Concerns over risk to pediatric participants leads to study's end

Review by four IRBs didn’t smooth the path for observational study

A controversial pesticide exposure study involving Florida babies and toddlers has been canceled in the wake of criticism that it targeted lower-income families, offered too much financial compensation, and exposed children to too high a risk of harm.

The Environmental Protection Agency (EPA) defended the Children’s Health Environmental Exposure Research Study (CHEERS) as a means of helping understand how children are exposed to pesticides used in the home.

But acting EPA administrator Stephen Johnson announced the cancellation in April, saying the agency “must conduct quality credible research in an atmosphere absent of gross misrepresentation and controversy.”

Johnson’s own career path became a part of the debate. The announcement of the study’s cancellation came only a few days after two U.S. senators, Barbara Boxer (D-CA) and Bill Nelson (D-FL), announced they would halt Johnson’s bid to be named EPA administrator unless the study was canceled.

In defending the CHEERS study, Johnson argued that it had been reviewed by four IRBs to ensure the study was designed in an ethical way.

The EPA first announced the details of the planned study in 2003. The two-year field measurement study would recruit families in the Duval County, FL, area, seeking a total of 60 children from two age groups: infants recruited into the study soon after birth and children recruited at about 12 months old.

The families would be asked about their use of pesticides during the eligibility screening process, and a field technician would inventory all pesticides being stored in the home.

Field staff would visit families accepted into the study five or six times over the two-year period, collecting air samples, surface wipes from various locations in the home, dust samples, and soil. In addition, parents would have to collect a urine sample, usually in a diaper, and put a piece
of clothing on the child that would be examined later for traces of chemicals used in the home.

Parents also would have to provide duplicates of food eaten by the child over a 24-hour period, keep a diary of the child’s activities during a five-day period, have the child wear an activity monitor for the five-day period, videotape their child, and keep monthly logs of pesticide use and cleaning habits.

Participating families would receive payments as part of each visit, with families who participating throughout the two-year period receiving up to a total of $970. They also would be able to keep the video cameras provided for monitoring.

Compensation, education questioned

When the details of the study became public, several criticisms were raised about the study’s design, including:

- **Study population** — Critics charged that the families being recruited were predominately lower income. EPA officials stated that CHEERS advertising was being conducted throughout the county, including in private pediatricians’ offices, magnet schools, and private schools.

- **High payments** — The EPA defended the $970 payment to families, noting that they were being asked to perform very labor-intensive tasks as part of their participation.

- **Pesticide education** — Wuerthele says she was very concerned that participants in the study wouldn’t get enough information about preventing their children from pesticide exposure.

The EPA fact sheet for the study states that a member of the research team would inventory any pesticides in a home, explain the importance of following label directions, and be sure participants were only using pesticides that were registered for use indoors. If participating children were found to have elevated exposures based on their urine samples, the EPA immediately would
step in to investigate the cause and correct the problem.

But Wuerthele says the agency has an obligation to go further — to explain to participants that pesticides are neurotoxicants, and that they should minimize their children’s exposure to them.

“Literally, there’s no risk to be in the study, but there’s a whole lot of risk if you use pesticides around your baby,” she says.

- **Study funding** — News reports stated that about $2 million of the $9 million cost of the study was to be provided by the American Chemical Council, raising criticism from environmental groups.

The design of the study does raise ethical issues, says Harold Y. Vanderpool, PhD, ThM, a professor of history and philosophy of medicine at the Institute for the Medical Humanities at the University of Texas Medical Branch in Galveston.

Vanderpool, who reviewed the CHEERS study design published on the EPA website, says that because participation in the study wouldn’t increase the risk to the children involved, it wouldn’t fall under the federal guidelines regarding research involving children. But he says that researchers also are bound to look to general ethical principles, including the principle of a “duty to warn” a person of risk of harm.

“In this case, what you have is research going on with babies and toddlers that could very likely indicate that some of the pesticides used around them are anything from neurologically damaging to growth limiting, maybe even affects their brightness mentally — who knows what all these effects of pesticides might be?”

