consent process.

"In my head all I could hear was my own voice repeating, 'Omygod, omygod, omygod.'"

The third area of difficulty is that subjects are inexperienced with the process of clinical trials. They need a basic understanding of the study, the consent process, the rights of a subject, and of the kind of support available to them for the duration of the trial.

Educating them about formal guidelines that are in place to protect them as subjects and explaining the larger, often national, operation of clinical trials empowers the subject. It encourages a greater sense of responsibility and cooperation with the goals of the study.

Says one father, "We didn't want our daughter to be a guinea pig. The more we got to know the physician and the more we learned about the trial, the more we felt like we were participating in an intelligent scientific process."

If a researcher takes the time to acknowledge the emotional state of the potential subject and educate the family about the medical condition and how clinical trials work, there is greater likelihood of successful study participation.

A researcher's job?
It may not seem to be the researcher's "job" to handle these aspects of the subject's experience, but it is appropriate and often necessary. The researcher is often one of the doctors with whom a subject will spend a fair amount of time. Because of this relationship, it is appropriate for the researcher to offer basic information about the subject's illness. In the third instance, educating the subject about the clinical trial process clearly falls within the purview of the researcher and study staff.

We Can families consistently describe their need for guidance and their desire to forge a relationship built on trust and understanding. The physicians have research studies in which they want us to participate. It is their responsibility to get us to a place emotionally and intellectually where we can truly cooperate. As they meet our needs and earn our trust, they gain willing participants.Δ

News notes

Discussion paper: Research ethics in developing countries

The Nuffield, England, Council on Bioethics has published another in a series of discussion papers related to international research issues. The paper, "The ethics of research related to healthcare in developing countries," is available at ***http://www.nuffieldbioethics.org***.

The council says that applying international guidance on healthcare-related research in developing countries in practice is often fraught with difficulty. Existing guidelines are often inconsistent and inappropriate for the developing-country setting.

"When the guidelines were compared, we found that they are markedly inconsistent in some areas," said one of the authors, **Professor Peter Smith**, Department of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine. "In addition, faithful adherence to some of the provisions within the guidelines is often unachievable."

Readers of Minority Engineer *say DOE among best employers*

Readers of *Minority Engineer* recently were asked to name the organizations for which they would most like to work, or that they believe would provide a positive working environment for members of minority groups. Results are listed on the Equal Opportunity Publications Web site ***http://www.eop.com/metop50.html***. DOE placed 8th among government agencies, and Sandia and Argonne national laboratories both made the top 20.

"Inefficient, arbitrary, inconsistent"

A frank look at how some investigators view IRBs and a few suggestions for improvement

The following was part of the presentation during a panel discussion at the last PRIM&R/ARENA meeting.


Elizabeth Hohmann

*The first is by **Elizabeth Hohmann**, who provided a disgruntled investigator's perspective as a somewhat exaggerated role playing exercise. She is chair and director of the Partners Human Research Committee, which consists of six IRB panels reviewing for Massachusetts General Hospital and Brigham and Women's Hospital in Boston, Massachusetts. She is an associate professor of medicine and infectious diseases at Harvard Medical School.*

*The response is by **Jonathan Woodson**, associate professor of general surgery at the Boston Medical Center and associate chief medical officer at Boston Medical Center. He has chaired Boston University Medical Center's IRB for eight years.*

Elizabeth Hohmann

IRB reviews may be viewed by investigators as uninformed, inefficient, arbitrary, and inconsistent as well as lacking in perspective. These are generalizations, but there may be kernels of truth in them, and IRBs need to acknowledge these issues and do their best to counter them.

I can appreciate the problems faced by people on IRBs, and I understand that they never get sufficient thanks for participating in this important process. In some instances one wonders if they may be overly conservative as a result of being out of their depth reviewing complicated studies in challenging areas of medicine such as gene therapy, stem cells, and minimally invasive approaches. Outside ad hoc consultants may be helpful in some instances like this.

Redundancy?

Many of the studies being reviewed have already been examined by experts in the field—by panels or by consensus groups. Yet, after this, the protocol review is done all over again by the IRB. Some investigators think that the IRB would do better to stick solely to considerations of ethics.


Jonathan Woodson

Also, it often appears to investigators that the IRB office staff don't prioritize well, nor do they understand medical issues or timeliness. It may be difficult for investigators to find people in IRB offices who have sufficiently advanced knowledge to answer sophisticated questions about protocols and the increasingly complex review process.

