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Chemicals in Our Community

News and Information

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Our Approach to Endocrine Disruptors

Lynn R. Goldman, M.D.

Dr. Goldman served as Assistant Administrator of the Office of Prevention, Pesticides and Toxic Substances from the Spring of 1993, and chaired the Endocrine Disruptor Screening and Testing Advisory Committee. She left the Agency on December 31, 1998.

Recently, increased scientific and public attention has focused on the potential effects of synthetic chemicals on the hormone, or endocrine, systems of humans and wildlife. The endocrine system consists of the glands and the hormones they produce that help guide the development, growth, reproduction and behavior of humans and animals. Concerns are about potential health effects, like cancers and developmental toxicity, as well as adverse effects on species in the environment. Since we do not know enough about the complex interactions of chemicals and hormone systems, EPA's first efforts in dealing with the emerging issue of environmental endocrine disruptors were in the area of research.

EPA has been a leader within the federal government in developing the science related to endocrine disruption. EPA held two workshops in 1995 to determine what research was needed to respond to human health and ecological questions associated with endocrine disruptors. EPA initiated the following actions identified from the workshops:

(1) In 1996, established a research program on endocrine disruptors that grew to $14 million per year, $8 million of which is dedicated to research in academic laboratories;

(2) Assessed the scientific literature related to endocrine disruptors and published a report entitled, *Special Report on Environmental Endocrine Disruption: An Effects Assessment and Analysis* in 1997;

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(3) Chaired an interagency committee to develop an inventory of federal research on endocrine disruptors; and

(4) Funded a National Research Council study on the science of endocrine disruption.

Fourteen federal agencies participated in the development of the inventory, which will be used to coordinate research efforts and identify issues that are not funded. The U.S. inventory has become the model for an international inventory to coordinate research among other countries.

In August 1996, the Congress concluded that research was not enough. Concerned by the unexplained rise in breast cancer and other diseases that seem to be related to the endocrine system, Congress included a requirement in the Food Quality Protection Act (FQPA) that EPA screen pesticides for estrogenic effects on the female reproductive system that may contribute to disease. Just a few days after the passage of the FQPA, Congress passed amendments to the Safe Drinking Water Act which contained similar provisions to screen drinking water sources for estrogenic endocrine disrupting chemicals. Both bills also authorized EPA to test for other endocrine effects.

Faced with the challenge of developing a screening program ... I thought that a consensus-based approach, while difficult, would be the best way to proceed.

Faced with the challenge of developing a screening program in an area where so many questions were still unanswered by scientific research, and with the hope that a consensus would speed acceptance and implementation by industry, I thought that a consensus-based approach, while difficult, would be the best way to proceed. The Agency appointed an advisory committee to assist in determining how to set priorities for substances, what short term screening and analytical tools the Agency should use, and what tests could be employed to enable the Agency to fully assess the hazard of suspected endocrine disruptors.

We tested the breadth of support for this approach by convening a meeting with our major stakeholders on May 15, 1996. All stakeholders endorsed forming an advisory committee and on October 16, 1996, the Endocrine Disruptor Screening and Testing Advisory Committee, better known as EDSTAC, was formed. EDSTAC was composed of 39 members representing the pesticide and commercial chemical industries, small businesses, state

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In This Issue

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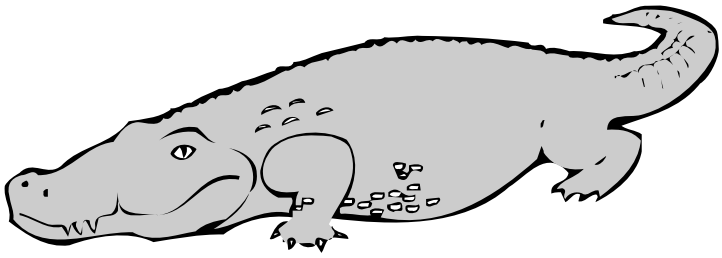
The Endocrine Disruptor Story

Gary Timm

The endocrine system is a chemical communication system that coordinates and regulates the processes that make the life of a multicellular organism possible. An endocrine system is essential to the life of multicellular animals and is found in all mammals, birds, fish and invertebrates. Hormones are produced by various glands and travel through the blood to receptors which are located in various tissues throughout the body. Hormones are biologically very potent molecules, and are therefore effective at small concentrations (e.g., parts per trillion). Much like a lock and key, hormones act by binding to receptors that are produced within cells. The hormone-receptor complex switches on or switches off specific biological processes in cells. The receptors are quite specific for the appropriate hormone but they can interact with molecules that are similar to the natural hormone. Over 50 hormones have been identified in humans and other vertebrates. Examples of biological processes controlled by hormones include sexual differentiation, growth and function of reproductive organs (testosterone and estradiol); control of blood sugar (insulin); and body growth and energy production (growth hormone and thyroid hormone).

