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After a quarter century, the Belmont Report holds up as ethical framework

One challenge: Report needs to be used more widely

Despite its relative brevity, the Belmont Report has withstood the test of time as a framework for ethical decision making about human subjects research, experts in research ethics say.

The Belmont Report resulted from the National Research Act of 1974, which created the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. The commission met monthly from 1974 to 1979, the group's tenure culminating in the creation of one of the most influential human subjects research documents in the United States.

"The big benefit of the Belmont Report was that it put proper emphasis on the importance of the ethical handling of human research," says former U.S. Rep. **Paul G. Rogers**, JD, a partner in Hogan & Hartson in Washington, DC. Rogers had been a Democratic congressman from Florida for 24 years and helped to write the National Research Act. Rogers also chaired the committee on health and environment in the House of Representatives.

Special Report: Belmont Report at 25 Years

While experts in research ethics roundly acknowledge the improvements that have occurred as a result of the Belmont Report, they also note some problems that still prevent the research community from meeting the report's ideals.

One challenge cited by experts involves disparities in how the report is used.

For instance, the FDA does not promote the Belmont Report, says **Barbara Bigby**, MA, CIP, director of the Scripps Office for the Protection of Research Subjects and an IRB administrator at Scripps Clinic in La Jolla, CA.

"So problems come when we have federally funded research, and the community doctors are doing FDA-related research," Bigby explains.

"Our federally funded doctors are very well aware of the Belmont Report because it's part of their federalwide assurance, and they say, 'When we accept federal funding, we accept the Belmont Report,'"

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Editorial Questions

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

Bigby says. "But on the other hand, the FDA has a statement of, 'I will follow good clinical practice,' which is terribly important, but is not an ethical framework."

Also, while human subjects protections are improved for federally funded research and research conducted at major research institutions, there remains an ethical gray area with regard to research that is privately funded and conducted at small facilities, notes **Elizabeth E. Hill**, RN, MS, DNSc, director of clinical research management program and assistant professor at Duke University School of Nursing in Durham, NC.

"If you don't have studies that are funded federally, what are the protections for people who don't follow the guidelines recommended in the Belmont Report?" Hill asks. "I teach a research methods class and have students from all different places, and some are from small hospitals, and they'll say, 'So and so is doing a study and it hasn't been through the IRB, but it's not a federally funded study.'"

Another challenge that remains is that clinicians who conduct research still have trouble understanding the differences between their clinical practice and research, says Hill.

For example, she learned of a situation at another institution in which a hospital physician had submitted a protocol to the IRB for the study of different treatment methods of a vulnerable population. When his protocol was deferred until he met further requirements, the physician ignored the IRB procedure and conducted the research as he had initially planned.

Although no patients were harmed, the IRB investigated the physician's actions, assigning a fellow physician to head the investigation, Hill recalls.

At first the investigator was skeptical that the researcher's actions amounted to improper conduct, but he quickly changed his perspective, she adds.

"He said, 'When I first started this I saw it as ridiculous because no one was hurt, but now when I look at the regulations and read the Belmont Report, I can see that what he did was very wrong,'" Hill says.

Issue of informed consent

While the Belmont Report established sound criteria for informed consent, including the three elements of information, comprehension, and voluntariness, there continue to be problems

today with how informed consent is carried out, says **Camille Nebeker**, assistant vice president for research at San Diego State University.

"I'm a principal investigator on a National Institutes of Health-funded grant, and I'm an IRB administrator and I oversee research administration, and the only role I haven't played is the federal one," she says. "So I can look at the informed consent process from different vantage points, and I can see that it looks good on paper and in practice we all think it's working, but there are some challenges in the application of the process."

More needs to be done to identify whether the process results in an informed participant, Nebeker says.

The informed consent process could benefit from considerable improvements, suggests **Michael Kalichman**, PhD, director of the research ethics program at the University of California-San Diego in La Jolla.

"It may be an unrealistic goal, and yet the whole system is based on a premise that our subjects will understand what it is they're risking by being involved in a study and that they'll understand what the benefits are," he says.

Nebeker has both participated as a healthy subject in a clinical research study and she has conducted focus groups with key personnel involved in the conduct of the research protocol. Based on her experience, she has found that the informed consent process has the potential to be compromised.

Preliminary findings from focus groups indicate that the process may rely more on the form than the process of describing the study in a manner that is conducive to good decision making, she notes.