Inconsistency

IRBs also suffer from inconsistency. One day a study will get a favorable review, the next day or with a different panel, the same study can get an unfavorable review. Later reviews may contradict earlier reviews. Last year the IRB wanted separate consent forms for different populations in the study; this year they want a single form!

> *Investigators who get contradictory or inconsistent directives may come to believe the entire process is flawed and inconsistent.*

Investigators who get contradictory or inconsistent directives from different panels may come to believe that the entire process is flawed and inconsistent. "The target is always moving and standards are always changing," is a common investigator complaint. Investigators need to be kept informed about changes in policies and procedures.

Possible changes

There are changes that might improve the process. A frequent request from investigators is that IRBs allow verbal presentations by researchers. Investigators feel this format can more efficiently present the important points. There also could be more ➢

subspecialty panels established for complicated areas of research. Turnaround times should be shortened.

Most research today is multicenter and thus is involved with multiple IRBs. Investigators feel it is torture to seek approval from multiple IRBs when multiple institutions have jurisdiction. Investigators provide the same information over and over; there seems to be no learning curve.

Perspective
Further, investigators feel that IRBs lack perspective. All issues are treated with the same level of scrutiny. A brain biopsy study is a lot different than a registry study. Do we really need a sample-size calculation for an anonymous questionnaire study with nonsensitive materials? How much oversight do these latter types of studies really need?

IRBs should take maximal advantage of expediting and exempting appropriate research. Making the approval process a convoluted production does not always make it a better process. Some investigators feel it has become self-important, working for the sake of working and not actually making anything better or safer.

Research can facilitate care
IRBs may not be up to-the-minute with knowledge of how clinics or medical groups function. IRBs may be unwilling to admit that, in many instances, our health care system offers inadequate care and that a research study may, in some instances, facilitate better care for those involved in the study.

At some institutions, for example, it is very hard for a child to get an appointment for psychiatric care. But if you enter a pediatric psychiatry study, you can get an appointment immediately. This is a failure of the health care system, but it's something IRBs need to consider.

I'm optimistic that if IRBs take more time to understand the investigator perspective, IRBs and investigators can get along.

Jonathan Woodson

The question here is how to maximize collaboration and minimize confrontation between investigators and IRBs.

Step back and ask the fundamental question: if we're all humans, why don't we see things in the same way? A look at the IRB process predicts why we have communication issues.

Confrontation and collaboration
The system is perfectly designed to minimize—not maximize—collaboration and to maximize—not minimize—confrontation, and so we shouldn't be surprised by the friction that sometimes results. We're trying to convey information during an ethics review.

But it's important to understand that all messages sent are not necessarily received, or at least not as they were intended to be received.

Think about how an investigator feels when told that the proposed protocol language might be perceived as coercive. The investigator says to himself, "My IRB said the language in my protocol sounds a little coercive, but I'd never coerce a patient."

The IRB's intention in questioning the language may merely be to suggest that the language tends to oversell a protocol.

The view depends on where you sit
For the investigator, however, the image of "coercive" is negative and derogatory. And in this way you develop a problem in communication. The problem occurs because your view of the world depends on where you sit. One view is from the IRB's perspective. Another is from the investigator's. They are not necessarily the same.

The investigator is looking from the vantage of advancing science, so she or he takes the same sentence and arrives at a different meaning.

Sometimes you see the world and you can't take a step back and see how others view it. The investigator is looking from the vantage of advancing science, so she or he takes the same sentence and arrives at a different meaning.

Bad experience
Further, if the investigator has had a bad experience with an IRB, the next question she or he gets from an IRB will almost automatically be viewed negatively, even when it's not.

How does the IRB contribute to poor communication? This depends on the IRB's dynamic. It depends

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A frank look at how some investigators view IRBs

—Continued from page 13

on the rigor of the review. Who's doing it, how much scientific background they have, the rigidity or willingness of the IRB to allow the investigator to come with language they're not used to.

Prominent individuals

Another factor is how prominent any one individual is in the IRB dynamics. If there is a very strong-willed person who is a statistician, then you will often see many more protocols disapproved that are heavy in statistics.

The board should be eclectic, including lay people, scientists, statisticians, clergy, administrators, and others. With this kind of mix, it's certain to produce debate. It typically will not produce total agreement. The best it can usually hope for is consensus.

Given the mix of people and the varied dynamics, things are not always going to be consistent. IRBs would like to spend a lot of time on one protocol, but time pressure and the workload mean it can't do that, so the members have to reach a consensus and move on.