The evidence of endocrine disruption is substantially stronger for fish and wildlife than for humans. A series of field and laboratory investigations with marine snails demonstrates that compounds like tributyltin, which are used in antifouling paints on ships, can have significant hormonal effects on some snail species at concentrations 1,000 times lower than lethal exposure concentrations. These compounds can irreversibly induce male sex characteristics on females (masculinization) which can lead to sterility or reduced reproduction. Field investigations in many parts of the world suggest this class of compounds may be responsible for localized reductions in specific snail populations. Feminized males and hermaphroditic fish (fish having reproduction organs of both sexes) have been observed in rivers below sewage treatment plants. Scientists



suspect that natural human estrogens, synthetic estrogens in birth control pills, and substances used in the manufacture of certain detergents are involved. Researchers have documented masculinization, altered sexual development and decreased fertility for some fish species near pulp and paper plant discharges. In many cases specific causative agents have not been identified. However, correlative data supported by laboratory studies in many cases suggest that compounds such as alkyl phenol ethoxylates, their degradation products, chlorinated dibenzodioxins and difurans, and polychlorinated biphenyls (PCBs) could be the causative agents.

One of the most fully documented examples of ecological effects caused by disruption of endocrine function was reported for alligators in Lake Apopka, Florida. Detailed field and laboratory investigations revealed that a mixture of pesticides (dicolfol, DDT, and its breakdown product, DDE) associated with a spill in 1980 was responsible for a variety of developmental effects that indicate a demasculinization of male alligators and "super-feminization" of females. The effects of the spill also included detrimental effects on hatching success and population levels.

Some research shows instances of effects on mammals and birds. A variety of organochlorine insecticides have been implicated in eliciting feminization of male gull embryos, suggesting that these effects may be contributing to population declines and skewed sex ratios in Western gulls in California and herring gulls in the Great Lakes. Although the extreme sensitivity of mink, seals, and related species to adverse reproductive effects from exposure to some dioxins and PCBs is well known, and controlled laboratory studies demonstrate similar effects on rodents, research has not established a

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Small disturbances in endocrine function, particularly during certain highly sensitive stages of the life cycle (e.g., development, pregnancy, and lactation), can lead to profound and lasting effects.

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link between exposure to endocrine disruptors and population declines for wild mammalian populations.

Reports show that humans exposed to relatively high concentrations of certain contaminants suffered adverse effects. However, whether such effects are occurring in the human population from exposure to concentrations present in the surrounding environment, drinking water, and food remains unclear. Several conflicting reports have been published concerning declines in the quality and quantity of sperm production in humans over the last four decades, and there are reported increases in certain cancers in highly sex-hormone sensitive tissues (e.g., breast, prostate, testes). Such effects may have an endocrine-related basis, which has led to speculation about the possibility that these endocrine effects may have environmental causes. However, considerable scientific uncertainty remains regarding the actual causes of such effects. Nevertheless, there is little doubt that small disturbances in endocrine function, particularly during certain highly sensitive stages of the life cycle (e.g., development, pregnancy, and lactation), can lead to profound and lasting effects.

The body of scientific research on human epidemiology, laboratory animals, and fish and wildlife provides a plausible scientific hypothesis that environmental contaminants can disrupt the endocrine system, leading to adverse health consequences. A critical issue is whether surrounding environmental levels are sufficiently high to exert adverse effects on the general population. To answer this question we must understand whether or not there is a threshold dose, that is, a dose below which exposure is safe, or whether exposure to any level of some endocrine disruptors carries a risk. Government agencies, industry, and academia are currently conducting various types of scientific studies (epidemiology, mammalian toxicology, and ecological toxicology) to resolve many of the scientific questions and uncertainty surrounding the endocrine disruptor issue. Within a few years we hope to have a much better understanding of the nature and breadth of this problem.

Our Approach

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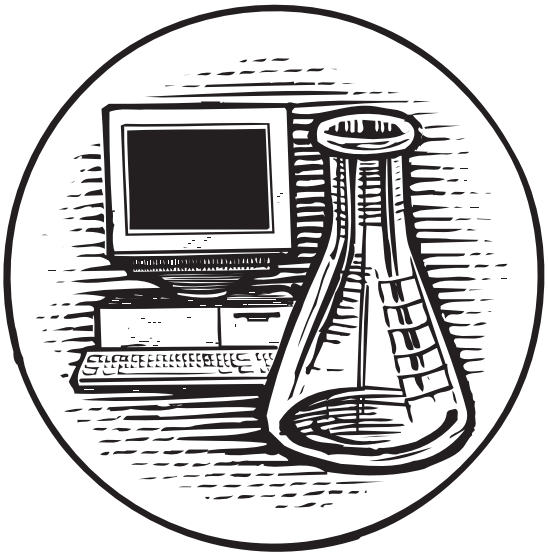
governments, Federal agencies, public health and environmental groups, and experts from academia. It was truly inclusive. EDSTAC held nine meetings from October 1996 until July 1998. These meetings were open to the public and held in major cities across the country to enable citizens to listen to the debate and offer comments to the Committee.