"This may be promoted by the IRB review process where the principal investigator is somewhat focused on getting a consent document put together that will be approved by the IRB," Nebeker says. "The IRB may assume that the document submitted by the PI takes into account the appropriate language and reading level and is appropriate for the target group."

When Nebeker volunteered to participate in a clinical study, she was presented with a 13-page consent form. While the nurse practitioner who presented it had done the type of job Nebeker would have expected, there was a great deal more information in the form than what was discussed in the one-on-one, she recalls.

Nebeker knew enough to read the form thoroughly and from that careful read, she discovered the form was written in a way that provided legal protection to the institution conducting the research, but did not provide a clear discussion about what Nebeker's rights were as a human subject in the event of injury.

"If I became injured as a result of participating in the study, it was very vague on what would happen, almost to the point that I wouldn't sign it," Nebeker says.

"I have asked study coordinators about the consent process and found that their understanding of what the participants' rights are if injured vary, and most tend to assume, from reading the text within the consent form, that the institution will cover costs associated with injury," she adds.

If study coordinators are confused, it's likely participants are not provided with accurate information at the onset, Nebeker notes. This is just one example of how information given to participants might be compromised during the process, Nebeker says.

Another Belmont Report principle that remains a challenge involves the third principle of justice, Kalichman says.

"Some questions have been raised about whether trials should be done in countries where citizens might not be able to take advantage of very costly treatment," he says. "The other side of it is why don't we ask the same question about trials that include those who are underinsured in this country."

The ethical question of justice concerns whether the outcomes of new therapeutics or approaches to understanding disease have sufficient benefit to outweigh the risks of testing a population that might not, under normal circumstances, benefit from the treatment, Kalichman adds.

"It's not that the principle is flawed, but we need to find clarity in some new way about how that principle needs to be applied," he says. ■

OHRP director discusses Belmont Report impact

Report has maintained its focus on ethics

[Editor's note: Clinical Trials Administrator *asked **Bernard Schwetz**, DVM, PHD, director of the Office of Human Research Protections (OHRP) to discuss the Belmont Report's successes and challenges as the 25th anniversary of its launching has passed.*

Schwetz offers his views in this Q&A.]

CTA: What do you believe are the two biggest accomplishments in human subjects protection that were achieved in the past 25 years because of the Belmont Report?

Schwetz: Well, I think one of them has to be to keep the focus of human subject protection on ethics and not just science or regulation. The fact that the Belmont Report was very clear in articulating the need to adhere to the three ethical principles, I think, has created a framework for conducting research involving humans in a way that has modulated the field so that we can continue to focus on those principles, rather than wandering all over and trying to identify a basis for protecting subjects. That clearly has to be No. 1.

Special Report: Belmont Report at 25 Years

I think the second factor that has created an environment for doing research that keeps the focus on protecting human subjects is the whole IRB system, the institutional review board. The regulations by themselves are important, but if you don't have a body of people within the research community to make sure the regulations are being followed, the regulations by themselves wouldn't be worth much, especially in this kind of system where compliance is voluntary. The whole thing is a system of trust, and the IRBs throughout the research community give credibility to the trust within the system.

CTA: On the other hand, where have the Belmont Report's ideals fallen short in research practice?

Schwetz: There are issues we're struggling with today that were not issues back in the middle '70s, and one example I would give is conflict of interest. Conflict of interest wasn't mentioned in the Belmont Report because at that time it had not surfaced as the particular issue it is today.

I had the opportunity to interview many of the members of the national commission and the support staff who helped to put together the various commission reports. One of the things I asked them all is, 'How up to date do you think the Belmont Report is? Does it have to be rewritten?' And despite the fact that there are issues like conflict of interest that weren't specifically addressed in their deliberations, they all felt the Belmont Report still is a logical basis for protecting human subjects today.

The other issues we've dealt with one-by-one by various forms of guidance from the government or non-government. So as long as we can continue to use the Belmont Report as a basis for decisions and provide guidance on specific issues, I think we're better off to leave it just as it is.

CTA: You've touched on an issue that some people have mentioned, and that is whether it would be helpful for the government to appoint a new commission to update the Belmont Report since we have so many new types of research, such as genetics research, to deal with today. What are your thoughts on why or why not that would be needed?

