"DANGEROUS DEPARTURES"

FDA BACKLASH OVER PROPOSALS

WASHINGTON, D.C.—Recent proposals to expedite drug-review procedures at the U.S. Food and Drug Administration (FDA, Bethesda, MD) are provoking a backlash within the agency and prompting an effort to refine the proposals. A sizable group of FDA medical officers contends that the suggested changes could weaken drug reviews and lower safety standards, according to a survey conducted by Sidney Wolfe, who is director of the Public Citizen Health Research Group (Washington, DC) and a frequent critic of both FDA and the drug industry. FDA commissioner David Kessler meanwhile has been meeting with staff members, devising ways to clarify and implement the proposals without undermining current standards.

Last November, Kessler unveiled several proposals intended to speed up evaluations of new drugs. Key among the proposals are plans for moving the testing of some candidate drugs from animal experiments into clinical trials without company sponsors first going to FDA for review, allowing some product reviews to be conducted by organizations outside the agency in the private sector, and accepting drug evaluations conducted by regulatory agencies in other countries instead of relying exclusively on those done within FDA (*Bio/Technology* **9**:1313, Dec. '91).

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Quayle's council under fire

Although these drug-review proposals officially emanated from FDA, they were generated as part of a wider top-down deregulatory effort by the Bush Administration. The White House Council on Competitiveness, chaired by Vice President Dan Quayle, is masterminding much of this effort, which has come under fire several times in recent months from organizations under the Ralph Nader umbrella. For example, these critics asserted in "All the Vice President's Men," a report released last summer, that Quayle's council has weakened "health, safety, and environmental protections." And they urged that the council "not interfere in the scientific and technical work of federal agencies."

Wolfe's recent criticisms focus specifically on the council's influence over FDA, arguing that the proposals for expediting drug reviews represent "sharp and dangerous departures from present agency policies." According to his poll of FDA officials, many of them apparently agree. He received 47 responses from the more than 120 officials who were contacted. More than 80 percent of the respondents said they disagreed or strongly disagreed with the three key proposed reforms for reviewing drugs.

Critics of the survey say it is both "biased" and "guilty of sampling error" because respondents represent only "those who are more disgruntled." Hence, its attempt to be quantitative leads to "uninterpretable gibberish," asserts one FDA official. "The reforms are saying that certain FDA efforts are superfluous, so some agency officials feel threatened and denigrated to a degree. But I see the reforms as positive evolution, streamlining the process and removing unnecessary government involvement without compromising public safety."

FDA officials react negatively

Whatever its quantitative flaws, individual comments contained in Wolfe's survey indicate that some FDA officials are reacting very negatively to the drug-review proposals. For example, on the proposal that institutional review boards (IRBs) be given principal responsibility for authorizing initial safety testing of new drug candidates in clinical trials, some FDA officials asserted that such a policy "could be a disaster" and that it would "compromise patient safety." Moreover, one official commented, IRBs lack "the needed expertise, time, and resources."

The proposal for farming out product reviews and evaluations to private contractors drew similar criticisms. "This is certain to lower the standards for approval of drugs," said one official. "Conflicts of interest may be impossible to avoid," said another. Moreover, "double reviews would likely impede the approval process," said another official, suggesting that such outside reviews may take more instead of less time.

In a similar vein, the third proposal calling for reliance on non-U.S. reviews of drugs would mean "lowering higher American standards," said an agency official in response to the Wolfe survey. "It is the right of the American people to have that standard upheld, no matter if other countries employ different standards," added another.

In interviews with *Bio/Technology*, some agency officials reinforced views represented in the Wolfe survey. For instance, the proposal to hand over candidate drug reviews to private contractors could slow rather than expedite the process and also might prove inequitable to product sponsors, several officials pointed out. Thus, they contend, sending reviews outside the agency could lead to analyses with considerable variability in quality and outcome. They also note that, even for product areas where the underlying science supposedly is static, surprises continue to pop up, arguing this is another point in favor of maintaining standardized product reviews with close oversight within the agency.

Kessler pushes ahead

Kessler, meanwhile, has been holding meetings with officials from the affected centers of the agency to explain the proposals and develop ways for implementing them. The picture that emerges is that the November reform announcement is more properly termed "a melange in varying stages of implementation and planning—not a coherent single proposal," says one FDA official. Thus, although the principles laid out last fall are "being taken very seriously" among top officials within the agency, a number of the reforms "can't be done as initially described," the official says.

Kessler is devising ways to implement the proposals without undermining current standards.

At this stage, the heads of the affected FDA centers are setting criteria for testing and eventually implementing some of the reforms. For instance, early on, IRBs may be asked to evaluate animal studies and authorize phase-I clinical studies in straightforward situations, such as when a sponsor is seeking a new indication for an already approved drug. The FDA centers also are to develop criteria for deciding which IRBs can be deemed "competent" for making such decisions rather than granting blanket authority to IRBs to assume this role. And instead of moving immediately to accept non-U.S. drug evaluations, Kessler has said that FDA will likely conduct more joint evaluations with sister agencies in other countries, as it did recently with the Canadian government for the approval of an AIDS drug.

—Jeffrey L. Fox