EDSTAC formed four workgroups to deal with the voluminous issues associated with endocrine disruptors and reported their recommendations back to the main committee. They were the Principles Workgroup, the Priority Setting Workgroup, the Screening and Testing Workgroup, and the Communications and Outreach Workgroup. EDSTAC submitted its final report in August l998 enabling EPA to meet the deadline specified in the FQPA for developing a screening program. The EDSTAC Final Report contained 71 consensus recommendations to EPA and detailed a step-wise approach to screening chemicals that begins with sorting, and proceeds to priority setting, screening, and finally testing. Our Science Advisory Board and the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) Science Advisory Panel consultants peer reviewed it in May l998; they will conduct a final review in early 1999. Testing is recommended on substances that possess endocrine disrupting properties identified during the screening phase. EPA has now adopted the EDSTAC's recommendations as the basis for its endocrine disruptor screening program and requested public comment on the proposal in the December 28, 1998 *Federal Register.* We have also published a draft implementation plan for notice and comment.

I want to once again express my gratitude to individuals who served on EDSTAC and its workgroups and gave so generously of their time and talent in helping EPA accomplish its mission of protecting the health of the American people and our environment. Chairing EDSTAC was one of the most rewarding experiences of my career at EPA.

Sorting and Priority Setting

Gary Timm



EPA formed the Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC) to help the Agency determine testing needs for endocrine disruptors. EDSTAC was asked to recommend which chemicals should be screened for endocrine disruption effects, and how to set priorities for reviewing these chemicals.

EDSTAC recommended that EPA consider 87,000 chemicals as potential candidates for screening. This huge number of chemicals includes over 600 active pesticide ingredients, 1800 pesticide inert ingredients (chemicals having little or no ability to react), over 75,000 chemicals in U.S. commerce, covered under the Toxic Substance Control Act (TSCA), and thousands of other chemicals including food additives, cosmetics, natural compounds in nutritional supplements, and drinking water contaminants. Although EPA has no jurisdiction over food additives, cosmetics, and nutritional supplements, EPA did commit to work with other agencies to test chemicals that fall outside EPA's jurisdiction. Because EPA cannot screen so many chemicals at one time, the Agency will prioritize and screen the results in batches and phases.

The first task is to develop a database to handle all of the data required for priority setting. The database will allow EPA to extract existing information (production volume, uses, monitoring data, physical and chemical properties, toxicity, etc.) from various sources and use it to sort and rank chemicals.

To winnow the number of chemicals from the 87,000, EPA will sort chemicals into four categories. These categories consist of the following:

- **Category 1,** known as the Hold Category, consists of compounds that are too big to penetrate the skin or other membranes — that is, polymers. Polymers are compounds of high molecular weight derived from the addition of many smaller molecules, or from the condensation of many smaller molecules when water, alcohol, or the like, is eliminated. Also included in this category are certain known non-toxic substances such as inert pesticides.

- **Category 2** consists of the chemicals needing screening level data to determine whether or not they have the potential to interact with the endocrine system.

- **Category 3** consists of substances known to have the potential to interact with the endocrine system, that is, those substances having data equivalent to some or all of Tier 1**,** but in need of data for hazard assessment. (For a description of Tier 1, see article, "How EPA is Reviewing New PBT Chemical Substances.") EPA plans to use available information, High Throughput Pre-Screening Steps (HTPS) data, and the Endocrine Disruptor Priority Setting Data Base to establish Tier 1 screening priorities. EPA anticipates, however, that the quantity and quality of exposure and effects information will be uneven for the majority of chemicals.

- **Category 4** consists of substances having complete test data that are ready for hazard assessment, risk assessment and possibly risk management.

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EDSTAC considered several different priority setting approaches to determine in what phase a chemical would be screened. In all of the priority setting approaches examined, EDSTAC considered both exposure and effects. The Committee rejected the approaches combining exposure and effects to give a ranking, because it felt that such an approach would cause EPA to focus on chemicals where there is little information. Chemicals having the least amount of information should be placed at a lower priority. The EDSTAC approach recommended that EPA group chemicals together based on like information, or information chemicals have in common, such as high production volume chemicals, chemicals found in drinking water, or chemicals that are released to the environment. This approach avoids "apples to oranges" comparisons, because the information used to group chemicals is the same information that is used to establish their ranking. EDSTAC called these groups of chemicals "compartments." A chemical can obviously fall into more than one compartment. After chemicals are sorted into compartments, they should be ranked for attention.

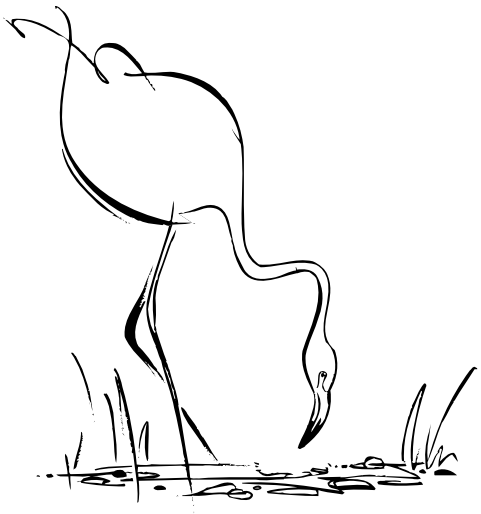
EDSTAC recommended that EPA consider 87,000 chemicals as potential candidates for screening.

