

private sources, and last month Brown Lab was gutted as part of an \$8-million renovation. Futrell says the NSF money was a definite help in enticing other donors, as well as in attracting topnotch faculty and students.

Such happy endings are likely to become more common thanks to the successful push for a larger program led by Mikulski. In keeping with the NSF's preference for research over infrastructure, the Administration's fiscal year 1995 request for the program was a modest \$55 million, half of its current budget. A frustrated Mikulski, who in past years has fought to revise NSF's requests upward by tens of millions of dollars, went even further this year. The bill that passed the Senate last month called for a \$300-million program—a figure that was reduced to \$250 million by a House-Senate conference (*Science*, 26 August, p. 1169).

Although Mikulski compromised on funding levels, she didn't give an inch on the strong language that she attached to her bill. She chided the White House for studying the problem of decaying facilities for 8 years without offering a solution. And she issued an unusual warning: The additional funds, which have been added to NSF's overall budget, will be withdrawn unless NSF requests at least as much for the program in the 1996 fiscal year as Congress gave it in 1995. The Senate report also requires the White House to lay out a 5-year plan for academic facilities renovation—exactly the sort of examination that Gibbons has now launched—before it will release the extra money.

As the NSF program grows, officials may come under pressure to relax some of its current rules, including those that require a strict merit-based review. Pitts, who was asked to submit a plan by 1 February, says he can imagine two scenarios. One would be to build a "virtual agency," with representatives from several research agencies meeting to decide jointly, and on a competitive basis, which projects will be funded. The second, more traditional, approach would create a model program that individual agencies could tailor to meet their own needs and preferences. The latter approach would put NSF on alert against even the whiff of pork because, as Pitts puts it, "some agencies have no history and no experience with merit review."

But Pitts is determined to try. "If we can get [other agencies] to accept the concept, we'll have made significant progress," he says. "Merit review is what NSF brings to the table." Even Futrell admits that, in retrospect, obtaining earmarked funds for the Delaware project would have been a bad idea. "Without merit review," he says, "you'd be making grants to institutions where the best people may not want to go. And that would be a waste of money." If Mikulski gets her way, universities will at least have a realistic alternative to the pork barrel.

—Jeffrey Mervis

AGRICULTURAL RESEARCH

USDA Holds Up Grants to Make a Political Point

The good news reached Harry Frank, a biophysical chemist at the University of Connecticut at Storrs, in June. Officials at the U.S. Department of Agriculture (USDA) told him his grant proposal had cleared peer review with a good score and passed all the technical hurdles. He would, they said, receive a check during the summer. Frank recruited a postdoc and waited for the money to arrive. And waited. And waited. University rules prohibit loans in this kind of situation, and Frank had no alternate source of funding. Finally, in desperation, last month Frank managed to find a teaching assistantship to pay the postdoc's salary, which meant the student could not fully devote himself to the lab. As of 2 September, Frank was still waiting for his grant.

Harry Frank is not alone. His grant, along with those of scores of other researchers, has apparently been used by Secretary of Agriculture Mike Espy as a pawn in a political chess match with Congress. According to four USDA staffers who spoke to *Science* on background, Espy put a "hold" on more than 800 research grants in July and August, worth about \$150 million. Most of the grants come from the \$100-million National Research Initiative (NRI), an office set up several years ago—ironically, as a small island of nonpolitical, peer-reviewed science within USDA.

Espy's decision to take NRI and other funds hostage came to light last week when Congress members led by Representative Pat Roberts (R-KS), ranking Republican on the House Agriculture Committee, accused Espy of an "unprecedented" use of research grants to bring pressure on Congress—specifically on himself and a group of conservative members who had been blocking an Administration bill (HR 3171) that would reorganize USDA. The bill would consolidate many offices and, Espy claims, save the government about \$3.2 billion. It cleared the Senate in April, but has been stalled in the House in a dispute over environmental regulations.