Schwetz: There is a federal advisory committee on genetics research. So I think that kind of federal advisory committee handles the questions that relate to new technology and new science. From that standpoint some of these new issues are being taken care of by the federal advisory committee on ethics. We have the federal advisory committee on human research protections. The one that deals with genetics is one that I think that even if we rewrote guidance today, within a period of time we'd have to revisit it because the technology is changing rapidly enough so that even if you gathered a group of people together, they would only deal with the issues that we have faced yesterday and today, but not necessarily be able to anticipate the ones a couple of years out. So at this time of more rapid change than it was 25 years ago, we're perhaps better off to deal with this in an ongoing basis rather than to try to anticipate what's going to be the question for society in 10 years.

CTA: Another area that we sometimes hear about is that the Belmont Report is a great ideal, but there is a lack of understanding of it among many clinical trials researchers, including the ones regulated by the FDA, and also that a lot of privately funded research isn't subject to the same kinds of ethical considerations that government-funded ones are because they're not regulated. What are your thoughts on those two concerns about human subjects protection?

Schwetz: In audiences, where it has been asked, 'How many of you have read the Belmont Report?' there is always a very high percentage of people who raise their hands. Now I don't know what the validity of that kind of test is but, nonetheless, my feeling is that the Belmont Report is very widely read because it's easy to read and it's short.

In contrast the regulations are lengthy and not

easy to read, and I think if you were to rank order the documents that have been read by the largest number of people, the Belmont Report would be at the top, the Declaration of Helsinki would be some place below it, and federal regulations would be below that — just because people go to the federal regulations for specific issues that they need to know. They don't go there for background. If they need to know a specific answer to a question that deals with prisoners or with children or the IRB structure they go directly to the piece of the federal regulations. By contrast, the likelihood that someone would have picked up the Belmont Report and read it front to back is pretty high.

CTA: How do you answer the concern that smaller research centers and private research are not adhering to the same codes that the larger institutions are?

Schwetz: It's possible that that's true, but it's also true that we don't have a good way of tracking what's going on in the community research centers because there's a very large number of them and the efforts to educate the research community have been largely focused on the academic research centers. Now the research is going beyond the academic health center and is going out into the community and private practice and small hospitals, and none of us has the resources to provide training programs locally at all of those sites.

But perhaps as importantly, we don't have good information about what's going on at those sites in terms of how well versed they are in the regulations. So we depend, for example if there is a study that's funded through the University of Maryland, but it's conducted in a small research site somewhere in the community, we have to depend on the University of Maryland for making sure that people who are collaborating on this study out in the community meet the standards of the University of Maryland. It has to be a partnership between the large health centers where we have spent a lot of effort providing training and the federal government who continues to remind those research sites that regardless of where the research is going on that we all have an obligation to make sure people are well trained.

CTA: Could you name a couple of challenges in human subjects protection that remain and is there any effort beginning now to meet these? Specifically, with all of the attention paid recently to FDA and the problems with Vioxx and antidepressant drugs for children, do you think there is a good chance we'll soon have a large public registry of all clinical trials, or is there some other type of achievement that might prevent some of the problems that have come up recently?

Schwetz: I'm sure that people within the medical product centers of the FDA are reviewing very seriously how they could help prevent any further problems with drugs being recalled; so I'm sure they're looking hard at that.

From the standpoint of protecting human subjects, that's a somewhat different issue. There are things I worry about there: One is the consistency of IRBs. We get a lot of comments back that IRBs are not consistent one to another. And it's a concern as the research becomes more complicated, and the science becomes more complicated, and the difficulty of obtaining good informed consent becomes more difficult. It's a concern that IRBs might not be as consistent as we want them to be. They do their jobs to protect subjects based on same regulations, so one of the things we're trying to get a handle on is how consistent IRBs are and what is the impact of protecting human subjects as IRBs do their work today. We can gather information on the length of time it takes to review protocols and how many cycles it takes to get a protocol reviewed and approved, that kind of information on how IRBs perform. But it's more difficult to get information on how well IRBs are doing their job, because we don't have agreed-upon criteria to even measure that.

That's one of the things that we're giving thought to and figure out how we might have a better handle on the performance of IRBs. We're looking at it within OHRP and we are reaching out to some other groups including the Secretary's Advisory Committee for Human Research Protections and others within the research community to get some momentum built on trying to take on this issue of how we can measure the performance of IRBs.

***CTA*:** Is there anything else about the Belmont Report and our reflecting on it 25 years later that you'd like to discuss?