Senior leadership

One of the keys is to get an institution's senior leadership involved in the process. If there is research community ownership of the IRB process, it will be a better process.

Experts are often long on data and short on judgment. If we get all the stakeholders involved in shaping the process, we can lessen the bureaucracy, get plenty of data, and more good judgment.

By lessening bureaucracy, we might suggest that low-risk protocols don't necessarily need all those things we obsess over.

Another improvement would be to educate everyone involved, early and often, without preaching.

We need to build into the systems a fundamental appreciation of protection of human subjects so that everyone grows up with it and it's not a mystery when they submit their first protocol.Δ

Web sites

International ethical guidelines, codes, declarations
http://www.nih.gov/sigs/bioethics/internationalresthics.html

Ethics of research related to healthcare in developing countries
http://www.nuffieldbioethics.org/go/ourwork/developingcountries/introduction

Research involving individuals with questionable capacity to consent: points to consider
http://grants.nih.gov/grants/policy/questionablecapacity.htm

IRB Forum—discussion and news forum
http://www.irbforum.org/

Fred Hutchinson Cancer Research Center—Institutional Review Office
http://www.fhcrc.org/admin/iro/irb/

Certification as an IRB professional
http://www.primr.org/certification/overview.html

National Cancer Institute: A guide to understanding informed consent
http://www.cancer.gov/clinicaltrials/conducting/informed-consent-guide

Bioethics and the National Institutes of Health (NIH)
http://www.nih.gov/sigs/bioethics/withinnih.html

NIH National Human Genome Research Institute, Ethical, Legal and Social Implications Research Program
http://www.nhgri.nih.gov/10001618

Centers for Disease Control & Prevention
http://www.cdc.gov/OD/ads/hsrdoc.htm

The President's Council on Bioethics
http://www.bioethics.gov/

Office for Human Research Protection
http://www.hhs.gov/ohrp/

Department of Health and Human Services (HHS) Office of Research Integrity
http://ori.dhhs.gov/

HHS Office of Research on Women's Health
http://www4.od.nih.gov/orwh/

Kennedy Institute of Ethics–Library and Information Services (with link to bioethics literature)
http://www.georgetown.edu/research/nrcbl/

Research ethics in medicine–University of Washington
http://eduserv.hscer.washington.edu/bioethics/topics/resrch.html

Beyond our borders

Different laws, different languages. Universal ethics?

During a panel discussion about the international research fueled especially by the AIDS epidemic, speakers considered the challenge of applying universal ethical principles to biomedical research in a multicultural world. The challenge is exacerbated by a multiplicity of health care systems, considerable variations in standards of health care, and diverse cultural traditions.


Amaboo Dhai

***Amaboo Dhai** is a professor of bioethics, medical law, and research ethics at the University of KwaZulu-Natal, Nelson A. Mandela School of Medicine in Durban, South Africa.*

***Jim Lavery** is a research scientist at the Centre for Global Health Research, and assistant professor in the Department of Public Health Sciences at the University of Toronto and Inner City Health Research Unit at Saint Michael's hospital.*


Jim Lavery

Amaboo Dhai

Yes, the principles are universal but the way we apply the principles are different from place to place.

Let me tell you a story about **Ntombi**, a young woman in her mid-twenties with little formal education. Each day she collects fuel and water and prepares food for her family. She has no access to clean water or electricity. She's been witness to and victim of much suffering, misery, violence, poverty, and disease.

80% are HIV+
Africa contains 33 of the world's 50 poorest countries. Living there are 690 million people—10% of the world's population living on less than 1% of the world's annual gross national product. Two-thirds of the people live in absolute poverty. Half lack safe water and 70% have no proper sanitation. In sub-Saharan Africa, 80% are HIV+. Africa has 22% of the world's annual deaths.

Ntombi lives for a year on the money that a person in the modern industrialized world lives on for a day. And she is aware of disparities in wealth and lifestyles. Those she sees living comfortably are mostly white; those who live like her are mostly black.

Ntombi is pregnant with her third child. During pregnancy she is approached by a team of health care workers, some from her own country, others from abroad. She's told there is a significant possibility she is HIV+ and that her child may get the virus either during pregnancy or breast-feeding.

Asked to take HIV test
She is asked to take a test to determine whether she is HIV+. She is told that if she is HIV+ she will be asked to participate in a trial of a drug that could reduce the chance that her infection will be transmitted to her baby. She is also told that if she is HIV+ she should not breast-feed.