R. Alta Charo, BA, JD, professor of law and bioethics at the University of Wisconsin Law School in Madison, compares the situation to a study that looks at people at risk for HIV. Those participants must be warned about the necessity of using condoms, even if they choose not to use them.

“I think you want to be very sure you want to explain to people in the course of enrollment, that there are these concerns about exposure to pesticides among children,” she says. “We don’t have all the answers — that’s why we’re doing the study. Certainly many people think that it’s better to simply avoid exposure for the children if at all possible. [Participants] would be encouraged to do exactly that.”

Vanderpool says there’s nothing the study design that indicates that the EPA would intervene if children were shown to be harmed by their exposure to pesticides — specifically, removing them from the study. In fact, he says, the structure of the payments provides a strong incentive to continue.

“They have a two-year protocol that has increasingly large payments, designed to do what? Designed to keep them in the study for two years,” Vanderpool says. “One could say that any observational study that observes that the subjects are being harmed should certainly have the duty to warn, and the duty to cease the study and begin educating.”

Charo says the issue of monetary compensation for research subjects is always tricky.

“We understand that the nature of the incentives should be such that it does not cause people to abandon their own good judgment,” she says. “So you’re walking a fine line between attracting people without making the offer so overwhelmingly tempting that a person of ordinary character would be unable to resist the temptation.”

Vanderpool says the study design posted by the EPA doesn’t contain information about existing animal and human studies that would justify or mitigate the need for this particular study.

“Were I serving on the IRB that looked at this protocol, I would say, ‘We defer this until the researchers come back and talk about the validity of this research, which freezes in place the lifestyle of these kids for two years and does it with the clincher of increasingly large payments to their families to keep them in the protocol,”’ he says. “Does the scientific validity outweigh that? And I suspect it would not, but I don’t know.”

Vanderpool says if his IRB had decided to allow such a study to go forward, he would have wanted a much smaller monetary compensation for participants.

**EPA contracts with IRBs**

Preuss, who is the EPA’s human subjects research official, says the agency doesn’t have an IRB of its own, but contracts with IRBs to review human research conducted by the agency or using agency grant money. All studies also must be approved by him. Four IRBs reviewed the CHEERS study:

- Battelle Memorial Institute, a Columbus, OH-based private company that was the contractor for the study;
- the University of North Carolina, which has a standing relationship with the EPA’s Human Studies Division, located on its campus;
- two IRBs at the Florida Department of Health and the University of Florida, because of
the location of the study.

Battelle officials declined comment for this article, referring questions to the EPA.

UNC's director of the Office of Research Ethics, Daniel Nelson, MS, says his board did not review the entire CHEERS study, but only a neurodevelopmental questionnaire that was to be used with parents in the study.

Jeff Goldhagen, MD, director of the Duval County Health Department, says approval had been received from the University of Florida IRB and was pending from the state Department of Health IRB when his agency decided to terminate its involvement in the study, based on the information that it was funded in part by industry.

Preuss says he sees no reason to change the current system of relying on outside IRBs for reviews of EPA human studies. "I think we are very comfortable with the work that the IRBs do—I don't see any change in that at all."

The controversy over the CHEERS study played out against the backdrop of another debate over how to deal with so-called third-party studies conducted by outside entities, often chemical manufacturers seeking to loosen EPA restrictions on their products by offering new research that shows lesser risk.

Preuss says the EPA is currently developing a policy that could subject such studies to closer scrutiny, including ensuring that the research has complied with the Common Rule.

Charo, who was the review coordinator of a National Academy of Sciences (NAS) report on the use of pesticides in research, says she believes the third-party debate has helped drive the controversy over the CHEERS study.

She says many opposing the use of third-party data were suspicious of the motives of the manufacturers, and skeptical of their claims that the research could benefit public health.