Schwetz: I'd like to reemphasize the importance of the ethical basis for our decisions in protecting human subjects. It's awfully easy to focus on the regulations as the basis for how we make decisions and lose sight of the ethical implications. So one message that I'm trying to get out to the community is that the regulations are important, but the regulations can't be taken in absence of a continual thought process about the ethics as the basis for our decisions. ■

Practice better closeout management in trials

Expert offers guidelines

Clinical trials administrators and other research staff could avoid common problems after research has been completed if they would follow a well-defined, closeout process, regardless of the type of award that was made, according to a research expert.

"Where I see institutions struggle is when they change their processes, doing one thing a certain way and another time doing it a different way," says **Tim Patterson**, manager of the Huron Consulting Group of Chicago. Patterson spoke about closeout management at the National Council of University Research Administrators (NCURA) conference, held Oct. 31 to Nov. 3, 2004, in Washington, DC.

"For example, if a university was doing a close-out for an award that had a financial report, they may do the closeout one specific way," Patterson says. "But if the closeout award did not have a financial report then they may deviate from the closeout process."

The same principles should be applied to both cases during the closeout process, Patterson adds.

"The same process should be used to close out every award and make sure things get done consistently across the board," he says. "When all is said and done, that's what sponsors want to see because it helps bolster confidence in the institution's practices."

Patterson lists these reasons why the closeout process often has problems and what might be done to improve it:

• Closeout is a low priority.

The reason research departments in universities often struggle to close out awards is because this process is the last step in the life cycle of an award, Patterson notes.

"Like many last things and different procedures, that's the one that can often get skipped because the burden is placed on setting up and producing financial reports," he explains.

• Research departments are understaffed.

Also, while the number of research dollars awarded to universities by federal and nonfederal sources are growing at a rate that has resulted in some institutions doubling or tripling their research award volume within the past decade, the administrative support for research has not grown at the same rate, Patterson says.

• Better training manuals are needed.

Another reason for problems with closeouts is that most institutions have not taken time to produce good training manuals or process improvement manuals for the clinical trials and research process, he notes.

"They find themselves relying on the people who've been there the longest," Patterson says. "And much like the game 'telephone,' when you're passing something down from one person to another, some things get missed," Patterson says. "Taking time to document a procedure or policy that's going to be in place beyond the length of time people are with an employer is invaluable because you make sure things are done repeatedly and consistently year after year."

• Time management is critical.

"You're in a position to support the researcher and provide him or her with guidance in terms of reliable items on projects and reliable costs," Patterson says. "But you also have a situation where you get a ton of e-mails from the department or sponsors, asking for things."

While new award set-ups, purchase order requests, and other details sit waiting in an administrator's in-box, the closeout process is invisible, he says. "No one puts a closing in your in-box, so if you don't specifically do this it'll fall off the radar and not get done."

• Ignoring closeout process increases audit risk.

When federal officials check a trial's balance or expenditures and compare this to the financial report or cash collected, there will be questions if they don't match, Patterson says.

"One reason they might not match is because after you issue the following report, perhaps expenses continue to post to the account, and because you don't have a good closeout process you don't realize this," he says.

"For federal awards, a lot of sponsors have a letter of credit authorization to draw down funds, and the individual drawing the funds will go off of what's posted to the account," Patterson explains. "If what's posted is greater than what's reported and you have a case of greater than cash receipts, the auditor will come in and say, 'What's going on?'"

• Ignoring closeout also poses financial risk.

"If expenses keep posting to an account and the window of opportunity to invoice or bill the sponsored entity has closed, then you may have

expenses that could have or should have been invoiced," Patterson says. "But because you didn't have a good closeout process, you didn't do a thorough review of expenses posted, valid post-term expenses, then you might miss that final payment posted to the account, and the institution now has to cover that cost."

• Document the closeout procedure.

"Develop a checklist that you will use every single time you close out the account," Patterson says.

It should include:

— Did you do the final invoice?

— Is the financial report done?

— Has all the cash expected come in and been received?

— Did expenditures to the account today match the expenditures you invoiced?

The closeout procedure should include checking to make certain all encumbrances or obligations are zeroed out to prevent other people in an institution from directing expenses to an award because they were ignorant of the grant and contract, Patterson says.

• Make certain PI and department agree on all costs.

Getting the confirmation of expenditures, which is a consensus from the PI and the department, is critical, Patterson says.

The clinical trials office and the person writing the financial report and invoicing must make sure when a file has been closed that the PI and department agree that all costs posted to that award are appropriate to that project, he adds.