> *"What will happen if I refuse to participate? If I accept, what will happen to me and the baby?"*

Ntombi wonders, "Who are these people? What are their intentions? Why are health resources so inadequate in my village? Is what these people are saying for my benefit or theirs? How will my life change? What will happen if I refuse to participate? If I accept, what will happen to me and the baby?"

What will spouse say?
She also wonders what effect failure to breast-feed will have on her baby. What will her spouse say about her participating? Can she rely on the explanations given by the researchers?

Should she consult with leaders she respects in her community? Should the community decide whether she should participate or should she decide for herself? How will it affect the relationship between her and her community? To whom can she turn for answers?

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When Westerners come with resources to do research, it is necessary for them to understand their own framework of thinking and the implications of that framework on very different mindsets and environments.

Western mindset
The researcher's mindset is fundamentally concerned with a biomedical approach to disease and a neoliberal approach to economics and trade. Remember that about 90% of health research is conducted on health issues causing only 10% of the global health burden. This suggests that the research agenda is driven by the profit motive, which is a view of the world that is not shared by those upon whom research is done.

Given the difference in world views and motivations, researchers must at the very least attempt to effectively communicate what they are doing.

Remember that about 90% of health research is conducted on health issues causing only 10% of the global health burden.

To do this, they must recognize barriers of culture and language and understand contextual differences. This understanding is the starting point of consensual discourse.

One of the problems we encounter with international research in Uganda is the socioeconomic inequalities between the researchers and the participants. It has a coercive effect because of the legacy of colonialism, which evokes a covert ethnic divisiveness. People are even suspicious of things such as whether HIV was brought in by foreigners.

Failure to involve local professionals
The problems we encounter include such difficulties as the failure to involve local health care professionals in protocol design. We also find protocols written in a language that research subjects don't understand. In addition, studies sometimes co-opt prominent local investigators not adequately trained in research. Studies sometimes also unfairly allocate duties to subservient junior staff members.

Therefore the primary issues of concern are informed consent, problems of justice, standards of care, what happens when the research ends, and the importance of local review.

In reference to local review, we have a problem with ethics shopping, in which researchers shop from community to community until they find a community that will approve their project. The problem, of course, is that the approval is motivated primarily by monetary gain.

The way to solve this is to develop review procedures that are on a par with reviews in the rest of the world. This is something that is developing now in examples such as the recently approved statutory requirement in South Africa for standardized ethical research practices.

Jim Lavery

The case I'm going to tell you about is an example of why we need more creative and proactive communication in ethics review of international research.

It involves a disagreement between a local host IRB and a remote Research Ethics Committee/Institutional Review Board (REC/IRB) about autopsy research involving malaria victims in Malawi, where a third of child deaths are due to malaria.

Autopsies of children
This was a study comparing autopsies of children dying from malaria with autopsies of children who died from other causes.

The community had a variety of concerns about the research, including the necessity for delaying burial and disfigurement of the body, particularly of the face, as a result of the autopsy. They also had concerns about treatment of internal organs.

Further, the community had concerns about the need for removal of the victims' eyes during autopsy. This was important because a complete retinal exam provides good prognostic information.

However, rather than disclosing that eyes were to be removed and replaced with prostheses, the investigators used a general disclosure statement, saying "It would involve taking samples from different parts of the body so that we can see what has happened throughout the body to cause the death.

"Although this would require cutting and then stitching the body, we would replace any parts that we have taken with natural appearing materials, and you would not see any marks or changes on the face."

This general statement was employed because the Malawian investigators and the local REC believed that local families would prefer not to know the ex-

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plicit details of the autopsy procedures, including removal of the eyes.

Concerns about fate of organs
Hence the rationale was based on the families' concerns about preservation of the deceased's physical appearance as well as about the ultimate fate of their organs.

The researchers and the REC knew these were important cultural issues, and it was believed that their concern was sufficiently great that explicit disclosure would frighten the community and end the study.

It was believed that their concern was sufficiently great that explicit disclosure would frighten the community and end the study.

Because malaria is such a serious public health threat in the region, both the researchers and the REC believed the studies were important enough that full informed consent would be counterproductive.

The local Malawian REC approved the study without explicit disclosure. The remote IRB, however, decided it would not grant approval without full disclosure.

Default with local ethics committee
The researchers would later write that "in situations where the application of a fundamental ethical issue is contentious, the final decision should fall within the jurisdiction of the local ethics committee (assuming it is properly constituted and can act independently)."

