Huge Testing Planned for Hormone Mimics

A committee assembled 2 years ago by the Environmental Protection Agency has completed work on an unprecedented plan to evaluate some 87,000 chemicals for their potential to disrupt hormones in humans and wildlife.

The plan comes in response to evidence that has emerged over the last 2 decades linking a wide variety of environmental pollutants to disturbing deformities and reproductive abnormalities in animals (SN: 1/8/94, p. 24). These pollutants, known as endocrine disrupters, mimic or block the action of hormones.

"I think that we have a lot of suggestive evidence but not enough to convict or acquit [specific chemicals]," says Gary E. Timm, a senior technical advisor at the EPA's Office of Pollution, Prevention, and Toxics in Washington, D.C. "The evidence for endocrine disruption is clearly stronger in wildlife than it is in humans."

Concerned about possible human health risks, however, the U.S. Congress amended two laws in 1996 to require the EPA to determine which chemicals might be endocrine disrupters (SN: 9/7/96, p. 159). The agency then formed the Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC). This month, the committee will release its proposal for EPA and public review.

The agency expects to begin the comprehensive screening by next spring.

At a Boston meeting of the American Chemical Society last week, Timm described the strategy proposed by EDSTAC. It relies on a two-tier process. The first screening, consisting of a battery of eight assays, would determine which substances have endocrine effects and whether they need further evaluation.

EDSTAC hopes that two of those assays can be done in a rapid, automated fashion. Of the original 87,000 compounds, the committee expects that an initial selection of 15,000 widely used chemicals, including all pesticides, will go through this high-throughput screen. "We might get a much better handle on what kinds of chemicals interact with the endocrine system to cause effects as we build that database," Timm says. The early, high-throughput results will help the scientists decide which chemicals to put through the full first-tier battery.

An estimated 1,000 chemicals are expected to pass on to the second tier of tests, which consists of in-depth studies on invertebrates, fish, amphibians, birds, and mammals. "We need to use all of that information to predict risk to humans," Timm says.

The first- and second-tier tests would cost, respectively, about $200,000 and $2 million per chemical, Timm estimates. The EPA would probably bear the cost of the high-throughput screening, he adds, but chemical manufacturers would be responsible for the rest.

"The plan is extremely comprehensive—if not to the point of overkill," says Paul Foster, a senior scientist at the Chemical Industry Institute of Toxicology in Research Triangle Park, N.C., and a member of the advisory panel that will review the final plan next year. "This is a huge amount of data that is being requested."

EDSTAC's plan, however, only examines effects on estrogen, androgen, and thyroid hormones, although endocrine disrupters can upset other hormones' actions (SN: 7/15/95, p. 44). With more time and money, the EPA could include other systems, says Timm, but "this is a reasonable scientific minimum to start with." The plan also recommends testing certain mixtures to see if the sum of many low doses can bring about adverse consequences (SN: 8/2/97, p. 69).

Many of the assays still need to be tested themselves to determine whether they are reliable and reproducible. This validation will be difficult, says EDSTAC member Michael D. Shelby of the National Institute of Environmental Health Sciences, also in Research Triangle Park. "This is an emerging area of toxicology. It's difficult to come up with reference compounds to gain assurance that the tests can discriminate endocrine disrupters from non-endocrine disrupters."

The validation should take 2 to 3 years, Timm says. "I would say that Gary is an optimistic man," Shelby remarks. —*C. Wu*

New strain of HIV appears in Cameroon

Cameroon, which has been a crucible for rare strains of HIV in the past, has earned that dubious distinction again.

French researchers report finding a novel strain of HIV, the virus that causes AIDS, in blood collected 3 years ago from a woman in this central African country. The new strain apparently evolved from either a more common HIV or its simian counterpart, SIV. The report, in the September NATURE MEDICINE, raises concerns that this subtype of HIV may be spreading gradually in Africa but not showing up on currently used diagnostic tests.

"It very likely will not have public health consequences," says Anthony S. Fauci of the National Institute of Allergy and Infectious Diseases in Bethesda, Md. Although the rare viral strain may not be picked up by initial screening, the national blood supply will continue to be protected by the many layers of controls currently in place, he says.

HIV-1 and HIV-2, the two known types of the AIDS virus, arose in East and West Africa, respectively. HIV-1, which more frequently causes a lethal disease, includes two broad strains, dubbed group M (for major) and group O (for outlier). Group M encompasses several subtypes, which together account for most HIV infections worldwide. Group O contains only a few uncommon but deadly viruses, appearing mainly in Cameroonians.

The newfound strain requires a new group. "This group is genetically distinct from group M and group O," says Francine E. McCutchan, a molecular biologist at the Henry M. Jackson Foundation in Rockville, Md. Scientists have named the puzzling strain HIV-1 group N, although it shows some genetic characteristics of SIV.

Researchers discovered the new virus in a frozen sample of the woman's blood taken in 1995. After characterizing the strain's DNA, they checked for its presence in 700 frozen blood samples taken from HIV-1-positive Cameroonians between 1988 and 1997. Most were infected with group M viral strains, and 65 showed group O. Among 16 samples that matched neither group, 3 had viruses strongly resembling the group N strain.

The new strain is as different from SIV as it is from known HIV-1 strains. "[It] can thus be considered as the prototype strain of a new human immunodeficiency virus group," say study coauthor François Simon of the Bichat Hospital in Paris and his colleagues.

Although the virus isn't widespread, it can be lethal. The woman who gave the original blood sample in 1995 died of AIDS later that year at the age of 40.

While it remains unclear whether the new strain evolved from HIV or SIV, scientists have clues as to why it arose in Cameroon. In the rain forest, people encounter many primate species, facilitating the spread of primate viruses into the human population, McCutchan suggests. In the same issue of NATURE MEDICINE, Simon Wain-Hobson of the Pasteur Institute in Paris suggests that the new strain, though rare, may "spread just enough to make life difficult for viral diagnostics." Tests may eventually have to screen for this new HIV strain, McCutchan says. —*N. Seppa*