Espy ordered the first of two delays in processing grants in July. The impact reached Congress the next month: Roberts, for example, claims that seven research proj-

ects at Kansas State University were held up. Since then, Roberts has also heard complaints from other academic institutions. But the pressure didn't seem to make Roberts more willing to yield. Instead, he fired off an angry letter to Espy on 19 August.

Espy didn't reply to queries from *Science* about the funding snafu, but a USDA spokesperson, Jim Loftus, said the secretary gave a full explanation in a letter to Roberts on 24 August. In that letter, Espy says that if Congress fails to pass the reorganization bill, USDA will have to reduce discretionary

spending by \$140 million in 1995. Research grants fall into this funding category. Espy continues: "Because of these budget realities, we have given all grant and loan programs within the Department closer scrutiny and review." Espy notes that the Cooperative State Research Service (CSRS), which provides the grants, was not the only division affected by the "review," which he insists was not in any way "partisan." He ends the letter by urging the House members to pass the

USDA reorganization bill "to avoid serious budgetary impact."

A department official who declined to be identified conceded that "the intent" of placing a hold on grants was to "deliver a wake-up call" to Congress; it was "a device to say, 'You have to pay some attention to this.'" The official added that it was "perceivable that a political process was going on." He conceded that it was a "double-edged sword," in that grantees may have been hurt, but claimed that the goal justified the means, because "it would be a disaster if [the reorganization] didn't get through." He said that the tactic may have been effective: In the next month, the House may go along with the reorganization, possibly by agreeing to attach it to a bill, now in conference, that provides crop insurance.

William Carlson, associate administrator of CSRS, says that when Espy's office sent out a memo ordering funding held back, it didn't explain the reason. However, "it certainly came out verbally" that the intent was to create political pressure, says Carlson, adding that the politicization of CSRS grants on this scale is "totally unprecedented."



Squeeze play. USDA Secretary Espy put 800 grants on hold.

As a result of the flap, Espy has now agreed to release the entire backlog, says Carlson. "We got it doubly confirmed. There's no hold on the grants in any way; the only problem now is the usual backlog we have at this time of year." Most grants will be processed in the next week or two.

And that will be renewed good news for researchers like Harry Frank and Tama Fox, a

postdoc doing research at Cornell University on iron uptake in pea plants. Fox says USDA is so late delivering a promised stipend check—which pays for groceries and rent—that she had to draw on laboratory funds. She plans to pay back the \$2500 before her fellowship ends.

While USDA officials claim that the whole flap has come to a happy end, some

staffers on Capitol Hill warn that this may not be so. Members of the appropriations committee may be upset to learn that USDA threatened to withhold funds that had already been appropriated for 1994, says an aide to Representative Roberts: "I expect there will be some kind of whiplash back on the department."

—Eliot Marshall

CHEMISTRY

EPA Campaigns for Safer Chemicals

Stephen DeVito is tired of being an environmental cop. He and his colleagues at the Environmental Protection Agency (EPA) have to identify and track hundreds of known toxic and carcinogenic substances released into the environment each year, as they move from air to water to land and back again. Instead, DeVito, a medicinal chemist by training, says he would rather replace his police uniform with a lab coat and promote research into ways chemists can redesign existing compounds to render them harmless to humans and the environment.

Last week, at the Washington, D.C., meeting of the American Chemical Society (ACS), DeVito and his EPA colleague Roger Garrett began that process by unveiling an EPA program called "designing safer chemicals." They are requesting between \$1 million and \$10 million to promote research into the mechanisms of toxicity with a view to redesigning compounds to make them less hazardous. A better understanding of what happens to industrial chemicals inside the body, says DeVito, should make it relatively easy to defang and declaw many toxic and carcinogenic dyes, paints, solvents, pesticides, weed killers, and other chemicals.

What does it take to turn a poison green? The first step is understanding how it is metabolized. Pharmacologist M. W. Anders of the University of Rochester notes that seemingly nontoxic compounds often convert to toxic metabolites. "Most of us would look at hexane [a solvent] and say this is the most innocuous thing in the world." However, it produces toxic byproducts that lead to neuropathy in those exposed to large amounts. In another instance, says Anders, researchers discovered that the fumes from a common paint thinner, dichloromethane, turn into carbon monoxide in the body.