Hence they concluded that this is a local issue, an issue about which we in the community should have the final say. But what guidance exists? There is nothing specific about how to resolve disagreement between RECs/IRBs in different countries. International guidelines are silent on the matter.

The Common Rule has "equivalent protections" provisions. There also is a Department of Health and Human Services report that is being reviewed by the agency. This is promising but is not an imminent solution for the short term.

What should we do in the meantime? Creative solutions are possible.

For example, after a 15-year clinical training exchange relationship between Moi University in Kenya and Indiana University, the two schools developed a memorandum of understanding for the ethics review of collaborative research.

A shared approach
The memo came out of a workshop held in Kenya after they had some experience with exchanging IRB personnel and recognized the need to develop a shared approach to ethics reviews. The goal was to enhance the ability to conduct research that would be sensitive to local values.

Schools in Kenya and Indiana developed a memorandum of understanding for ethics review in collaborative research.

Since the workshop, in addition to signing the memorandum of understanding, the two institutions have developed a handbook of standard operating procedures for institutional research and ethics committees at both schools. A Kenyan, who as a graduate student was trained by the Indiana faculty, now is the permanent human subjects administrator at Moi University.

So ethical collaborations are occurring. But it is important to remember that the Indiana/Kenya collaboration did not happen overnight. It came after a 15-year period in which the two had established a stable, trusting relationship with respectful engagement and dialogue.Δ

Web sites

Bioethics resources for health care organizations
http://www.mcw.edu/bioethics/presentation.html

Medical ethics: cross-cultural issues and diverse beliefs
http://eduserv.hscer.washington.edu/bioethics/topics/cross.html

DOE Office of Human Radiation Experiments
http://www.eh.doe.gov/ohre/

National Institutes of Health (NIH) Office of Extramural Research, Human Subjects Web Site
http://grants.nih.gov/grants/policy/hs/index.htm

NIH stem cell information
http://stemcells.nih.gov/policy/guidelines.asp

CITI training program

NIH grants fund expansion to cover international research and to fund Chinese, Spanish translations

The CITI (Collaborative IRB Training Initiative) Program in the Protection of Human Research Subjects has expanded to include course materials that have been translated into Chinese and Spanish.

Using enhancement grants for human subjects protection from the National Institutes of Health, CITI began the project because U.S. investigators collaborating with international sites needed training materials.


Karen Hansen

In addition, if a U.S. institution sends a subcontractor to an international site, the investigators there will have to confirm that they have had human subjects protection training. CITI training can be used to do that.

Karen Hansen, director of the Institutional Review Office at the Fred Hutchinson Cancer Research Center in Seattle, has for more than two years been overseeing CITI's expansion to incorporate international training.

New course modules

"In addition to the translations, we have also created a new course module for international research. It discusses the various codes, the unique cultural differences to be aware of, and other instances where guidance at an international site might be different than it is here."

The international module also includes an attachment with country-specific resources, including policies and regulations that apply to different countries.

"We've incorporated, as well, an analysis of different ethical codes, guidance about them, what's common and what's different regarding issues such as informed consent," **Hansen** said.

The purpose, she added, is to give investigators "a feel for how the requirements of ethical review are the same or different in various countries, whether some places require more or less."

Local authors in several countries

CITI has also arranged with authors in several countries to write articles for the training programs that will provide perspective about each country's review process and other aspects of conducting research.

"We had two people writing about conducting research in China," **Hansen** said. "Another is writing about South Africa, and another from Zimbabwe."

The CITI training program's international research component also includes links to a variety of resources, including the Belmont Report, the Declaration of Helsinki, the FDA, OHRP, and several articles about ethical conduct of research.

The training program is available free to the public. It is at *http://www.irbtraining.org*.

For additional information, contact **Karen Hansen**, khansen@fhcrc.org.Δ

CITI update

In mid-June, CITI completed the launch of its International Platform. It includes three basic modules with quizzes and two additional modules that include international guidance and general links to information that might be useful for those conducting global trial activity.

Among other uses, this may be helpful, for example, if a researcher in China with a federal subcontract from DOD needs to provide certification of human subject protection training. This site generates a certificate of completion.

Modules 1–3 of this abbreviated international training site are available in English, Spanish and Simplified Chinese text. Some but not all of the resource documents in modules 4 and 5 also are available in translation. Additional translations are to be available in the future in French, Russian, and Portuguese.

