

PROFESSION

HHS cutting red tape to speed clinical trials

Sweeping changes to regulation of human-subject research could streamline the review of protocols and stem the outsourcing of studies to developing countries.

By KEVIN B. O'REILLY, *amednews* staff. *Posted Aug. 15, 2011.*

Wide-reaching changes announced by the Dept. of Health and Human Services would speed up the process of approving and monitoring federally funded clinical trials.

The plans, which represent the first substantive revisions to the country's human-research subjects regulations since they were adopted three decades ago, could help ease the regulatory burden faced by the estimated 30,000 U.S. physicians who act as clinical investigators.

When the federal rules were adopted in 1981, nearly all U.S. clinical trials took place in academia. But a wave of commercialization, driven in part by the high costs of bureaucracy, has pushed about 70% of them to community-based settings, according to the Tufts University Center for the Study of Drug Development in Boston. The center says that nearly half of Food and Drug Administration-regulated trials now take place outside the U.S., where costs are cheaper, due partly to a lighter regulatory burden.

The rules, adopted after abuses in Tuskegee, Ala., and elsewhere came to light, initially took effect when most trials were conducted at a single site. Today, the vast majority are conducted at many different locations, yet federal rules require that each site's institutional review board scrutinize and approve the research protocol and informed-consent procedure. Critics have long argued that the process is redundant, does little to protect trial participants and adds to the cost of conducting badly needed clinical research.

A shift to central IRBs

The HHS proposal, announced in July, would mandate that all domestic sites in a multisite trial name a single review board as the IRB of record, legally responsible for complying with federal regulations and ensuring that trial participants are properly informed of the risks and protected from dangerous protocols. Local IRBs still could review protocols and consent forms and suggest changes, but they would have more of an advisory role. The idea, known as a "central IRB," already is practiced widely in privately funded clinical trials and recently was implemented by the Veterans Health Administration and the National Cancer Institute.

"Using a single IRB would greatly assist sites in dealing with so many of the problems that come from contradictory board assessments," said Kenneth A. Getz, senior research fellow at the Tufts center. "So many boards have different sets of guidelines they follow, and there is so much inconsistency. And, as a result, there is a lot of bureaucracy and inefficiency."

If the central IRB idea is enacted, it could make trials less costly to conduct and less headache-inducing for physicians, said Charles M. van der Horst, MD, associate chief of the infectious diseases division at the University of North Carolina at Chapel Hill School of Medicine.

"The central IRB could have a dramatic effect," said Dr. Van der Horst, who has conducted many multisite trials and is director of UNC's AIDS clinical trial unit. "Once a protocol's approved, then we can just start using it and that will make it a lot easier."

Reforming the human-research subjects review process is key to preventing the further outsourcing of clinical trials to developing countries, said Glenn McGee, PhD, editor-in-chief of *The American Journal of Bioethics*.

"If we can't build a less expensive, more intelligent IRB system in the United States, then we should expect -- along with the other economic rationales for [locating] clinical study in China or India or any number of other possibilities -- that it's just going to get worse and worse and worse," said McGee, bioethics chair at the Center for Practical Bioethics, a think tank in Kansas City, Mo. "Anything we can do to keep clinical research in the context of the United States' more broadly protective rules about human research subjects is good."

While seeking to lighten the regulatory burden, HHS plans to expand who is covered by federal rules. Currently, human-research subjects regulations apply only to studies funded by one of 15 federal agencies or to FDA-regulated trials. Under the HHS proposal, the rules would apply to all studies -- regardless of how they are funded -- that are conducted at a U.S. institution that receives any federal funding for human subjects research.

In addition to streamlining the study-review process, HHS plans to eliminate continuing IRB review for minimal-risk

studies that involve surveys or focus on education or the social sciences. Such studies receive "expedited review" from a single member of the principal investigator's local IRB, but the class of minimal-risk studies that would be exempt from such review would be broadened. For studies not exempted, continuing IRB review would no longer be required once the study gets to the data-analysis phase.

Revising informed consent

The HHS revisions also would limit the acceptable length of informed-consent documents, prescribe how information is presented, allow certain types of information to be included in addenda, slash legal boilerplate terms and make available standardized consent form templates. Such reforms are long overdue, experts said.