"In the NAS report, you'll see that committee struggling with this and finally concluding that there may very well be situations in which the public health and protection of the environment really is enhanced by a more accurate and nuanced appreciation of the way in which pesticide residues remain and the effects they have on people," Charo explains. "And on that basis, they came to the conclusion that this is research that should be done, where it is justified and properly controlled.

"I do think it is this underlying hostility that is part of why people are reacting so strongly as they are to [the CHEERS study], the most benign kind of study that is done on humans, which is a naturalist observational experiment."

Asked if he would have been comfortable had the EPA gone ahead with the CHEERS study in its original design, Preuss hesitates. "I think that's really hard to answer with a 'yes' or 'no,'" he replies. "Given the issues that have been raised, we might try to see now if there would be a different study design that would allow us to accomplish the same thing."

He points to the issues of compensation and selection of participants as areas where he might seek changes to the design.

Preuss says the debate served to sensitize the agency to some of the ethical issues surrounding such studies, despite his belief that much of the controversy was based on incorrect information.

He also contends the issues raised in the CHEERS study are useful for IRBs to contemplate.

"They also need to be sensitive about these kinds of public concerns, even without arguing whether they're correct or not," Preuss says. "The fact that there are these kinds of concerns is important for IRBs to be aware of, so they can look over these kinds of studies with an eye toward these kinds of issues."

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**Assembly continues to fight COI rules**

**NIH director supports changes**

A group of NIH researchers known as the Assembly of Scientists (AOS) is continuing organized opposition to implementation of stringent new conflict-of-interest rules slated for full implementation late this year.

The group recently dropped a planned court challenge following statements by NIH director Elias Zerhouni and Health and Human Services Secretary Mike Leavitt that indicate they are open to amending the rules. But they have retained the services of law firm Arent Fox to lobby Congress and the public in support of the assembly's position.1 2

"We do believe some regulation is necessary to prevent conflict of interest and ensure the integrity of federally sponsored research," Ezekiel Emanuel, MD, chief of clinical bioethics at the NIH's Warren G. Magnuson Clinical Center and chair of the AOS executive committee tells IRB Advisor. "But the current rules are so broad and overreaching that
they will hurt the ability of the NIH to attract and retain top scientists and impede the collaborations with industry and outside organizations that are necessary to ensure the sound dissemination and interpretation of research findings."

Many media reports have characterized the AOS as opposing any restriction on paid private relationships between NIH scientists on the federal payroll and companies in the pharmaceutical and biomedical industries.

That's not true, Emanuel says, adding that the rules are far broader than most people realize.

In addition to requiring top scientists to forego outside consulting, and divest of stock in pharmaceutical and biomedical companies, the rules require all NIH employees and their immediate family members to divest of stock worth more than $15,000 in any pharmaceutical, biomedical, food, and beverage company.

The new rules also bar employees from consulting with or accepting any payments from pharmaceutical, biotech, and medical device companies as well as universities, hospitals, and research institutes that receive NIH funds. This can prohibit accepting paid speaking engagements at health care organizations that receive NIH money, whether related to that person's area of work or not. Work with advocacy groups and service in leadership positions in many professional organizations also are affected, Emanuel says.

Since the rules were announced, some noted scientists have announced they will reconsider taking positions at the NIH or will leave the positions they currently have.

James Battey, director of the National Institute for Deafness and Other Communication Disorders, has said he intends to quit before the requirement for stock divestiture takes effect.

Pulmonary researcher David Schwartz of Duke University told The Washington Post that the new rules caused him to rethink taking the helm at the National Institute of Environmental Health Sciences.

The AOS has proposed alternative regulations that, Emanuel says, will effectively prevent researcher conflicts while preserving their ability to work collaboratively with academic institutions and private organizations, he says.

Among the differences:

• Researchers would be prohibited from holding stock in companies or organizations that support studies in that person’s field, or in any area in which they have oversight at the NIH. However, they would be permitted to consult or serve on advisory boards for companies unrelated to their area of research.

• Payment for outside writing and editing would be permitted as would service with professional organizations, but those in leadership and grants administration positions at the NIH could not be paid for doing so, and such employees would be barred from holding stock in any drug, biotech, or medical device company.