Edward Gabriele *gave the closing keynote address at the last PRIM&R/ARENA meeting, entitled, "Trust and Troth: Our Passion for Protecting Human Subjects." A humanist, philosopher, and academic theologian, Gabriele is an executive level research ethicist and research administrator who specializes in research integrity, policy formation, and the development of procedural norms for research administration and ethical oversight operations. This article, written by newsletter editor Timothy Elledge, is based on a series of interviews with Gabriele.*

Shifting the emphasis

Protection follows from trustworthiness

The most serious problem with human subjects protection is not technical noncompliance with regulations. Instead, it's the difficulty we have with the human ability to trust and be counted as trustworthy.

Those words—trust and trustworthiness—aren't necessarily found in the codes from federal agencies. You are more likely to find them in reference to friendship and other relationships in business, school, marriage, and family.


Edward Gabriele

If all we needed were regulations, by now we should have a perfect system of protection, because we have more regulations than we know what to do with.

So it is something else that we really need. That "something else" is connected to my belief that we care about protecting people—not because the task is grounded in compliance with regulations, but rather because our task is grounded in the willingness of vulnerable human beings to trust us.

As such, human subjects protection is about a sacred troth—the commitment that happens between the research community and those who entrust to us their lives, privacy, and personhood. But like any other relationship, trust has to be earned. When we meet a person in a research setting, there is a great vulnerability there.

A *sacramentum*

I am reminded that in the ancient world, when soldiers began their service for the emperor and the Roman Empire, they laid their hands on an altar and took their "oath of office," their commitment. They gave it their all. The Latin name for the soldier's oath was *sacramentum*, a sacred pledge of honor and commitment. Their "oath" became a "troth," a dedicated and almost sacred relationship of fidelity and honor. This same intention is captured for Americans today in the oath that our United States Marines take in the form of their motto, *Semper Fidelis*.

To be worthy of the trust that people bring to becoming research subjects, it will be necessary to retrieve the human face of research by attending to how we think about the formation of human values. For example, in developing the ethical direction of an organization, we need antidiscrimination procedures. But we cannot assume that having procedures in place will cure bigotry, which is the result of poorly formed human values. Establishing procedures can be done quickly; curing bigotry is a long and arduous task.

Putting the cart before the horse

Our society has tended to put the cart before the horse, regulations before values. The proclivity for establishing procedures has led to incessant worrying about protecting the liability of institutions. We mistakenly equate protecting human subjects with protecting an institution's liability. But if the focus is on protecting the institution, we miss human beings. Instead, think about it this way: if we protect human beings, we will protect the institution.

> *If we protect human beings, we will protect the institution.*

There is value in following regulations and seeking accreditation, but they alone will not ensure an ethical program. You can cheat on any of them. You can go through the PowerPoint slides, print out a certificate, and say you're qualified, but without the

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element of a troth of fidelity and honor, it is a hollow qualification.

One way to begin the process of understanding the difference between merely following regulations and really deserving trust is to think seriously about this question: what are the ultimate, foundational values for why I do what I do? Another important part is to ask: what is the ultimate need for what I do?

In seeking answers to these two questions, we can significantly enhance the ability of people to care deeply about the ethical dimension of protecting human subjects.

I'm not sure that people in this field fully understand how needed they are—how much the culture of research needs you. Some of the problem is that society has tended to put you in the role of regulator, or cop, one who enforces the rules.

If, instead, you think about the implications of what you do—the very important results of your doing this task well or poorly, then, when you are considering the implications of guarding the well-being of vulnerable people, you will see that it is not the regulations alone that are important. What is more important is your commitment to being worthy of their trust. Their protection flows naturally from your worthiness.

To truly help people, you can't do it politely from way out there—from an objective distance cloaked in procedures and regulations. It is necessary to be able to suffer with the poor and disenfranchised of the world, who continue to be made more poor and more disenfranchised. Our passion for protecting people has to go deeper than compliance with regulations

How do we do this? By being truthful, being compassionate, and being passionate about protecting human dignity. We do it by shifting the emphasis from compliance to ethics. We do it by becoming a community based on a compassionate character, a compassionate ethos. We do it by reminding society that we must maintain an authentic moral center, one that requires us to protect others in their lives and their fragility before protecting our own interests. The foundation for all of this is attending to the formation of values—in each of us and in others.Δ

Schwetz *—Continued from page 9*

protection of subjects of research, not protection of institutions against liabilities.

More is not better

There were some wrinkles then, but those shorter documents were better than the 20 to 80 pages we see now.

The additional pages don't have anything to do with protecting subjects; they serve merely to dilute the parts that provide meaningful safeguards.

We're following the regulations but have lost sight of how to make informed consent processes more protecting.