Unfortunately, EDSTAC's priority-setting efforts were incomplete due to the number of chemicals to be addressed in a short period of time. EDSTAC defined some compartments in its recommendations to EPA, but most have yet to be defined. Examples of compartments, include high production volume chemicals, chemicals in consumer products, chemicals found in biological tissue, pesticide active ingredients, formulation ingredients in pesticides, and chemicals found in sources of drinking water. EDSTAC specified that special compartments be established for mixtures, naturally occurring non-steroidal estrogens (estrogenic substances produced by plants such as soybeans), and public nominations. EDSTAC felt that nominations from private citizens would focus attention on chemical exposures at the community level rather than the national level.

EPA accepted EDSTAC's recommended compartment-based approach, and EDSTAC's recommendation to continue EPA's involvement with the public. EPA has not attempted further specification of the compartments.

To further develop the list of priority setting compartments, EPA plans to convene a multi-stakeholder technical workshop in January. Based on public feedback, and comments received on EPA's proposed policy statement, EPA will establish a limited number of compartments. EPA will sort chemicals into these compartments using existing information, and the criteria that define each compartment. EPA will then rank chemicals within the compartments according to criteria related to those for inclusion in the compartment. Finally, the highest priority chemicals in each compartment will form the group of chemicals going into the first phase of the screening program. One advantage of the phased approach is the ability to apply what is learned during the first phase to subsequent phases. Thus, EPA will reevaluate the screening program and make appropriate adjustments at the end of each phase.

This process will introduce the flexibility to apply what is learned from both the screening program and ongoing research. In this way, EPA hopes to guarantee a cohesive and consistent long-term program for endocrine disruptors.



Screening and Testing

Gary Timm

Commencing in 1995 and continuing into 1997, a series of workshops was held in the U.S. and overseas. The purpose was to identify short term laboratory analytical methods or assays that could be used to screen chemicals for their potential to disrupt the endocrine system of humans, fish and wildlife. One of the workshops, the mammalian workshop, looked at over 50 such assays. Some assays were *in vitro* (conducted with cell cultures in glassware) others were in *vivo* procedures (using live animals). Scientists evaluated each assay based on its:

- **validity** — Does it measure what it is supposed to?
- **reliability** — Can you get the same results from lab to lab and from time to time?
- **sensitivity** — Can it measure active compounds that have weak effects or only strong ones?
- **suitability as a screen** — Is it cost-effective and quick and easy to perform?

A consensus of the workshop participants concluded that no single assay is effective for use as a screen. A battery of assays is needed. Participants also agreed that the battery of assays should be composed of both *in vitro* and *in vivo* procedures. The advantages of the *in vitro* procedures are increased sensitivity, lower cost and shorter time frames. A disadvantage is that *in vitro* tests do not provide feedback about the workings of the endocrine system and provide only limited information on an animal's ability to metabolize or transform chemicals.

The Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC) built upon the efforts of these workshops and constructed a battery of Tier 1 screens to identify the potential of chemicals to interact with the endocrine system, and a battery of Tier 2 tests to generate the kind of data EPA needs for hazard assessment. EPA is proposing to accept EDSTAC's recommendations for screening and testing (*Federal Register*, December 28, l998) for effects on three hormone systems — estrogen, androgen, and thyroid — and will invite public comment on this approach.

Tier 1 would consist of three *in vitro* assays and five *in vivo* assays. To minimize the chances of missing an endocrine-active chemical, each of the three hormone systems is covered by at least two assays in the battery. The first two *in vitro* assays detect binding to the estrogen and androgen receptors. These assays can run automatically. EDSTAC therefore recommended that EPA conduct the automatic assays on 15,000 chemicals so that the Agency could use the results to set priorities for the remaining chemicals in Tier 1. EPA could run the rest of Tier l on a smaller set of chemicals, at a minimum, because it would take far longer to run the full Tier 1 battery (eight assays) on so many chemicals. EPA expects substantially fewer chemicals than 15,000 would go through the full Tier 1 screen. The third *in vitro* assay in Tier 1 (steroidogenesis) detects the potential of the test substance to interfere with the enzymes that are responsible for making the steroid hormones, i.e., the two sex hormones and others that are derived from cholesterol. If the body cannot synthesize these hormones in adequate amounts, or makes too much, serious developmental consequences can result.

Of the five *in vivo* screens, one is a relatively short-term assay in females that

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EPA is proposing to accept EDSTAC's recommendations for screening and testing for effects on three hormone systems — estrogen, androgen, and thyroid — and will invite public comment on this approach.

Screening and Testing

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measures estrogenicity (the uterotrophic assay). Another is a short-term assay in males that measures androgenicity (the Hershberger assay). The most complex assay is a 20-day assay in immature females that follows them through puberty to detect potential estrogenic effects and thyroid effects. The frog metamorphosis assay also detects thyroid effects since tail resorption depends on adequate amounts of the thyroid hormone. Fish are included in the screening battery because they are the oldest class of vertebrates and are the farthest removed from mammals.

EPA is quite confident that chemicals that test negative in the Tier 1 screening battery are not likely to interact with the estrogen, androgen, or thyroid systems. Therefore, chemicals that test negative in Tier 1 would not be tested in Tier 2. Chemicals testing positive in Tier 1, however, will generally be required to be tested in all Tier 2 tests. Tier 2 will contain representatives of all major types of animals. It will include testing for reproductive effects in mammals, fish, birds, amphibians, and invertebrates. The Agency will use data from the mammalian reproductive study to assess the risk to humans and to mammals that live in the wild. Data from the other tests will be used to assess the risk to fish, birds, and invertebrates.