Once you know the mechanism of toxicity, it is often possible to disarm the compound with the simplest sort of substitution. And SUNY-Stony Brook chemist Scott Sieburth says he can sometimes preserve the original function of a chemical if he uses a substitution that keeps the original molecular shape intact. At the ACS meeting, for example, Sieburth announced a

redesign of a common pesticide that was killing fish. With the help of an insect physiologist, he says, he was able to replace some carbon atoms with silicon to create an equally effective but fish-friendly version of the compound.

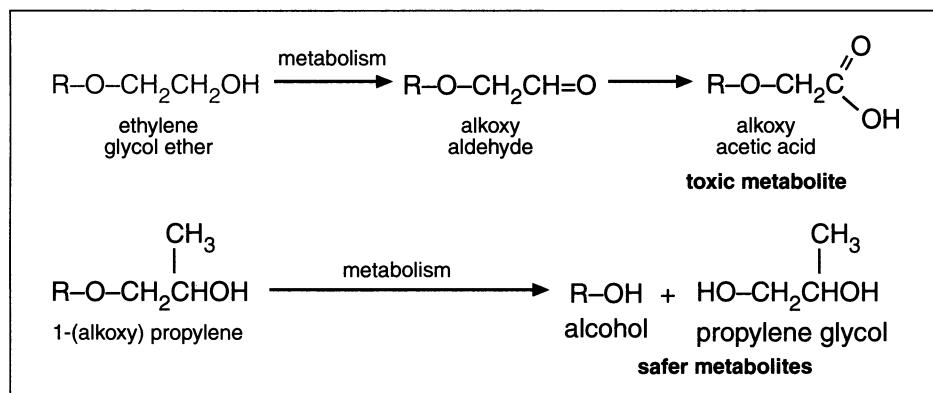
One technique that Nicholas Bodor, head of the Center for Drug Design at the University of Florida, has employed to prevent drug side effects is to create an inactive relative of the drug that is activated by enzymes present at the site where it's needed—the eye or skin, for example. That technique could in principle also result in safer pesticides, says Bodor, by creating inactive compounds that become an active poison only on contact with chemicals unique to the biochemistry of a particular pest.

Bodor also uses a process called retrometabolic design, in which he looks for a harmless and inactive metabolic product of a drug that has some harmful side effects. Then he redesigns the original drug starting from this inactive product. Surprisingly, this often re-

processes. In that program, EPA chemists worked with the National Science Foundation, which awarded \$6 million in grants in a search for cleaner, synthetic pathways. One result, says NSF's Margaret Cavanaugh, was a new way to make quinoic acid—a building block in photographic developing agents and other chemicals. The new process incorporates a bacteria and releases sugar where it used to release benzene. Another research effort resulted in a paint made with supercritical carbon dioxide in place of some of the toxic solvents.

So far, however, industry has reacted cautiously to the new program. Michael Pierle, Monsanto's vice president for environment, health, and safety, warns that it's no simple matter for industry to embrace the substitutes that might result. For one thing, Pierle says, if researchers from another company invent a safer version of one of Monsanto's products, the result could be a costly and lengthy fight over patent rights.

Garrett believes, however, that industry will come to see the benefits of EPA promoting research rather than imposing rules. But he himself points to one practical obstacle:



Making nice. A small change in a glycol ether prevents its metabolism into a substance that can cause developmental toxicity and hematotoxicity.

sults in an active and equally effective new drug. He's applied this approach recently to a steroid drug that reduced inflammation of the eye without causing a buildup of fluid that, in the worse case, might lead to glaucoma.

DeVito and Garrett say they want to apply these approaches to chemicals, modeling their efforts on a 3-year-old EPA program to reduce hazardous waste in manufacturing

The redesign work will require a new breed of chemist, one who understands both synthesis and enough toxicology to recognize trouble within a chemical structure. And it will take time to train them. But Garrett and DeVito are not in any hurry. "The session at the ACS meeting was just the first step in a long road," he says.

—Faye Flam