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EPA FOR YOUR INFORMATION

Screening and Testing Chemicals for Endocrine Disrupting Properties

In recent years, some scientists have proposed that chemicals might be disrupting the hormone (endocrine) systems of humans and wildlife, resulting in reproductive disorders, birth defects, immune dysfunction, and other harmful effects. A variety of chemicals have been found to disrupt the endocrine systems of animals in laboratory studies, and compelling evidence has accumulated that endocrine systems of certain fish and wildlife have been altered by chemicals that contaminate their habitats. With few exceptions, however, such effects have not been conclusively demonstrated in human beings to date.

Because of the potentially serious consequences of human exposure to endocrine disrupting chemicals, Congress included a mandate to EPA in the Food Quality Protection Act of 1996 and the 1996 amendments to the Safe Drinking Water Act to develop an endocrine disruptor screening and testing program. We formed an advisory committee, the Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC), to develop recommendations for such a program, which were finalized in August 1998. We then used EDSTAC's recommendations to design our endocrine disruptor screening and testing program. This document summarizes some of the key EDSTAC recommendations and the actions we are taking.

What is the endocrine system?

The endocrine system consists of glands and the hormones they produce that guide the development, growth, reproduction, and behavior of human beings and animals. Some of the endocrine glands include the pituitary, thyroid, and adrenal glands, the female ovaries and male testes. Hormones are chemicals, produced by endocrine glands, that travel through the bloodstream and cause responses in other parts of the body. An example is estrogen, which is essential for female reproductive function. Hormones can produce both positive and negative effects. For example, some types of breast cancer are exacerbated by estrogen, but studies also indicate that estrogen has a protective effect in combating heart disease and osteoporosis- related fractures in older women.

What are endocrine disruptors?

Chemicals that interfere with the normal functioning of this complex system and cause harmful effects are known as "endocrine disruptors." Disruption of the endocrine system can occur in various ways. For example, some chemicals may mimic a natural hormone,"fooling" the body into over-responding to the stimulus or responding at inappropriate times. Other chemicals may block the effects of a hormone in parts of the body normally sensitive to it. Still others may directly stimulate or inhibit the endocrine

system, causing overproduction or underproduction of hormones. Certain drugs are used to intentionally cause some of these effects, such as birth control pills.

Has EPA ever required endocrine disruptor tests before now?

We currently screen new pesticides and industrial chemicals prior to their introduction into commerce and seek to control any which may pose an unreasonable risk to human health and the environment. New pesticides are routinely tested in animals for effects on reproduction, fertility, and the developing fetus before they are approved for use. Older pesticides are tested as part of our ongoing re-registration program, a comprehensive reevaluation of all pesticides first approved before 1984. The growth and development of offspring are also evaluated, including an assessment of birth defects or other abnormalities. Although these tests are not specifically designed to identify endocrine disruption, they can detect certain reproductive and developmental effects which may result from endocrine disruption. Once re-registration is completed in 2002, we will re-examine all pesticides every 15 years.

At the same time, we are also reassessing all tolerances (maximum limits for pesticide residues in food) and tolerance exemptions for both active and inert pesticidal ingredients to ensure they meet the new safety standards established by the Food Quality Protection Act (FQPA) of 1996. The FQPA tolerance reassessment will be completed by 2006.

What gives EPA legal authority to test for endocrine disruptors?

Authority for screening and testing endocrine disrupting chemicals is based on the Food Quality Protection Act and Safe Drinking Water Act Amendments, both passed by the United States Congress in August 1996, which require us to:

...develop a screening program, using appropriate validated test systems and other scientifically relevant information, to determine whether certain substances may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or such other endocrine effect as the Administrator may designate...

The law requires us to implement this program by August 1999. In addition EPA has broad general authority to require testing under the Toxic Substances Control Act and the Federal Insecticide, Fungicide and Rodenticide Act.

What was the EDSTAC?

The Endocrine Disrupter Screening and Testing Advisory Committee (EDSTAC) was a federal advisory committee formed in 1996 to make recommendations on how to develop the screening and testing program called for by Congress. The EDSTAC was composed of representatives from industry, government, environmental and public health groups, worker safety groups, and academia. These committee members were charged with developing consensus-based recommendations on a scientifically defensible screening and testing program that would provide us the necessary information

In addition to addressing human health effects, the EDSTAC agreed to broaden its scope to consider effects on wildlife. The committee also agreed to consider not only estrogenic effects, but those related to the androgen and thyroid hormones, as well. The committee also recommended that we consider common mixtures in addition to pesticides and industrial chemicals.

about certain endocrine effects of chemicals to *make regulatory decisions about them.*

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Members thoroughly reviewed and discussed scientific information and sought the opinion of other experts and members of the public during its two-year deliberations. The EDSTAC presented its final report to us in September 1998.

