FEDERAL BUDGET

House Panel Homes In on NIH

Biomedical researchers got a nasty shock last week when the House Budget Committee outlined proposals for slashing $190 billion in federal spending over the next 5 years to pay for the tax cuts House Republicans promised in their "Contract With America." Among the targets was the National Institutes of Health (NIH). The committee suggested cutting NIH's $11 billion budget by 5% in 1996, followed by a spending freeze for the rest of the decade.

The proposed NIH reduction was the most significant threat to research in the committee's list of what it calls "illustrative" ways to finance the tax cut. The National Aeronautics and Space Administration (NASA) and the Department of Energy would also be hit. And there's more to come: Budget Committee Chair Representative John Kasich (R–OH) promised more detailed proposals, entailing even deeper cuts, in May, when the committee is due to submit a plan to pay for tax cuts and balance the federal budget by 2002.

Opening shot. Rep. John Kasich says more cuts are needed.

This unhappy fiscal news, however, doesn't mean that deep cuts in research budgets are right around the corner. The package the committee outlined last week must go to the full House, then to the Senate, then to conference, and ultimately to President Clinton. Whatever emerges from that obstacle course would simply serve as a guideline for appropriators, who write the actual spending bills. NIH and its supporters therefore have plenty of opportunities to counter the threat; indeed, congressional staffers predicted that the NIH budget would be one of the first programs taken off the chopping block if the Senate, as expected, opts for a less drastic reduction in federal spending.

But even the threat of a decline in NIH's budget caught the biomedical research community by surprise. "There were rumors of proposed cuts in indirect costs," says Dave Moore of the American Association of Medical Colleges, which were not part of last week's bill. "But we hadn't expected anything that targeted NIH."

The idea for cutting the NIH budget was apparently taken from a recent report by the Congressional Budget Office (CBO), which each year is required to prepare a list of programs that could be trimmed, along with an explanation of the effects of such cuts. This year's CBO report describes the impact of a 10% cut in NIH's budget, citing lower success rates and smaller grants, as well as additional curbs on university overhead charges. "We thought 10% was a bit steep," says one congressional aide, "and NIH has a lot of bipartisan support, so we went with a smaller figure."

Other proposals in Kasich's budget package include:

- *NASA*. Save $1.2 billion by reforming the agency's human space flight program. A NASA report released on 16 March proposes turning over space shuttle operations to a private contractor, a move agency officials say will save money, although it is not clear how much. NASA's shuttle and space station programs consume almost half the agency's $14 billion annual budget. The plan also recommends $326 million in cuts to the agency's Mission to Planet Earth program.
- *Energy Department*. Cut $2.3 billion from energy supply research and development. This $3.4 billion account includes solar and nuclear research, as well as fusion and environmental programs.
- *National Oceanic and Atmospheric Administration*. Restructure agency to yield $1.2 billion in savings.
- *Interior Department*. Dissolve the National Biological Service, saving $326 million.

The budget committee's plan is expected to be debated next week on the House floor.

–Andrew Lawler and Jeffrey Mervis

HEPATITIS CLINICAL TRIAL

Panel Clears NIH in Patient Deaths

A panel put together by the Institute of Medicine (IOM) has written what is expected to be the final chapter in a tragic saga of a clinical trial that went wrong. The panel, in a report issued last week, concluded that the deaths of five patients in a test of an experimental drug to treat hepatitis B were not the result of mistakes by researchers at the National Institutes of Health (NIH) who conducted the study. On the contrary, the panel found that the NIH researchers halted the 1993 trial as soon as they discovered the drug—fialuridine (FIAU)—was causing severe liver damage.

The IOM report is the third review of the case. Its findings agree with those of an NIH panel, which concluded last summer that the tragedy could not have been averted because of FIAU's novel toxicity (*Science*, 10 June 1994, p. 1530). Subsequent studies have shown that FIAU binds to DNA, where it remains active in the body longer than researchers had realized. An earlier review by the Food and Drug Administration (FDA) came to a different conclusion, however. The FDA report, issued in December 1993, contended that data indicating liver toxicity "were not analyzed or reported in a way that might have led to some understanding of FIAU's possible hepatic or pancreatic toxicity."

The IOM and NIH panels disagreed with that assessment. "I don't see much that could have been done differently in light of the promising anti-viral effects and the lack of hints that this kind of toxicity could occur," says IOM panelist Michael Saag, an infectious-disease specialist at the University of Alabama. Indeed, says Saag, "if investigators weren't paying as close attention as they were, more patients would have been exposed and more probably would have died."

The lead author of the FDA report takes a different view. Scientists can do a better job of monitoring safety during a clinical trial, says FDA clinical pharmacologist Roger Williams. "Investigators shouldn't automatically attribute away an adverse event to a cause other than a drug." But Williams adds that FDA "did not want to pass judgment on the NIH researchers."

FIAU, a nucleoside analog similar to the AIDS drugs AZT and ddI, was developed by Oclassen Pharmaceuticals as a treatment for hepatitis B, which each year infects about 200,000 people in the United States. About 5% develop a chronic infection that can result in lethal cirrhosis and liver cancer. In short-term animal and human tests, FIAU reduced blood levels of hepatitis B viral DNA and had few side effects.

The trouble began in June 1993, when 10 patients in a longer term NIH trial began developing side effects such as nausea and vomiting. On 25 June, one patient developed liver failure and lactic acidosis, a condition also seen in a man who had died in a previous trial. Although lead NIH investigator Jay Hoofnagle halted the trial the next day, it was too late to prevent deaths: By 1 September, 5 patients had died of complications from liver failure.

In its report, the IOM panel does recommend several changes to clinical trial design and monitoring, such as ensuring that trial safety data are routinely analyzed during a trial rather than after a patient has completed a course of therapy. But panel members say the changes would not likely have prevented the tragedy.

–Richard Stone