Sweeping bioethical reform proposals contemplated for trials

Although their recommendations are yet to be presented formally, key US bioethicists are poised to recommend sweeping reforms for how both publicly and privately sponsored clinical trials are handled not only in the United States but also in developing countries. Whether and when these putative reforms are implemented depends in part on how quickly the new Administration and Congress begin to focus on the rarefied but generally bipartisan issue of protecting human subjects who participate in clinical trials.

Some recommendations being contemplated by members of the presidentially appointed National Bioethics Advisory Commission (NBAC; Washington, DC) are vulnerable to rejection through disregard, particularly as the commission is set to disband early in October 2001. Meanwhile, the draft NBAC reforms call for establishing a single, independent office with jurisdiction over all—whether federally or privately funded—domestic research involving human subjects; developing a single, uniform set of rules to govern all such research; creating a new framework in which to analyze concerns involving research subjects who may have special vulnerabilities; developing means for compensating individuals who are injured through their participation in research projects; better educating investigators and members of institutional review boards (IRBs) on these matters: changing the membership of IRBs to include more nonexperts and community representatives; and improving the scrutiny of those research protocols that are likely to present notably high or uncertain risks to participants.

Greg Koski, who recently assumed directorship of the new Office for Human Research Protections (OHRP) within the US Department of Health and Human Services (HHS; Washington, DC), endorses many of these reform measures. For instance, he agrees with the notion of bringing jurisdiction of all federal agencies and departments conducting research involving human subjects into a single office.

HHS, and thus OHRP, already has broad jurisdiction over clinical research, including a considerable proportion of it within the private sector, according to Koski. For example, officials in the US Food and Drug Administration (FDA; Rockville, MD) within HHS can hold companies in the private sector that are developing drugs, medical devices, and similar products and testing them in humans to the same bioethical standards that federally sponsored investigators follow, he says. Nonetheless, he says that the federal system for protecting research subjects is "somewhat dysfunctional." One reason is that the US National Institutes of Health (NIH; Bethesda, MD) emphasizes "front-end assurances of institutions" as its principal means for protecting research subjects, whereas FDA officials rely mainly on "post-hoc audits" to evaluate the effectiveness of comparable protective measures. Those separate focuses leave "a gaping hole in the process," he says. It will be "important to bridge this important gap."

Currently, the system operates largely through scattered IRBs, whose members have frontline responsibility for evaluating clinical trial and similar research proposals. "I don't believe that IRBs are particularly well positioned to protect human subjects," Koski says. For one thing, those boards have little or no direct contact with the participants while the projects are under way —neither with the subjects of the research nor, for that matter, with the researchers conducting the projects. To change this practice, he favors a "new, collaborative model [in which] everybody bears responsibility" and in which protecting subjects is the "critical focus."

To implement this admittedly "idealistic" alternative system, "proper education and training is needed at all levels," Koski says. And, to ensure that such training will be effective, he calls for "independent certification" as well as "uniform standards that are recognized nationally for all IRBs, along with universal guidance and performance-based evaluations." Even while outlining these plans for IRB reforms, he also says there are no plans to "abandon the current system." Instead, "OHRB will provide broad leadership and catalyze efforts" to introduce changes "in a timely manner" within limits specified by legislation and rules now governing NIH, FDA, and other agencies. And he envisions on-site inspections being conducted locally at "deputized outposts" in different regions of the country.

On a more-immediate level of reform, a working group within NIH has drafted a prototype "informed consent" document for wide use, according to Mary McCabe of the National Cancer Institute at NIH. It is intended for many different kinds of clinical research protocols, and is framed in relatively simple language that is candid about risks to participants and takes care not to overstate potential benefits. The template document also is designed to be culturally sensitive, specifies that participants be promptly notified about new information pertinent to ongoing clinical trials in which they are involved, and assigns categories of risks as another way of better informing them about research being done.

Meanwhile, NBAC members are considering reform measures affecting clinical research conducted outside the US. For example, a draft report recommends unusual principles for researchers and corporate or government sponsors of clinical trials to follow when planning, conducting, and following up research projects in developing countries. One such recommendation calls for sponsors of research projects to continue supplying successfully tested therapeutic products to those who participated in evaluative trials for some period thereafter, with terms such as cost and duration to be negotiated. Individual researchers would be ethically bound at least to encourage such arrangements by the sponsors.

Another proposal being contemplated goes further. It suggests that, in the aftermath of a research project conducted outside the US, sponsors should provide additional knowledge and benefits—that is, go beyond supplying a specific drug or treatment—to the relevant host communities and countries. Here again, although researchers are not themselves expected to furnish those additional benefits, they are considered ethically bound to see that such matters are broached and negotiated between the research project sponsors and host country officials. "I believe the obligation to sponsors goes beyond the clinical trial in meeting [local] health needs," says NBAC chair Harold Shapiro, president of Princeton University (Princeton, NJ). The terms of that obligation will vary, he adds, suggesting each case likely will entail extensive negotiation.

The subject of bioethics reforms for participants in clinical trials, although perhaps not an immediate priority for the reconfigured US Congress and Administration is "ripe for discussion and change," says Michael Werner, Bioethics Counsel and Director of Federal Government Relations for the Biotechnology Industry Organization (BIO; Washington, DC). Although BIO has no specific response to the NBAC proposals or other reforms now under development, those efforts to reevaluate the system for protecting human subjects are "appropriate," he says. Meanwhile, BIO is "doing a policy analysis…and plans to "participate actively in that debate next year."

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