"Let's face it. Informed consent in this country is broken," said Ernest D. Prentice, PhD, who for 30 years chaired the IRB at the University of Nebraska Medical Center in Omaha and is now the university's associate vice chancellor for academic affairs.

"Back in the early 1980s, we saw consent forms in single-site trials that were maybe three or four pages long, at most. Now we've got 15-, 20- or 30-page consent documents, and they're so complex that you practically have to go to medical school to understand them."

Among the other changes planned: Investigators would be required to get participants' approval to keep their biospecimens for future research; the process of monitoring clinical trial data for potential adverse events would be simplified; tighter security regarding patient information would be mandated; and the guidance given to investigators would be uniform across federal agencies.

The HHS announcement marks a big step to moving human-research subjects regulation "into the 21st century," said Ann C. Bonham, PhD, chief scientific officer at the Assn. of American Medical Colleges. The Pharmaceutical Research and Manufacturers of America declined to comment on the proposal to *American Medical News*, although a spokeswoman said the organization will file comments with HHS.

The deadline for public comment on the HHS advanced notice of proposed rule-making is Sept. 26. That 60-day comment period is "grossly inadequate," said Sidney M. Wolfe, MD, director of Public Citizen's Health Research Group. He said that considering the sweeping nature of the changes, the public should have at least until Thanksgiving to comment.

An HHS spokeswoman wouldn't say if the deadline would be extended. Once comments are received and reviewed, HHS will issue a proposed rule.

ADDITIONAL INFORMATION:

Changing research rules

Here are the most significant changes HHS is seeking as part of a wide-ranging effort to reduce the regulatory burden physicians and other investigators face when conducting federally funded research. The HHS plan would:

- Require a single institutional review board of record for multisite studies to avoid conflicting IRB recommendations that slow the approval process.
- Require shorter, easier-to-understand informed-consent documents that contain all the key information and cut out legal boilerplate terms.
- End the requirement for continuing IRB review of a study after the medical interventions have been completed.
- Apply human-research subjects regulations to all studies -- whether funded privately or by the government -- conducted at any American institution that receives federal money for human-subjects research.
- Update and clarify the list of minimal-risk research -- such as educational or social-scientific studies -- that can be reviewed on an expedited basis and make it easier for researchers to be exempted from review.
- Create a single government website to allow electronic reporting of all clinical-trial adverse events and let investigators meet all federal reporting requirements.
- Apply specific data-security protections to all research based on how identifiable the patient information being collected is.
- Require written patient consent for any biospecimens for use in future research, because even after stripping them of patient names, they still can be identified by DNA analysis.

Source: "Regulatory Changes in ANPRM: Comparison of Existing Rules with Some of the Changes Being Considered," Dept. of Health and Human Services Office for Human Research Protections, July (www.hhs.gov/ohrp/humansubjects/anprmchangetable.html)

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"Regulatory Changes in ANPRM: Comparison of Existing Rules with Some of the Changes Being Considered," Dept. of Health and Human Services Office for Human Research Protections, July (www.hhs.gov/ohrp/humansubjects/anprmchangetable.html)

"Human Subjects Research Protections: Enhancing Protections for Research Subjects and Reducing Burden, Delay, and Ambiguity for Investigators," advanced notice of proposed rulemaking, *Federal Register*, Vol. 76, No. 143, July 26 (www.gpo.gov/fdsys/pkg/FR-2011-07-26/pdf/2011-18792.pdf)

How to submit comments on the Dept. of Health and Human Services proposal on clinical trials (www.hhs.gov/ohrp)

[/humansubjects/submitanprmcomment.html](#))

"A National Cancer Clinical Trials System for the 21st Century: Reinvigorating the NCI Cooperative Group Program," Institute of Medicine, April 15, 2010 (www.iom.edu/reports/2010/a-national-cancer-clinical-trials-system-for-the-21st-century-reinvigorating-the-nci-cooperative.aspx)

"Principles on Conduct of Clinical Trials and Communication of Clinical Trial Results," Pharmaceutical Research and Manufacturers of America, revised in July (www.phrma.org/sites/default/files/105/042009_clinical_trial_principles_final.pdf)

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