EPA's Strategy for Priority Persistent, Bioaccumulative, and Toxic (PBT) Pollutants

Kathy Davey

EPA has developed a draft strategy to further reduce risks from persistent, bioaccumulative, and toxic (PBT) pollutants. These PBT pollutants are highly toxic, long-lasting substances that build up in the food chain to levels that are harmful to health in humans and the ecosystem. Health warnings about eating fish due to PBTs in the U.S. increased by 80% in four years, from 1,278 in 1993 to 2,299 in 1997, primarily because states are doing a better job of monitoring and setting protective levels. PBTs are associated with a range of adverse human health effects, including effects on the nervous system, reproduction, and fetal and child development. PBTs have also been linked to cancer and genetic impacts. EPA is especially interested in protecting children and women of childbearing years, and in restoring the valuable quality of our nation's waterways. EPA's challenge in reducing risks from PBTs stems from their ability to travel long distances, to transfer easily among air, water, and land, and to linger for generations.

The first main element of EPA's strategy is to develop and implement national action plans that reduce risks from select PBTs. These plans will use all of EPA's tools, across all media. EPA's first national action plans will be developed for the 12 priority PBTs named in the Canada-U.S. Binational Toxics Strategy. EPA has already developed a draft action plan for mercury (see article in this issue), and will be developing plans for the remaining 11 substances named in the Binational Toxics Strategy — aldrin-dieldrin, benzo(a)pyrene, chlordane, DDT (+DDD+DDE), mirex, hexachlorobenzene, alkyl-lead, octachlorostyrene, PCBs, dioxins and furans, and toxaphene.

The second element of the strategy is to select more priority PBTs for future national action plans. The third element is to stop the flow of new PBTs into commerce. The fourth and final element of the strategy is to develop improved right-to-know measures of progress for the public, so people can tell whether we are achieving our national goals and commitments.

To date, EPA actions to reduce risks from PBTs have largely consisted of individual EPA offices each using their separate authorities to control PBTs in one media (air, water, land) at a time. What is new in EPA's PBT strategy is a truly multi-media approach. Since these substances move among air, water, and land, we need to use all available tools — voluntary, regulatory, enforcement and compliance, research, and international — in combination with each other to break the cycle of transferring pollutants from one place to another. As an example, once state-based voluntary efforts retire more mercury from circulation and use, a national approach is needed for what to do with the mercury. Re-using mercury commercially is not a viable answer. States will also need national help to address the mercury blowing in from other countries.

Near-term actions under the PBT Strategy are underway to prevent the introduction of new PBTs in commerce, encourage voluntary reduction of PBTs in hazardous waste, increase the public's right-to-know about local sources of PBT emissions and mercury emissions from utilities, and evaluate fish in U.S. water bodies for PBT contamination.

EPA cannot do this alone. We will work closely with our regulatory partners and engage in partnerships with industry, environmental groups, and the public to get the PBT job done.

EPA is especially interested in protecting children and women of childbearing years, and in restoring the valuable quality of our nation's waterways.

Reducing PBT Chemicals in Waste

PBTs

Douglas Heimlich

On November 9, 1998, EPA published in the *Federal Register* a Notice of Data Availability on the Draft RCRA Waste Minimization PBT Chemical List. The list contains 53 chemicals which will be the focus of source reduction and recycling activities aimed at reducing persistent, bioaccumulative, and toxic (PBT) chemicals present in hazardous waste. Comments on the Notice are due on February 16, 1999.

The List, also known as the RCRA PBT List, includes certain PBT chemicals that may be present in some industrial hazardous wastes regulated under the Resource Conservation and Recovery Act (RCRA). PBT chemicals do not readily break down or decrease in potency after they are released to the environment. Over time, these chemicals are likely to accumulate in soils or other environmental media, be absorbed or ingested by plants and animals, accumulate in animal and plant tissue, pass through the food chain, and potentially cause long-term human health or ecological problems (such as cancer and birth defects in humans, or reduced ecological populations). PBT chemicals are internationally recognized as a global environmental concern.

The Agency aims to use the List to raise government, industry, and public awareness of the potential effects of these chemicals in the environment, and focus coordinated public and private actions to reduce the generation of these chemicals in hazardous waste by 50 percent by the year 2005. The emphasis will be on source reduction and recycling activities to get the job done. The 50/2005 goal was established in the Waste Minimization National Plan, which EPA developed with extensive input from states, industry, environmental groups, and private citizens. The Plan also aims to avoid transferring these PBT chemicals from one environmental form to another (e.g., from air to water).

The List can be a valuable resource for state and local governments, citizen organizations, and individuals to promote reductions in the amount and toxicity of PBT chemicals contained in hazardous wastes. EPA also plans to use the List in working with states, industry, environmental groups and other stakeholders to identify a variety of implementation approaches for promoting progress toward the 2005 goal. The List will be promoted in workshops, technical assistance, progress reporting, developing partnership agreements, regulatory reinvention projects, and other venues.