We spend a lot of energy complying with regulations, but the excess time and energy spent in documenting things aren't to protect the subject. An example is the emergence of experimental design committees in institutions. When a proposal has been through the design committee, IRBs are saying they don't have to look at it because it's already been through a review process.

Yet nobody on the design committee looked at the proposal from the standpoint of minimizing risk to subjects, because they were looking only at whether it was good science.

In regard to issues of conflict of interest, it's entirely possible to have institutional conflicts that are permissible from the standpoint of compliance. It's permissible, but that may be only because we haven't dug into the issue to find out whether there might be better ways to state the regulations to better protect subjects.

For those of us who are regulators, we have to uphold the regulations, but uphold them with a sensitivity based on the foundation and overlay of ethics.

For those who are not regulators, you should engage with full knowledge of the regulations, but also with knowledge of the ethics that overlay the work.

The public expects us to facilitate research that's in the best interest of all of us, not just some of us. We can't do that without both ethics and compliance.

The key, therefore, is to find ways to reach a better balance between understanding the regulations and thinking about the ethics of what we're doing.Δ

***Lori Abrams** is senior lecturer at the University of Minnesota's Carlson School of Management, Department of Strategic Management. She is also an organizational consultant in conflict management, leadership, and communication and organizational change.*

Thinking about difference

It's not possible for researchers and subjects to think alike. They necessarily have different perspectives on whatever the project is. But there are ways to improve communication.

Principal investigators usually do not think like their research subjects, no matter how hard they try.

When they do try to understand how another person is thinking, the efforts tend to be confounded by several factors, the most important of which is that the investigator is focused on one thing—research—and the subject is focused on something else.


Lori Abrams

These problems in communication occur because people tend to have inaccurate perceptions (of each other), and they are unaware that their perceptions are inaccurate.

Nonverbal communication

This is true of both verbal and nonverbal communication. Patients, or research subjects, will assign meaning to nonverbal forms of communication as readily as they will to what is actually said.

One way of describing the communication that goes on in research relationships is to think in terms of a functionalist and an interpretivist perspective. The first is more objective, the second more subjective.

In the functionalist perspective, the concern includes things such as being clearly understood, issues related to data collection, the mechanics of the project, money, who participates, and so forth.

The interpretivist perspective is the one that has concern for how the other person feels, and from a subject's position it is most likely feeling understood, trust, wanting something, and hope.

These are two very different ways of being in a relationship, and the best we can hope to do as researchers is to find a middle ground between the two, a place to collect data and at the same time find some real connection with subjects.

Unique relationship

Good communication also depends on who we're communicating with, as well as on the goal of communication. For obvious reasons, the relationship between patient and doctor is unique, and nonverbal forms of communication are significant.

For example, if the doctors sits down, or doesn't sit down, the patient assigns meaning to it. If the doctor wears a white coat or not, the patient will assign meaning. And the nature of the relationship then grows out of those and other perceptions.

If the doctor sits down or doesn't sit down, wears a white coat or not, the patient assigns meaning.

From the researcher's perspective, the subject is here to help us get data. But, often, from the patient's perspective, the feeling is "I'm here to get well."

This is the same sort of perspective difference that we find in our personal relationships: "I wouldn't have done that if you hadn't done that."

The social world that we create in our minds is based on interactions between ourselves and others. It's not something that's set in concrete. It changes all the time, based on interpretation of events.

Being understood vs. feeling understood

It's important, for example, to realize that there is a difference between being understood and feeling

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understood, a difference between confirmation of information and perceived empathy. If you have been diagnosed with breast cancer, the doctor might know what that is, but does the doctor understand how you feel about it?

Feeling understood focuses on the subject, who wants to feel accepted, appreciated, and respected. When this climate is created, subjects are more likely to cooperate.

In dealing with communication strategies, people tend to fall into one of three groups. One is what we call the noble self. In this self, black is black and white is white. A physician in this self is saying "This is the news; what you do with it is up to you."

People tend to fall into one of three groups: noble, rhetorical sensitive, or interpersonal.

A second is the rhetorical sensitive self, which focuses on the demands of the relationship. People in this group understand complexity and know what to say and how to say it. As we get older, we tend to become more rhetorically sensitive.

The third type is the interpersonal, which we tend to save for our loved ones, where special rules apply. The opposite of this is the impersonal, the way you often treat people at a store, for example.

Impersonal style brings problems

Problems arise when you respond to subjects in the impersonal style. I think we need to be somewhere in the middle. It will never be interpersonal, but maybe you can move in that direction.