"They must agree on the final tally of costs," Patterson says. "They're the only ones who know because they are responsible for administering the award, and no one in central administration is going to be able to say whether all expenses are posted."

• Review summary list in validating expenses.

Review a project status report or an awards status report that lists the expenditure type that is posted to an account, Patterson says.

The research staff should provide the PI with information about how the costs have added up and what the remaining balance is for a particular account, he suggests.

For clinical trials, research staff should validate from the researcher that all cash that is expected to come in on the account has been received, he adds.

"The critical point is to make sure they agree that all final, expected payments have been received, because if you close it out before you receive a payment then you will hurt the institution's ability to post a payment," Patterson says.

• Notify PIs and staff of closeout time.

There's a great deal of value in sending a notification letter to the PI and department staff to tell them that the award referenced in the letter will be going to term in 60 days, 30 days, or two weeks, Patterson says.

The letter could request that if the PI hasn't already done so, then he or she should begin doing a process of review to make sure the cash has been received and the expenses are appropriate, he says.

"Some PIs will come back and say, 'I lost track of time and didn't realize the invoice was in 30 days — I need more time, how do I go back to getting more time?'" Patterson notes. "So you work with them in terms of a no-cost extension." ■

Has FDP really improved research bureaucracy?

There have been benefits and losses

The Federal Demonstration Partnership's (FDP) latest incarnation in its nearly 20 years has the goal of reducing administrative burden in research and reducing bureaucracy, lofty objectives that clinical trial administrators and others could be forgiven for greeting with skepticism.

After all, the successes the FDP has had thus far in reducing unnecessary paperwork have been offset by the increase in new documentation requirements under the U.S. Patriot Act, including the unfunded mandates regarding the handling of biohazardous materials, exporting materials to foreign countries, and recruiting foreign scientists and students, some FDP members say.

However, the research administrators, faculty, and investigators who participate in phase IV of the FDP say they are enthusiastic that some of the new goals will be achieved and that others at least will be discussed with federal officials for the first time.

"FDP is one of the few, if not the only forum that serves the purpose of getting groups together to talk about burdens that some federal regulations may have created either inadvertently or knowingly," says **Thomas Higerd**, PhD, professor of

microbiology and associate provost of institutional research and assessment at the Medical University of South Carolina (MUSC) in Charleston.

"The main success in this latest phase is what we're trying to do is work with federal officials to either eliminate or streamline or simplify nonvalue-added research compliance requirements, such as payroll certification or subrecipient monitoring," says **Elizabeth Mora**, associate vice president for research administration department at Harvard University in Cambridge, MA.

The FDP is a faster way to bring researchers' and research administrators' ideas to the attention of federal regulatory officials, notes **John Bain**, associate director of cost analysis and compliance department at Harvard University.

"Federal agency representatives also are a part of FDP so there is a joint working arrangement for understanding the areas of regulations that need changing," he says. "This was a very constructive approach; rather than just writing letters or using lobbyists — we can meet with the federal agencies directly."

One of the bigger successes has been the expanded authority, which allows successful initiatives that are piloted by FDP institutions to be rolled out for all institutions, Bain says.

"That was one of the early big wins that allows much more streamlined changes and modifications of grants, which federal authorities have agreed to," he adds.

There have been numerous successes since the project began in the mid-1980s as the Florida Demonstration Project, says **Dillard Marshall**, director of the Office of Research and Sponsored Programs at MUSC.

"One of the cornerstones of FDP is the intent to reduce administrative burden of conducting research while sustaining or promoting public accountability for research funds," Marshall says. "So there has been extensive work where we've been able to reduce a lot of bureaucracy."

For example, some of the changes promulgated by FDP has eased the burdens of faculty and staff who handle grants, including the use of expanded authorities, says **Marvin Paule**, PhD, professor and interim chair of biochemistry and molecular biology at Colorado State University in Fort Collins.

"It eliminated a lot of silly paperwork that we needed to do to administer our grants," he says.

Also, current members of FDP are working potential solutions to some major sources of regulatory burden to research institutions, including changing the way effort reporting occurs, improving the process for recruiting foreign scientists/students, and improving space surveys. **(See story on potential improvements to regulatory process, p. 9.)**

Where FDP has worked

Paule and some of the other current members of FDP provide these examples of some of the research burdens that have been improved:

• **Reducing paperwork for subrecipient monitoring:** "What we've done on subrecipient monitoring has been the most successful of all of the efforts," Mora says.