The Draft RCRA PBT List is an important component of the Agency's PBT Strategy, which integrates all of EPA's activities focusing on priority PBT chemicals and aims to measure collective Agency progress on reducing uses and releases of PBTs nationally.

How EPA is Reviewing New PBT Chemical Substances

Ken Moss

PBT chemical substances possess characteristics of persistence (P) in the environment, accumulation in biological organisms (bioaccumulation (B)), and toxicity (T) that make them priority pollutants because of their potential risks to humans and ecosystems. EPA developed a category of PBT chemical substances by defining what it means for a chemical to be persistent, bioaccumulative, and toxic. The category statement includes the boundary conditions that would determine inclusion in (or exclusion from) the category, and standard toxicity and environmental fate tests to determine if a chemical fits within those boundaries.

Chemical substances characterized as suspected persistent bioaccumulators may need to undergo testing on "P" and "B" endpoints which, if confirmed, would be followed by appropriate toxicity testing to classify "PBT chemical substances." Establishment of this category helps the Agency gauge the flow of PBT chemical substances through the New Chemicals Program and measures the results of its risk screening and risk management work.

Defining a PBT category helps EPA to gather additional information as needed about persistence and bioaccumulation and tailor regulatory requirements as appropriate to protect human health and the environment. Depending upon the level of certainty for the PBT properties of a new chemical (e.g., measured vs. estimated values), the magnitude of Agency concerns, and conditions of expected use and release of the chemical, control action by EPA may be needed in varying degrees, up to a total ban on production of the chemical.

The criteria for banning a chemical from being produced are equivalent to those that have been used internationally to eliminate from commerce new chemicals that are known PBT substances, chemicals like the polychlorinated biphenyls (PCBs) and the pesticide DDT. For new chemical substances meeting these criteria, EPA's concern is higher than for other PBTs and the Agency looks carefully at any and all environmental releases. Because of the increased concern, more stringent control action would be a likely outcome, including a ban on commercial production, until data are submitted which allow the Agency to determine whether the level of risk can be appropriately addressed by less restrictive measures.

With specified controls, EPA might allow a new chemical categorized as a PBT to enter the market. For example, EPA might allow a Premanufacture Notice (PMN) submitter (anyone wanting to manufacture a "new" chemical) to commercialize a substance upon signing a negotiated and legally binding consent agreement. Stipulated in the agreement could be annual reporting requirements on environmental releases of the PMN substance and specific limits on exposures, releases or uses while test data are being developed.

In many cases, the PBT status of the new chemical is ambiguous and testing is needed. EPA has developed a testing strategy for this category of new chemical substances which describes test data that EPA believes are needed to evaluate the potential persistence, bioaccumulation, and toxicity of a PBT chemical substance. The tests are tiered. Depending upon the circumstances, such as magnitude of environmental releases, results of testing already conducted, or what we know about other chemicals with similar chemical structures (an approach called Structure Activity Relationships or SARs), EPA will require additional testing in order to screen the chemical.

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- **Tier 1.** If, based upon SAR and professional judgment, EPA scientists identify a new chemical as a possible PBT chemical, the chemical manufacturer first needs to conduct simple tests to measure its tendency to partition towards either water or fish tissue (scientifically described as biological lipids or fat) and its ability to readily degrade in the environment. Once the chemical is dissolved in water, the organic solvent octanol (thought to have properties that mimic body fat) is then placed in the test vessel and the entire two-phase (water phase and organic phase) system is shaken to mix everything up. After everything settles, the amount of the test chemical is measured in both the water and the octanol phase. The ratio of the amount in the octanol phase over that in the water phase is called the octanol-water partition coefficient, or Kow. The lower the Kow, the more likely it is that the chemical dissolves easily in water and therefore is available to natural breakdown processes in the environment; the higher the Kow, the more likely the chemical is to partition to biological lipids like fish tissue, where it might concentrate in biological organisms, or bioconcentrate. If the test result is a low Kow, or a "ready biodegradability" test shows that the chemical rapidly degrades (which means it is not persistent in the environment), no further PBT-related testing is required. If the chemical has a high Kow and does not pass the ready biodegradability test, the chemical would proceed on to Tier 2 testing.

- **Tier 2.** In this next tier, a more sophisticated measure of biodegradability is determined according to a test called the "shake-flask die-away" test, or an equivalent test. This test measures how long it takes for the chemical to disappear by chemically breaking down. The potential of the chemical to bioaccumulate (be taken up in fish by any route, through the gills or the gut) is determined by experimental measurement of the bioconcentration factor. A fish bioconcentration test is the most convenient way to experimentally measure bioaccumulation and refers to how well the chemical concentrates in the fish tissue. If the measured biodegradation half-life is greater than 60 days and the measured bioconcentration factor is high (greater than l000), the chemical is expected to linger in the environment (be persistent), and concentrate in fish tissue. As a result, the chemical manufacturer is then required to do Tier 3 testing. If only one condition is met, releases and exposure are further considered to determine if additional testing is required.