The level of restriction should vary based on the influence the particular employee has over funding decisions or pursuit of specific types of research within the institutes, Emanuel states.

The group submitted their recommendations more than two months ago, but have yet to receive any response, he says. Meanwhile, the current rules are in force, with the exception of the requirement for stock divestiture, which has been postponed until October.

References


Study needed on consent process

Personal presentations more effective

A review of nearly 40 years of research of interventions intended to improve informed consent for research participants found mixed results for some of the most popular methods studied. It also revealed a significant lack of good, methodologically sound studies of these informed consent interventions to see which ones work best, says one of the authors.

"I think each one of them [the interventions] could use a very, very good rigorous test," says Ezekiel Emanuel, MD, PhD, chief of clinical bioethics at the NIH's Warren G. Magnuson Clinical Center.

"That would be a great way to spend money, and they're not expensive studies to do, comparatively. If I had enough money, I would invest the
money in making sure each of the studies is really good methodologically, so that the data are really reliable at the other end."

In the meantime, Emanuel says, IRBs can draw some conclusions about what works to improve informed consent — and what doesn’t.

“For IRBs, if there is one take-home message, it’s not at all clear that more, and especially more boilerplate informed consent documents, helps,” Emanuel says. “And there is some suggestion from the literature that more boilerplate doesn’t help, that actually you can improve understanding by just getting rid of that boilerplate.”

Extended discussion helpful

The review, which was published in the Journal of the American Medical Association, looked at 30 studies from 1966-2004 that described 42 trials of practices intended to improve research participants’ understanding.

The authors broke down the various studies into categories — multimedia projects, enhanced consent forms, extended discussion with study staff, testing participants on their knowledge and a group of miscellaneous interventions.

They examined each type of intervention to see which resulted in the greatest improvement in understanding. Among their findings:

— The “extended discussion” option — having the research participant talk about the trial with study staff — resulted in significant increases in understanding in three of the five studies in which it was used. The interventions ranged from a 30-minute telephone conversation with a nurse to multiple counseling sessions lasting up to two hours.

— Multimedia projects, which asked patients to watch videos or interact with a computer program, showed less success, with only three trials out of 12 showing significant improvement in understanding.

— Enhanced consent forms, with improvements ranging from condensed formats to larger type and more graphics, resulted in improvements in only six out of 15 trials in which they were used. The study notes that five of the six successful trials were of “limited quality,” casting doubt on their usefulness.

— Test/feedback interventions, in which patients were tested on their knowledge of the trial, showed successful results in all five trials in which it was used. But the authors said that those patients were tested using the exact wording in the intervention and questionnaire. “This is a serious methodological flaw, because any improvement in the test score would reflect rote memorization of the answers to questions, rather than increases in real understanding,” the study notes.

Researchers attracted to high tech

Emanuel says it’s not surprising that the most-tested methods of intervention — multimedia presentations and enhanced consent forms — were ultimately the least successful in trials.

“There’s an attraction to new high-tech solutions for all sorts of reasons,” he says. “They don’t require extra labor — you can give it to a person and you don’t have to actually have a [staffer] there. And lots of people, not just in the research world but in the education world, somehow think that computers enhance learning.”

Conversely, Emanuel says, the extended discussion intervention is more labor-intensive, and more complicated to study. But he says it shouldn’t come as too much of a surprise that it was a more successful intervention in actual use.

“What this data did for me was to make me stand back and say: ‘Do I learn better by looking at a computer?’ No. A computer tends to be pretty passive. I tend to go to sleep. I don’t actually like it, personally,” Emanuel says.

“When did I learn most? Well, mostly sitting in classrooms where I could interact with people and ask questions,” he says. “In some sense, the result becomes intuitively obvious, once you’ve been forced to step back and look at the data.”