"We as prime recipients of federal funds are responsible for compliance requirements of all of our subrecipients," Mora explains. "If we contract with Brown University, and they have a problem on our award, then we're responsible to make sure they pay back any money owed or we need to increase oversight in that area."

The old and time-consuming way of providing this oversight was for the main grant recipient to write letters requesting updates from the subrecipient, Mora says.

This took time away from other research administrative duties and resulted in extra loads of paperwork, and it added no value to compliance goals, she adds.

So thanks to FDP, this process has been simplified: Rather than write letters to subrecipients, the main grant recipient can check the Federal Clearinghouse web site and use that site's information as the monitoring tool. If the subrecipient has any problems to report, they will be posted on the Clearinghouse web site, Mora says.

"The Clearinghouse uploads the detailed results of all of our audits into one place so that any sponsor or member of the public can look and see how we're all doing," she says.

If a subrecipient has a problem, then the main grant recipient can follow up, and if there are no problems, then no additional action needs to be taken, Mora adds.

This change along has saved Harvard one-half a full-time equivalent position, Mora says.

• **Permitting no-cost extensions:** Budget revisions were a costly part of the process for institutions before the FDP paved the way for easy no-cost extensions, Marshall says.

Previously, it might take institutions weeks to receive word on no-cost extensions even though 99.9% of them were approved, he adds.

Now, institutions can make the decision locally, giving a study a one-time no-cost extension for up to 12 months and reporting this extension to federal officials prior to the grant's expiration date, he says.

"There's no additional cost to the government," Marshall adds.

For example, if an investigator is collecting data from 1,200 patients and the region is hit with bad weather, resulting in many no-shows to the clinic that cause the work to be delayed, then the research institution can provide a no-cost extension so the investigator can complete the work, he explains.

FDP members want more improvements

They're raising questions about biggest burdens

Members of the Federal Demonstration Partnership (FDP) are aiming high in their latest efforts at improving efficiencies and reducing unnecessary paperwork during research.

For one example, researchers, professors, and administrators in the FDP have made it clear to federal officials that they need clerical help to carry out many of the regulatory requirements, says **Marvin Paule**, PhD, professor and interim chair of biochemistry and molecular biology at Colorado State University in Fort Collins.

"Just the clerical aspect of taking care of all this [documentation] is quite onerous," he says.

For example, investigators who have a number of different studies at one time may have particular paperwork that has to be filed each, only each document is different, Paule notes.

Since they may not fill out a particular report more than once or twice a year, they will have to look up instructions for each report, and all of this adds to their time burden without providing any value to the research, he says.

In addition, many researchers will have to file paperwork for each of their postdoctoral assistants to the point where the burden becomes onerous, Paule says.

"One of my colleagues filed 18 reports in one year because he had post-docs and undergraduates doing research, and it snowballs to the point where I don't think the agencies realize how much time we're spending on that kind of stuff," Paule adds. "It's gotten worse and worse and it detracts from what we're trained to do."

However, federal grant rules prohibit researchers from using grant money to hire someone to handle the paperwork burden.

"A lot of researchers are saying, 'If we could have a super tech, a project coordinator that is elevated and could fill out a lot of these forms, then that would relieve the high-paid faculty member to do research,'" says **Thomas Higerd**, PHD, professor of microbiology and associate provost of institutional research and assessment at the Medical University of South Carolina in Charleston.

Also, if the regulations would allow researchers to have an expert coordinator handle the paperwork, it would benefit the government in the long run by increasing the amount of research that could be done, he adds.

A solution would be to use direct grant funds to hire an expert coordinator who would not only file some of the paperwork, but answer questions for researchers about paperwork that they will continue to file themselves, Paule says.

The FDP has begun to entertain discussions about this issue with the possibility that a potential solution will be initiated on a trial basis, Higerd notes.

"That's probably the No. 1 issue that I glean from the faculty side," he notes. "The tremendous amount of paperwork has become so burdensome that some researchers may even stop doing research."

Likewise, researchers and administrators would like to change effort-reporting requirements for investigators, FDP members say.

"It's very hard for physicians and other scientists to understand the concept of effort," says **Elizabeth Mora**, associate vice president for research administration department at Harvard University in Cambridge, MA.

"They want to think, 'If I work 80 hours a week then that's 200% effort,' but the government says that whatever amount of time you work is 100%, whether it's 30 hours or 70 hours," she explains.

Also, investigators have difficulty determining exactly how much time they've spent on any particular project, Mora notes.