Another way of thinking about this is to contrast the pragmatic and the humanistic. The pragmatic involves confidence, immediacy, expressiveness. The humanistic encompasses openness, empathy, supportiveness, positiveness, equality.

And, again, I think the best way to be as a researcher with subjects is somewhere in the middle.Δ

Doing research in traditional cultures

—Continued from page 2

Other societies can be different. The traditional African view of the person is relational and communitarian. The person is extended in space and time, embedded in social and communal relationships. To be a human is to participate in a community of similar selves.

The highest value is placed on positive human relationships; they take precedence over all else.

This is captured in many African proverbs: you only become human by recognizing the human in the other. The person is born for the other. That emphasizes the expectation of participation in community.

The highest value is placed on positive human relationships; they take precedence over all else.

There is also a notion of a divine element inherent in you as human. This means that people will often request their tissue be returned to them because it has divine element.

Endless transformations

Traditional societies also believe that human life is a series of endless transformations that don't begin at birth and end at death. This has implications for research, and especially for organ donation and research involving human tissue.

For example, the request for the tissue to be returned to the participant could possibly raise complicated ethical problems if the tissue has been sent to international laboratories for analysis, where it might have been discarded because researchers do not necessarily share this religious perspective.

Further, the family is the most important aspect of one's social identity, apart from which personhood is almost inconceivable. A deep respect for elders is specially cultivated, which gives them a socio-moral responsibility to promote communal well-being. Elders don't dictate to the community, but they preside over the process by which decisions are made.

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Deference to authority
Among the ethical implications of this is that there may be a strong deference to authority. Investigators must have thought about how they will deal with this. And, further, people expect a relationship to continue once it has begun, which means they want to be able to count on researchers to help not just now but in the future as well.

There are accompanying important implications for the consent process. You should consider whether consent should be individual or "communal," allowing time for the person to discuss the research with significant family members before consenting to participate.

The latter sees consent as a negotiated process. It is difficult to make the decision about the informed consent process in advance, because one must first become familiar with the forms of family organization and community governance (e.g., consensus decision-making by means of *imbizo* or *baraaza*—a community gathering to discuss and debate issues and to ensure checks and balances on power).

The following questions may have to be addressed: What are the ramifications of not engaging the family and the community in obtaining informed consent? What is to be consented to by the community, the family and the individual? Failure to take these issues into consideration could lead to research participants being victimized or ostracized by their communities. Researchers should demonstrate that they have given these issues the critical thought they deserve. Engaging local social science expertise is often useful.

Critical gaze
Most importantly, when considering ethical practice one should not simply rely on principles. Instead, think of this as an ongoing dialogue, as a process in which you continuously engage. Think of it as a process of critically gazing on your practice, assumptions, and philosophical traditions.

I suggest that you become trained in what the Greeks referred to as *phronesis*, that is, knowledge of how to engage with the other, as opposed to technical knowledge that merely applies principles according to predetermined plans.Δ

Web sites

University of Minnesota Research Subjects' Protection Programs
http://www.research.umn.edu/subjects/

Resource for people considering participation in research
http://www.med.umich.edu/irbmed/research.htm

Consortium to examine clinical research ethics
http://csmeh.mc.duke.edu/cecrelndex.htm

Protecting Human Subjects

This newsletter is designed to facilitate communication among those involved in emerging bioethical issues and regulatory changes important to both DOE and the human subjects community.

DOE Human Subjects Protection
Interim Program Manager Michael Viola, M.D.

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Meetings

Southwest Regional Conference on Institutional Biosafety Committee
August 18–19, 2005
San Antonio, Tex.
For information, contact Janet Cole, jcole@utsystem.edu

Just Doctoring: Can Medical Education Address Racial and Ethnic Disparities in Health Care?
October 6–8, 2005
Maywood, Ill., Loyola University Chicago Stritch School of Medicine
For information, see http://www.bioethics.net/events.php?viewEvent=153

International Health Care Ethics Colloquium
October 17–20, 2005
Washington, D.C., Georgetown University
For information, see http://clinicalbioethics.georgetown.edu

American Society for Bioethics and Humanities—2005 Conference
October 20–23, 2005
Washington, D.C., Omni Shoreham Hotel
For information, see http://www.asbh.org/

2005 Annual HRPP Conference—Ethics & Trust Across Boundaries
December 3–6, 2005
Boston, Mass.
For information, see http://www.primr.org/about/cal_05.htm