Emanuel says if he were pursuing a very complicated study, with important risks he wanted to ensure participants understood properly, “I would say you ought to recommend to the researchers that they ought to consider more time or second contact with these subjects, just to see if they have more questions or anything. That would be my recommendation.”

More studies needed

But Emanuel says this review hardly is the last word on the subject of informed consent interventions. For one thing, many of the studies were methodologically flawed, so it’s unclear whether the results might have been different had the studies been better designed. Some of the studies reviewed were never even peer reviewed.

Even with a finding such as the success of the extended discussion intervention, it’s not clear
how much discussion helps, and how it should be best carried out.

Emanuel says he’s still interested in studying enhanced consent forms, particularly those that have been condensed to rid them of what he considers unnecessary and complicating boilerplate language.

“We, as a department, still have a great interest in doing a study of short forms,” he reports. “But I actually think, for example, that none of the short form studies [reviewed in the study] are very good; in part, because I don’t think their short forms were very well designed.”

He does think that the findings regarding multimedia projects should make IRBs sit up and take notice.

“I’ve seen some organizations that require videos or computer interaction, and they’re willing to pay $100,000 to create it,” Emanuel says. “At least from this data, I think I’m in a strong position to say there’s no evidence it’s going to work.

“If you see someone who wants to make a video, I would say as an IRB, ‘Why don’t we evaluate how effective that is?’”

Ultimately, Emanuel would like to see several well-designed, rigorous studies of each of the interventions identified in this review.

“I think you could do that for just a few million bucks, and it would be a huge benefit to the research community,” he says. “We’re spending billions, if not tens of billions on clinical research. A few million to figure out which of these interventions give you the biggest bang for the buck would be well spent.”

Reference

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VA develops patient handbook for research

Early studies indicate it’s effective

Staff within the Veterans Affairs (VA) research arm have produced a handbook for veterans considering involvement in clinical trials.

The booklet, which still is being tested for eventual use in a clinical trial, has shown success in an early study of its usefulness among pharmacy students who read it. A second study, testing an elderly patient population, still is under review for publication.

Dennis Raisch, RPH, PhD, associate center director for scientific affairs at the VA Cooperative Studies Program’s Clinical Research Pharmacy Coordinating Center in Albuquerque, NM, says he hopes to continue with a third study as part of an actual clinical trial.

The VA Cooperative Studies Program (CSP) is a research organization within the Veterans Health Administration’s Office of Research and Development. The CSP works on large-scale multicenter clinical trials, primarily within the VA system. Raisch’s center is the pharmacy coordinating center, which makes sure drugs being tested are distributed to various sites.

“For a number of years, we’ve been concerned that patients in the VA and in all sorts of clinical trials may not fully understand the informed consent that they’re signing or have a very good background and understanding of the consent process,” he says. “And that’s really where the initiation of the idea for this project came.”

Raisch says that the higher profile clinical trials have in the public mind these days doesn’t necessarily translate into more willingness to participate.

“It makes the public’s awareness of clinical trials heightened, but it also makes their fears of clinical trials heightened,” he says.

One key issue he wanted to address was patients’ understanding that signing up for a trial doesn’t obligate one to finish it.

“Patients need to understand that before they’re even considering a trial,” Raisch says. “Your right is to make choices as you go along. I think that’s a fear that people have — ‘If I get in this trial, they won’t let me out. The doctor will treat me differently if I get out of the trial.’”

He says the idea was to provide a booklet with basic information about clinical trials presented in an easy-to-understand format. The first draft was written by then-pharmacy student Agatha C. Graham, PharmD, now clinical assistant professor of pharmacy practice at the University of Wyoming School of Pharmacy in Casper.

Graham says she looked to the National Cancer Institute’s clinical trials booklet and other similar published materials to come up with the general organization of the VA handbook. After discussions with staff, the format was changed to a question-and-answer style with questions such as: What is a clinical trial? What should you
know before participating in a clinical trial? “It actually is a fairly generic booklet,” she says. “It does talk a little bit about the CSP program, so it’s specific to the cooperative studies program.”