- **Tier 3.** This tier looks at the chemical's ultimate fate in the environment and toxicity to animals up the food chain, i.e., animals that eat fish, including birds and mammals, and human beings. Possible toxicity tests include long-term toxic effects on fish and water fleas; testing to evaluate effects on other living creatures, such as birds and organisms dwelling in the sediment of streams and lakes; and testing of effects such as potential for endocrine disruption (potential effects of synthetic chemicals on the hormone systems of people and wildlife). Environmental fate testing determines how the test chemical interacts with the environment, including transport and transformation. These kinds of tests permit scientists to draw more accurate and reliable conclusions about how the chemical will act in natural aquatic environments than is possible with lower tier test methods, and allow EPA to screen potentially toxic chemicals prior to entering commerce that have, in the previous testing tiers, been confirmed as persistent and bioaccumulative.

Defining a PBT category helps EPA to gather additional information as needed about persistence and bio-accumulation and tailor regulatory requirements as appropriate to protect human health and the environment.

This article describes a process by which EPA screens new chemicals and decides what controls should placed on PBT chemicals prior to their entry into the marketplace. The process is also applied to other new chemicals, and works to ensure that chemical companies develop products that are safer to human health and the environment.

Progress of the Great Lakes Binational Toxics Strategy

Dan Hopkins, EPA Region 5

The Great Lakes Binational Toxics Strategy (BNS) was signed by the United States and Canada in April 1997. The process of implementing the BNS did not begin until January of 1998. At that time, the U.S. and Canada, with suggestions from stakeholders, drafted an implementation plan for the BNS.

The implementation plan called for the formation of substance-specific workgroups consisting of environmental organizations, states, industry, tribes, and governments to address the challenges set out in the BNS for the Level One substances. The Level One substances are as follows: mercury and mercury compounds, dioxins and furans, polychlorinated biphenyls (PCBs), hexachlorobenzene and benzo-a-pyrene, alkyl-lead, octachlorostyrene, and pesticides. The pesticide work group is specifically addressing chlordane, aldrin/dieldrin, DDT, mirex, and toxaphene. To date, there have been two meetings of all BNS stakeholders, a steering group referred to as the Forum. The purpose of the Forum is to establish and maintain the workgroups, assess progress to date under the Strategy, and exchange information and ideas leading to further reductions in these substances.

In addition to the substance-specific work groups, an Integration Workgroup composed of similar stakeholders has been formed to discuss cross-cutting issues such as how to address contaminated sediments and account for long-range transport of the Level One substances. Discussions about these issues included providing incentives for stakeholders to voluntarily undertake reductions which are then discussed with management officials of EPA and Environment Canada. The Integration Work Group met in June 1998 and was scheduled to meet again in January 1999.

Partnerships among stakeholders are another important marker of progress in implementing the BNS. Since the development of the BNS, several partnerships have formed. In the U.S., the American Hospital Association and EPA have signed a Memorandum of Understanding (MOU) to work together toward the virtual elimination of mercury from hospital waste, to provide education, and to develop a model waste management plan. In another partnership agreement, three northwest Indiana steel mills, the Lake Michigan Forum, the Indiana Department of Environmental Management, and EPA signed an agreement to conduct an inventory of mercury in equipment and wastes, and to develop mercury reduction plans. The Chlorine Institute, on behalf of its members, committed to reduce mercury use in the chlor-alkali industry by 50% from 1990-1995 levels, aiming for an annual reduction in mercury usage of 80 tons by the year 2005. Six Ontario hospitals in Canada signed an MOU for the voluntary reduction and elimination of mercury. Several additional hospitals have indicated an intention to sign this MOU.

A number of other activities related to the reduction of the BNS Level One substances have taken place. These activities include the promulgation of new regulations by EPA, reductions achieved by Great Lakes stakeholders resulting from earlier initiatives, and EPA and state-funded activities such as pesticide collection programs. In addition to actual reductions and newly formed partnerships, the U.S. and Canada have achieved significant strides to improve source and emission inventories for the BNS Level One substances, and to identify opportunities for further reductions of many of the substances.

The American Hospital Association and EPA have signed a Memorandum of Understanding to work together toward the virtual elimination of mercury from hospital waste.

Update on EPA's Fish Contamination Program

Jeff Bigler

During 1997-98, the FCP conducted one of the largest site-specific fish contamination studies ever undertaken by EPA.

State and tribal officials monitor fishing waters and fish for contaminants and issue health advisories to the public if fish consumption is deemed unsafe. EPA's Fish Contamination Program (FCP) provides technical assistance to states, tribes, and others on matters related to persistent bioaccumulative toxics in fish and wildlife and associated potential health risks to consumers. Through this program, EPA publishes guidance documents; develops and manages national databases; holds national forums, conferences and training workshops; provides grants for advisory development; conducts special studies; develops outreach materials; and assists in the issuance of advisories informing the public about safe amounts of fish to eat. Since 1992, the FCP has worked closely with state and tribal agencies to establish a national consistency in the development and management of advisories. It helps establish approaches, methods, and protocols for assessing contaminants in fish and wildlife.

The FCP has published and revised a four-volume set of guidance documents titled *Guidance for Assessing Chemical Contaminant Data for Use in Fish Advisories.* Used together, these four volumes provide an approach for writing risk-based, scientifically sound, and cost-effective advisories. Over the past eight years, the number of states using this risk-based approach has increased from 10 to approximately 40. FCP continues to work with the remaining states to achieve the goal of national consistency in fish consumption advisories. This national consistency goal is an Action Item included in the *Clean Water Action Plan*, announced by President Clinton and Vice President Gore.