For example, a researcher might be conducting studies at a university, holding clinical trials at a teaching hospital, teaching at one or more universities, and have a Veterans Affairs appointment or private practice, notes **John Bain**, associate director of cost analysis and compliance department at Harvard University. "Trying to keep track of all of those

parts of their work quantitatively is very difficult."

Nonetheless, federal grants require investigators to break down their time per project and report how much effort they put into each project, Bain and Mora say.

This has posed problems for some institutions when effort reporting has been done incorrectly and is later audited by federal officials.

A better solution might be to use the annual progress reports as a proxy to effort reporting, Mora suggests.

Instead of expecting investigators to punch time clocks for each study, it would be better to look at the big picture of whether or not they are producing research and publishing their findings, Mora and other FDP members say.

"No matter how much effort someone says they are spending on a study, if they are not showing results then it doesn't matter," Mora says. "My peers will not refund me, so there are built-in checks and balances."

An FDP subcommittee is reviewing different options for replacing effort reporting, and the next step will be to meet, discuss these options, and listen to feedback from federal officials, Bain says.

Another issue FDP members would like to address involves the required space surveys, he adds.

"We've had a couple of different meetings about it and have tried different models and approaches, but have not yet landed on a recommended resolution," Bain says.

Space surveys require institutions to measure the facilities where research takes place and then allocate the portion of those facilities that are used for organized research in order to recover facility costs, including utilities and maintenance, he explains.

Conducting space surveys is complicated and expensive, Bain adds.

The goal is to come up with a method that is cheaper, easier, and more efficient for institutions to use, he says.

"Our goal is not to get more money out of the government, but to spend less of our money on compliance," Bain says. "The administrative cost recovery has been capped since 1993 or so at 26%, so if your administrative costs exceed 26%, which in most cases it does, then the additional costs come out of your own pocket."

Another concern of research administrators and investigators, which they hope to discuss at FDP meetings, involves the new problems they are having with recruiting foreign students, Paule says.

"The federal government has really cut back on visas for foreign students, and we are seriously falling behind the rest of the world in recruiting the best and brightest minds outside of the United States," he says. "If you look over the past few decades, you will find that many of the major achievements in basic science have been made by foreign students in the United States." ■

Willingness to participate in trials varies by race

Non-Caucasians more suspicious of true intent

Non-Caucasian cancer patients, while just as interested as Caucasian patients in learning about clinical trials, approach their decision to enroll in one differently, according to new study.

They tend to talk to family, friends, and other patients while considering enrollment rather than looking to sources such as the Internet. They are less likely to sign up for a trial unless the chances are high that they'll benefit from it.

And non-Caucasian patients are more than twice as likely as whites to believe that they have been treated as part of a clinical trial without their knowledge — likely a legacy of the infamous Tuskegee study that ended in the 1970s, says the study's lead author, **Charles Wood**, MD, a radiation oncologist at the Hospital of the University of Pennsylvania in Philadelphia.

Wood presented the study in October at the annual meeting of the American Society for Therapeutic Radiology and Oncology.

He says the challenge for investigators and IRBs is to recognize the differing attitudes of white and nonwhite patients and to address them, particularly during the informed consent process.

"I think it's our responsibility to get better," Wood says. "We think we communicate much better with patients than we actually do. If this is going to improve, it's not going to be making the non-Caucasian patients change their attitudes. It's going to come from us."

He also noted that patient-to-patient networks that allow prospective participants to talk to patients who already are part of a clinical trial could be helpful in recruiting minorities.

Wood's group surveyed 166 cancer patients over eight months in 2003 at two radiation oncology clinics regarding their attitudes toward

clinical trials. Patients ranged in age from 15 to 84. The most common cancer diagnoses were breast, prostate, and head and neck cancers.

Wood says that his study didn't initially focus on race, but looked at a variety of factors, including gender, age, and the differences between patients at the two clinics — one a Veterans Affairs hospital and another at the University of Pennsylvania.

But it was the attitudes expressed by patients of different races that became clear in analyzing the data, he says:

— While both groups showed about the same interest in learning about clinical trials, Caucasians were more likely to seek out more information from the Internet (31% vs. 11% for non-Caucasians) or from their doctors (50% vs. 34%).

— Non-Caucasians were more likely to talk to other patients about enrolling in a clinical trial (25% vs. 12% for Caucasians).