Raisch says the booklet was written from the perspective of the type of patients who would be in the VA system.

“From the perspective of ‘Why would you as a veteran want to participate in this type of thing?’” he says. “But with a few changes, it could be used in other types of facilities.”

**Students tested better**

The booklet was tested among pharmacy students at the University of New Mexico, which collaborates with the CSP in training students in pharmacy.

In the controlled study, students in the experimental group were given 15-20 minutes to read the handbook, then given a questionnaire that included 25 true/false questions testing participants’ knowledge of clinical trials. Also included in the questionnaire were questions regarding attitudes about clinical trials and motivation toward participation in a hypothetical clinical trial.

Students in the control group were given the questionnaire, but not the handbook.

The experimental group’s knowledge scores were higher (89% vs. 83% for the control group), as were their positive attitudes. There was no difference between the groups in their motivation to participate in the hypothetical clinical trial.

Raisch says it’s noteworthy that even among pharmacy students, who are more sophisticated about the research process, the handbook increased understanding of clinical trials.1

He explains the decision to start with a student group, rather than immediately attempting to test the booklet in a real clinical trial.

“What if our booklet had actually affected people’s perceptions in a negative way?” Raisch says. “Of course we assumed it would have a more positive impact on people’s thoughts about trials. But if it had had a negative impact, it could have affected the enrollment in the main study.”

While he couldn’t release details yet from the study of more elderly patients who read the booklet — a group that included patients who were at the VA for other reasons — he said they found it easy to use.

“They stuck with it, they read the whole booklet — it took them maybe 20 minutes,” he says. “We’re pretty pleased with their response.”

Raisch says ease of use is key to creating a successful handbook for clinical trial participants. The most recent form of the booklet includes color photos, graphics to explain some concepts and boldfaced type of key terms, with a glossary at the back for reinforcement.

“The most challenging part of it was getting it down to that seventh-grade reading level,” he says. “It seemed like most of that was the short sentences. It’s the long sentences that bring you up into a higher-grade reading level.”

Graham suggests that institutions attempting a similar project should seek feedback from as many different perspectives as possible, including people currently participating in clinical trials.

“Just ask [the patients] what kind of things they have questions about that they’d like to see in written format,” she says. “Definitely get a group of people working on it so you can get feedback.”

**Reference**


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**Stem cell research needs separate oversight**

**National Academies release guidelines**

The National Academies have released a set of recommended guidelines for research using human embryonic stem cells, advising research institutions to establish separate oversight committees for such research. Those involved in the report say that the extra layer of oversight is essential to enhance public confidence in stem cell research.

“While we were hesitant to recommend another bureaucratic oversight entity, the burden in this case is justified, given the novel and controversial nature of embryonic stem cell research,” committee co-chair Jonathan D. Moreno, PhD, said in a statement. Moreno is a professor of biomedical ethics and director of the Center for Biomedical Ethics at the University of Virginia in Charlottesville.

While an institution could choose to involve IRB members on a so-called Embryonic Stem Cell
Research Oversight (ESCOR) committee, it should be a separate entity, the report recommends.

"The ESCRO committee should not be a sub-committee of the IRB, as its responsibilities extend beyond human subject protections," the guidelines state. “Furthermore, much [human embryonic stem cell] research does not require IRB review."

The guidelines, which were a joint project of the National Academies' National Research Council and the Institute of Medicine, were released in late April.

The guidelines apply to stem cell lines derived from blastocysts made for reproductive purposes and later donated for research as well as those created specifically for research.

They spell out the responsibilities of IRBs in the course of human embryonic stem cell research, including:

- Reviewing procurement of all gametes, blastocysts or somatic cells for the purpose of generating new stem cell lines.

"Requests to the ESCRO committee for permission to attempt derivation of new [stem cell] lines from donated embryos or blastocysts must include evidence of IRB approval of the procurement process."

- Ensuring proper informed consent to donors regarding the potential uses of the stem cells, the potential for the release of any traceable information about the donors and possible risks to the donor.

