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.

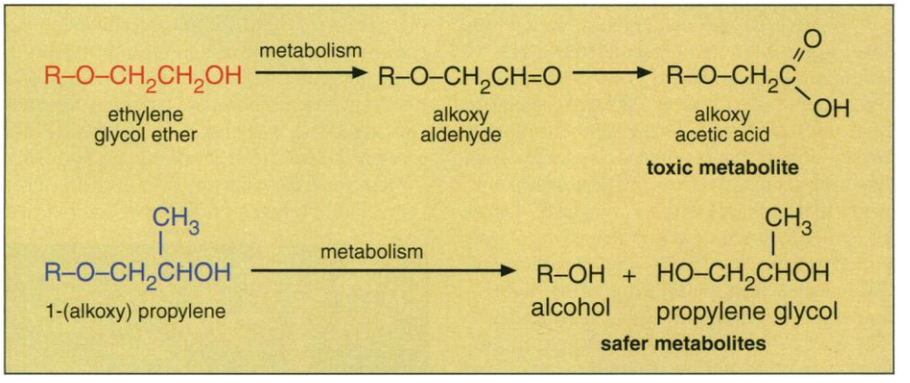
Bodor also uses a process called retrometabolic design, in which he looks for a harmless and inactive metabolic product of a drug that has some harmful side effects. Then he redesigns the original drug starting from this inactive product. Surprisingly, this often results in an active and equally effective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



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