What were EDSTAC's recommendations?

The EDSTAC identified approximately 87,000 chemicals to be examined for initial sorting and priority setting. EDSTAC recognized that deciding which chemicals to screen and test first would be the first challenge.

Which Chemicals Should We Test First?
We will test the potentially riskiest chemicals first. However, there are many chemicals for which there is little endocrine-related data we can use to evaluate their endocrine-disrupting potential.

In order to identify high-risk chemicals we know little about, EDSTAC recommended that we, in partnership with industry, conduct roboticized assembly-line chemical assays, called "high throughput pre-screening," on approximately 15,000 pesticides and industrial chemicals to obtain information quickly on whether these chemicals can interact in certain ways with the endocrine system. This will enable us to prioritize them for further screening and testing.

The high-throughput screen data will be incorporated into other existing data in a specialized data base that will help us identify chemicals with the potential to disrupt the endocrine system . By comparing the characteristics of known endocrine disruptors with those of a chemical for which we have little or no data, we will be able to identify potential endocrine disruptors based on characteristics like chemical structure and other properties.

Based on existing information, we will sort chemicals into four categories:

- **Tier One Screening Group**, consisting of chemicals for which there is insufficient endocrine-related data. If the high-throughput screens indicate endocrine disruption potential, or other indicators exist, the Tier One screening tests will provide more data to show whether a chemical can interact with the endocrine system and if more in-depth testing is warranted;
- **Tier Two Testing Group**, consisting of chemicals for which enough data exists to show the potential for endocrine disrupting properties. These chemicals will proceed directly to reproductive and developmental testing. These tests will show us what kind of effects the chemical can cause;
- **Risk Assessment Group**, consisting of chemicals for which enough data already exists to support a full risk assessment; and
- **Polymers**, which will be placed on "hold" status. Because of their large molecular size, it is unlikely that they can be absorbed through membranes. We will first test their building blocks (monomers and oligomers), which are more likely to interact with an organism's biochemical processes.

What will the screening process consist of?
Tier One Screening will consist of short-term

tests *in vitro* (outside the living body and in an artificial environment) and *in vivo* (in the living body of an animal). These tests are designed to identify chemicals that may interact with the endocrine system.

What will the testing process consist of?
Tier Two Testing will consist primarily of longer-term, *in vivo* reproductive and developmental tests that will determine whether a chemical causes harmful endocrine-mediated effects in humans and wildlife.

How will risk be evaluated?
A chemical can cause harmful effects at one exposure level, and have little or no effect at another. Thus, we have to determine the relationship between possible exposures to a chemical and the resulting harmful effects. To estimate exposure, we use data gathered from agricultural field studies, industrial use statistics, water and wildlife monitoring studies, chemical production volumes, and other relevant sources.

If humans or animals will not be exposed to levels of a chemical that have been shown to cause problems, we conclude that the chemical is not likely to cause harm. On the other hand, if exposure levels exceed or come close to those suspected or known to produce problems, we will expect the chemical to cause harm. We will then take regulatory action to reduce risk to acceptable levels. The endocrine disruptor testing data will be incorporated into our ongoing FQPA pesticide tolerance reassessment process.

Will the public have any say in which chemicals will be tested first?

Yes. The EDSTAC recommended that citizens concerned that adverse health effects in their area might be linked to exposure to endocrine disrupting chemicals be permitted to nominate chemicals for top priority testing. This will ensure that low-production chemicals that affect small groups in localized areas, for example, will not fall through the cracks of the core priority setting process, which will focus on high-production chemicals with national impact.

How will EPA use EDSTAC's recommendations?

We will use EDSTAC's recommendations to design our comprehensive endocrine disruptor screening and testing plan. In accordance with the provisions of FQPA, we will solicit public comment and scientific peer review by the FIFRA Scientific Advisory Panel and the EPA Science Advisory Board, two blue-ribbon panels of external experts and scientists, by March 1999; and we will report to Congress on the program's progress by August 2000.

We will continue to work with other federal agencies, state agencies, the private sector, and non-governmental organizations to develop, standardize, and validate screening and testing methods as we fully establish the program.

Consistent with EDSTAC's recommendations on communications and public outreach, we will provide information to members of the public and interested stakeholders on the screening and testing program itself, screening and testing results, and about the nominations process.

Where Can I Go For More Information?

For a free hard copy of the EDSTAC report, call EPA's TSCA Hotline at (202) 554-1404. All EDSTAC documents are available from the EDSTAC web site at http://www.epa.gov/opptintr/index.htm. Or contact us at: Communication Services Branch, Office of Pesticide Programs, U.S. EPA (7506C), 401 M Street, SW, Washington, DC 20460, (703) 305-5017
or visit our general web page at: http://www.epa.gov/pesticides