- Reviewing any reimbursements to women who undergo hormonal induction to produce eggs for research purposes. The guidelines state that only the cost of the procedure should be reimbursed; similarly, no payments should be provided to couples who donate stored blastocysts for research.

Once stem cell lines have been derived, the ESCRO committee and other relevant committees, such as an institutional animal care and use committee or an institutional biosafety committee, would monitor the use of the lines in research.

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**Trying to reign in a few difficult PIs?**

*Here are tips for dealing with them*

Every compliance department has encountered the occasional investigator who causes staff to pop antacid pills the minute he or she walks into the room. And such personalities may have been tolerated in the past, with today's tighter focus on research compliance and ethical concerns, such personalities now can be a real problem.

There are several common personality and behavior problems that clinical trial staff might encounter among investigators, including the following:

- "Rules don't apply to me."
  
  "One of the biggest concerns is a scientist who feels the rules don't apply to him," says Cindy Kiel, JD, CRA, director of sponsored projects at the University of Nevada, Reno.

  "A lot of times these are brilliant people," she explains. "When dealing with cutting-edge research, what most researchers are doing is pushing what is known, disproving what people thought they knew."

  Because of the maverick personality needed to succeed in this type of research, often the successful investigators also are people who are more creative than bound to rules and conventions, Kiel explains.

  "Sometimes that can flow over into the compliance world where an institution might end up with legal and liability concerns if the individual feels the rules don't apply to him or that they were made to be broken," she says. "There are times when you need to think outside the box and times when you need to play inside it."

  The solution to dealing with an investigator who refuses to follow rules and regulations could be terminating the person's position or contract; although with university tenure tradition, that is extremely difficult to do, Kiel notes.

  "If the person causes extreme liability then you need to go down that road, but if the person will listen to reason, then the team approach sometimes will work," she suggests.

  By this, Kiel means that research administrators assemble a group of people at the institution sit down with the investigator, explain what the problem is and why it's a problem, and let the person know that if things don't change there will be severe repercussion, such as a job dismissal, she notes.

  "Hearing stories about extreme examples of what happens with noncompliance does help," Kiel says.

  For instance, when federal officials brought criminal charges against faculty at another institution because of their inaccurate effort reporting, that got the attention of researchers, she notes.

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"When our faculty saw their colleagues facing criminal sanctions they started calling our office to say, ‘Tell us what the rules are because we want to follow whatever the rules are, and we don’t want to get close to the edge,’” Kiel recalls. “It has much more of an impact when it’s someone they know who gets into trouble.”

- “Don’t bother me with details.”

“A second variety of difficult scientists is the individual who feels like, ‘I’m only here to do my science, and don’t bother me with the business details — that’s not why I was hired,’” Kiel says.

The most effective way to cope with these types of personalities is through proper training of the roles and responsibilities, especially when the person is first hired or learning to become a researcher, she says.

- “It’s not my world, and I don’t want to have to do it.”

Then there’s the type of investigator who simply refuses to follow some rules and obligations, such as taking time for mandatory training courses, Kiel says.

“A lot of institutions have made training mandatory, and those sometimes are the ones who have been hit with legal or audit findings,” she notes. “That gives them the clout on campus to say, ‘We will make this training mandatory.’”

Still, there always are the scientists who will say the rule shouldn’t apply to them because they haven’t gotten into trouble or because they are so low on the federal radar screen that no one will be looking over their shoulders, Kiel says.

One solution is to make the training as pertinent and valuable as possible for investigators, so they cannot use the argument that they wouldn’t learn anything from it.

Recent stem cell bill forbids cloning

More stem cell legislation surfaced in April on Capitol Hill in yet another effort to sidestep President Bush’s almost 4-year-old restrictions, as the latest bill seeks to safeguard the use of nuclear transfer for research while banning human reproductive cloning.

Introduced in the Senate, it’s called the Human Cloning Ban and Stem Cell Research Protection Act of 2005. While the use of somatic cell nuclear transfer for creating stem cell lines is legal in the United States, no federal funds can support such work. The bill would reverse that.

