NIH, FDA favor better "management" of conflicts of interest

Despite a smattering of heated rhetoric calling for wholesale reform of federal conflict-of-interest rules affecting biomedical researchers, top officials at the US National Institutes of Health (NIH; Bethesda, MD) and the US Food and Drug Administration (FDA; Rockville, MD) appear more inclined to tweak those rules while urging universities and other research institutions to develop better means for handling such matters locally. Although the outcome of the current debate over strengthening these rules and more aggressively enforcing them is far from certain, it could have a substantial impact on both the biotechnology and pharmaceutical industries as they pursue a wide and still-expanding array of consulting arrangements, technology-transfer deals, product-evaluative clinical trials, and development of new companies based on research at universities that is often, at least in part, federally sponsored.

Federal agencies in general and NIH in particular carry a "deep obligation to protect the public investment in science," said NIH acting director Ruth Kirschstein during a two-day Conference on Human Subject Protection and Financial Conflict of Interest, held at NIH, August 15–16. According to long-standing NIH policy, objectivity in research "must not be compromised"—either by financial considerations or other temptations, such as the pursuit of personal fame. Although this policy remains intact, NIH is "not trying to stop a changing world" that, through technology-transfer legislation enacted two decades ago, has helped to "fuel the biotechnology industry," she said. "Either too weak or too strong protections are a risk."

Individuals who receive NIH support and the institutions where they work "must comply with federal regulations and policies," Kirschstein said, and they are being urged to "eliminate, reduce, or manage conflicts of interest." Acknowledging that there may well be "gaps in the system," NIH officials have begun visiting research institutions throughout the country to review their approaches to such conflicts as a way of learning what practices are particularly workable and perhaps subsequently developing consensus guidelines based on those "best" practices.

Clinical trials represent an especially sensitive node in the research system where both real and potential conflicts-of-interest can cause serious damage, risk arousing unwarranted skepticism about outcomes, and come under particularly sharp scrutiny, according to FDA Commissioner Jane Henney. Because clinical trials play such a vital role in bringing new therapeutic products to market, they need to be "above reproach" at every stage to prevent the "erosion of public confidence," she said. Both Kirschstein and Henney indicated that disclosure of real and potential conflicts of interest is a critical, and possibly the best path, to retaining public confidence in clinical trials and the associated lab research needed for evaluating therapeutics, vaccines, and other biomedical products.

Meanwhile, William Raub, deputy assistant secretary for science policy in the Department of Health and Human Services (HHS) reemphasized the need for FDA to gain authority from Congress to levy penalties against researchers and institutions if they fail to meet federal regulations—an initiative announced earlier this year (*Nat. Biotechnol.* **18**, 709, 2000). However, even in reiterating this much-criticized plan for legislative authority for assessing civil monetary penalties, Raub sounded similar conciliatory notes as his HHS colleagues Henney and Kirschstein, saying that the "challenge is not to arrest…but modulate" current trends involving financial arrangements between clinical investigators and their corporate sponsors, and to better "harmonize these new monetary realities with patient protections."

Clinical trials represent an especially sensitive node in the research system where both real and potential conflicts-of-interest can cause serious damage.

But newcomer Gregory Koski, who now heads the new Office for Human Research Protections (relocated and renamed from a similar agency at NIH) within HHS, was not so conciliatory, suggesting a potentially far more aggressive path for federal conflict-of-interest policies to pursue in the near future. Koski leans more toward practices that would avoid rather than "manage" such conflicts in the context of clinical trials—a stance that sides with policies recently adopted, for example, by the leaders of the American Society of Gene Therapy (ASGT; Milwaukee, WI).

The ASGT policy states, in part: "All investigators and team members directly responsible for patient selection, the informed consent process and/or clinical management in a trial must not have equity, stock options or comparable arrangements in companies sponsoring the trial." Elsewhere in the private sector among members of the biotechnology industry, conflict-of-interest policies are under development but have not been formalized, according to Angus Grant of Aventis (Frankfurt, Germany), speaking on behalf of the Biotechnology Industry Organization (BIO; Washington, DC).

Surprisingly, one of the strongest proponents for fundamental reform of the federal mechanism for dealing with such conflicts is Representative Dan Burton (R-IN), who chairs the House of Representatives Committee on Government Reform. However, his concerns focus almost exclusively on advisory committees that help officials at FDA and the Centers for Disease Control and Prevention (CDC; Atlanta, GA) to review new vaccine products. Rep. Burton convened several hearings over recent months to explore vaccine safety issues, delving into questions involving harmful side effects associated with several such products.

As an upshot of those hearings, the committee issued a critical report, and Rep. Burton sent it with a blistering letter to HHS Secretary Donna Shalala in mid August, insisting that she implement reforms that he says will correct conflict-of-interest problems affecting two specific advisory committees that were instrumental in reviewing and approving a rotavirus vaccine that was subsequently withdrawn by its developer, Wyeth Lederle, a division of American Home Products (Madison, NJ). In part his letter states, "For the public to have confidence in the decisions made by their government, they must be assured that those decisions are not being affected by conflict of interest." Although top HHS officials agree about that goal, they also insist that their advisors are experts in the scientific issues surrounding the products that they are called on to evaluate.

Jeffrey L. Fox