— Minority patients were more likely to feel that they would need a better than 50% chance of benefiting from a clinical trial to agree to it (64% vs. 45% for Caucasians). Both groups, however, had similar expectations regarding potential side effects from the treatment.

— Non-Caucasian patients were more than twice as likely as whites to believe they had been treated in the past in a clinical trial without their knowledge (22% vs. 9%).

That last statistic leapt out at the researchers, Wood says. "We put the question there almost as an afterthought because we didn't think we'd get much of a response. And that was when our jaw dropped."

Trust not inherent

Wood, who is Caucasian, says he believes the attitude expressed in the question relates directly back to the U.S. Public Health Service's Tuskegee syphilis study, in which black male patients in Alabama were enrolled in a 40-year study to examine the effects of syphilis.

The men enrolled in those studies weren't told they had the disease or given effective treatments for it. The study ended in 1972, after word of it was leaked. Patients' families sued, and won a $9 million settlement. In 1997, President Clinton formally apologized to the victims.

Wood says the effects of the notorious study still resonate in the minority community decades after it ended. Knowledge of the Tuskegee study combine with conspiracy theories about other public health threats — AIDS, drug addiction, Agent Orange — to create a deep well of distrust that doctors may not be aware of, he says.

"We have the expectation that trust for us on the part of the patient is inherent — that they're automatically going to trust us because we are their doctor," Wood says. "We need to understand that we are not automatically trusted and at least according to this question, [some of the time], we are not trusted at all."

He says if researchers know that mistrust exists, they can work to overcome it, and that an understandable, unpressured informed consent process can be a key tool in doing that.

"The non-Caucasian patient sees [informed consent] as a legal loophole for the physician to be protected, regardless of how he acts," Wood says. "I think when you go before the IRB board, they should put a lot of emphasis on the consent form being educational to the patient — explaining in very basic language why they're doing the trial, what you could get out of the trial, and how the trial might hurt you. I think the IRB is a crucial step."

Wood says patients shouldn't be pressured to sign the form immediately, but encouraged to take it home and discuss the clinical trial with friends, family, and community members.

He's unsure how to address the finding that non-Caucasian patients want a higher chance of benefit from a study.

"It's not like you can make any guarantees in the trial," he says. "You shouldn't put any more emphasis on the positive vs. the negative. Just have the knowledge that non-Caucasian patients expect more from the trial."

Wood advocates for an organized patient-to-patient contact that would allow people considering a clinical trial to talk to those already in it. Patients interested in being contacted could give consent to have their names released.

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"Patients trust other patients, perhaps more than they trust physicians, because the patient's interest is in getting well," Wood says. "A patient might think the physician's interest is financial, or fame, or any number of other things. I think a patient-to-patient network would just be a huge help."

Most importantly, Wood says, researchers and IRBs need to place the burden of overcoming attitudes such as those identified in this study squarely on themselves. "We're targeting ourselves because we're just not getting the job done." ■

CE/CME objectives

The CE/CME objectives for *Clinical Trials Administrator* are to help physicians and nurses be able to:

- review pertinent regulatory mandates;
- develop practical clinical trial oversight strategies;
- review best practices shared by facilities that successfully conduct clinical trials. ■

CE/CME *questions*

Physicians and nurses participate in this medical education program by reading the issue, using the provided references for further research, and studying the questions at the end of the issue.

Participants should select what they believe to be the correct answers, then refer to the list of correct answers to test their knowledge. To clarify confusion surrounding any questions answered incorrectly, please consult the source material.

After completing this activity at the end of each semester, you must complete the evaluation form provided and return it in the reply envelope provided to receive a certificate of completion. When your evaluation is received, a certificate will be mailed to you. ■

1. Which of the following is an achievement resulting from the Federal Demonstration Partnership?
A. FDP has reduced paperwork for subrecipient monitoring.
B. FDP helped give institutions flexibility in providing no-cost extensions to research.
C. Both A and B
D. None of the above

2. The Belmont Report established sound criteria for informed consent, including which three elements?
A. Information, comprehension, and voluntariness
B. Honesty, risks/benefits, understanding
C. Clarity, flexibility, cultural sensitivity
D. Justice, beneficence, do no harm

3. A clinical trials expert advises administrators and investigators to improve the trial closeout process by developing a checklist that is used each time. Which of the following should be included on the checklist?
A. Did you do the final invoice?
B. Is the financial report done?
C. Has all the cash expected come in and been received?
D. All of the above

Answers: 1-C; 2-A; 3-D.