The proposal was written by Sens. Orrin Hatch (R-UT), Arlen Specter (R-PA), Dianne Feinstein (D-CA), Ted Kennedy (D-MA), and Tom Harkin (D-IA).

Michael Werner, the Biotechnology Industry Organization’s chief of policy, said a similar bill is expected to soon come forth in the House of Representatives as well.

Such bipartisan unity is a common theme with several of the recently introduced bills, which seek to establish federal funding for embryonic stem cell research through grants from the NIH.

That’s certainly the case for one House bill, co-sponsored by Reps. Mike Castle (R-DE) and Diana DeGette (D-CO), which has nearly 200 other House members on board. It stipulates that
embryos must have been produced at in vitro fertilization clinics and be in excess. It also says donors must have received proper informed consent and there must be no financial incentives to offer embryos.

For the most part, the myriad congressional bills aim to supplement funding efforts already under way in a number of states "to fill the vacuum," Werner said, created by the President's limit on federal funding.

In contrast to efforts to ease stem cell research restrictions, two other bills on the legislative agenda have been introduced to prohibit all cloning, for research and reproduction. One was written by Sens. Sam Brownback (R-KS) and Mary Landrieu (D-LA), and the other is from Reps. Dave Weldon (R-FL) and Bart Stupak (D-MI). The former has 26 Senate backers, and the latter has 113 supporters in the House. ▼

leukoencephalopathy. As a result, drug safety was a central theme during a senate committee hearing on Crawford's nomination to lead the FDA on a permanent basis.

At that hearing, and again at the conference, he defended the FDA.

"It is important that these concerns do not distort the fact that drugs are safer today than they ever have been before," Crawford said, "and that millions of Americans each day benefit from them."

Efforts to improve the agency's product surveillance include the newly established Drug Safety Oversight Board as well as its soon-to-be-unveiled DrugWatch web page to better provide the public with emerging data and risk figures. ■

FDA head says better communication needed

Sounding a call for a more communicative culture at the FDA, its acting commissioner, Lester Crawford, addressed a lunchtime crowd gathered at the BIO-Windover 2005 conference held April 25-27 in Washington, DC.

The public, Crawford said, is looking to the FDA as a reliable source of information. Safety, of course, is the chief issue that has raised consciousness about the FDA's role, and he acknowledged that "there's been a lot of public scrutiny over this issue."

That topic has gained attention during the past year, largely due to product recalls of the once-popular COX-2 painkiller drugs. More recently, the agency approved Biogen Idec Inc.'s Tysabri, only to see the company withdraw the drug months later due to the discovery of deaths linked to progressive multifocal

CE/CME objectives

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

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

COMING IN FUTURE MONTHS

- Collaboration helps network of IRBs work more efficiently
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- Overseas studies: Taking cultural difference into account in informed consent
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Physicians, nurses, and others participate in this continuing education program by reading the article, 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. The semester ends with this issue. 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.

21. A pesticide exposure study involving Florida babies and toddlers was cancelled due to charges that it:
A. offered too much financial compensation
B. targeted lower-income families
C. exposed children to too high a risk of harm
D. All of the above

22. A review of studies testing various interventions to improve research participants’ informed consent found which of the following to be the most successful?
A. Extended discussion between the patient and study staff
B. Multimedia presentations such as videos or computer programs
C. Enhanced informed consent documents
D. None of the above

23. Under the new guidelines for research using human embryonic stem cells, IRBs would NOT be responsible for:
A. reviewing procurement of gametes, blastocysts or somatic cells for the generation of new stem cell lines.
B. ensuring proper informed consent for donors of materials used to create stem cell lines.
C. reviewing reimbursements to donors.
D. overseeing actual research done with the stem cell lines.

24. Women who undergo hormonal induction to produce eggs for research can be reimbursed only for the cost of the procedure.
A. True
B. False

Answers: 21-D; 22-A; 23-D; 24-A.