In February 1998, the Administration published the *Clean Water Action Plan: Restoring and Protecting America's Water*, providing a blueprint for restoring and protecting the nation's water resources. A major premise of the Plan is that informed citizens and officials can make better decisions with clear, accurate, and timely information. Beginning in 1993, the FCP began publishing the National Listing of Fish and Wildlife Advisories (NLFWA). This database includes all available information describing state, tribal, and fish consumption advisories issued by EPA and other federal agencies in the United States for the 50 states, the District of Columbia, and four U.S. territories. It has been expanded to include the 12 Canadian provinces and territories. The NLFWA contains information provided to EPA by the states, tribes, and Canada as of December 1997.

In addition to the development of national guidance and database management, the FCP organizes national conferences on chemicals in the environment, conducts training workshops, and sponsors the Annual State/Tribal/Federal Forum on Contaminants in Fish. This Forum is attended by representatives from all 50 states, 30-40 tribes, several federal agencies, and various environmental and industry groups. The next Forum will be held in May 1999.

The FCP is also involved with the conduct of special studies, which currently includes studies of subsistence villages in Alaska, the effectiveness of fish consumption advisories, and comparative dietary risks. During 1997-98, the FCP conducted one of the largest site-specific fish contamination studies ever undertaken by EPA. Fish, shellfish, and marine plants were collected from the Cook inlet area of Alaska to determine if oil and gas activities were affecting the quality of the food supply. The study will provide the information needed to characterize health risks from fish and wildlife harvested from Cook Inlet by members of four native Alaskan villages dependent on marine resources as a source of dietary food items. The study design, methods, and protocols are based on the FCP guidance series mentioned earlier in this article. This human health risk assessment is part of a larger EPA effort to characterize human health risks from pollutants associated with offshore and coastal oil and gas Industry practices. EPA will issue a final report in the Spring of 1999.

The FCP is working with EPA's Office of Research and Development (ORD) and the State

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of Wisconsin on a second study, to assess the awareness about and effectiveness of the advisories. The study, which is national in scope, will use focus group techniques to interview women of childbearing age in states issuing mercury advisories to determine:

- their fish consumption habits;
- the channels by which they receive health information;
- how they prefer to receive advisory information;
- how they perceive health risk due to consumption of sport fish; and
- what they view as the central risk message that needs to be communicated.

The study will lead to a protocol which states and tribes may use for effectively communicating targeted mercury fish consumption advisories to women and children. Based on the focus groups, EPA will determine how to distribute intervention materials, design an intervention tool (advisory), and then determine if the tool is effective in lowering this sub-population's fish consumption habits and/or mercury body burden levels. A draft report is expected in 1999.

The third special study, Comparative Dietary Risk, involves the collection and assessment of data concerning health risks and benefits of behavior changes due to fish consumption advisories. This study will provide a comprehensive document on what is known about health risks from consumption of contaminated fish, health risks from lack of fish consumption, health benefits of consuming fish, general problems associated with comparisons of these risks, and a proposed approach to evaluate the risks and benefits of fish consumption and other dietary food items. This research should lead to a better understanding of the impacts that fish consumption advisories could have on an individual's diet. Local risk managers and ultimately individual consumers could evaluate a broad range of dietary information before making decisions about whether to consume fish from contaminated areas. Furthermore, states and tribes may use the results to assess local populations and conditions and tailor fish consumption advisories to better reflect the local conditions. EPA will hold a workshop of national and international experts during the Winter of 1998/1999 to develop the final draft document. Prior to completing the document, EPA will ask the Science Advisory Board or another peer review group to comment on the approaches and methods included in the document.

The FCP is also involved with the development and dissemination of outreach materials. In collaboration with the ATSDR, the FCP will be writing to health care professionals nationwide to emphasize the need to be aware, and to ensure the public is aware, of the possible health consequences to those who consume contaminated noncommercial fish (i.e., fish caught through sport or subsistence fishing). This effort is also part of the President's *Clean Water Action Plan.* This Plan provides a blueprint for a new cooperative approach to identify and solve pollution problems and to inform citizens and officials about the quality of water bodies, and the safety of the fish and drinking water that come from them, as well as the beaches that surround them. Attached to the letters to health care providers will be copies of the brochure, *Should I Eat the Fish I Catch?,* developed by ATSDR and the FCP to provide information to consumers about how to reduce health risks from eating fish containing chemical pollutants. It is part of the Action Plan and is available in three languages (English, Spanish, and Hmong).

Lastly, the FCP assists in the issuance of individual advisories to ensure adequate protection of public health. In 1997, the FCP, in collaboration with ATSDR, coordinated the development and issuance of the first federal fish consumption advisory. The State of Michigan was prepared to issue an advisory which EPA determined did not provide adequate protection of public health, particularly for women and children. EPA printed and distributed a total of 1.2 million copies of the federal advisory to fishing license holders and health care facilities throughout the State of Michigan. In 1998, Michigan issued a new advisory providing adequate protection of women and children. The FCP continues to work with other states to ensure advisories are issued that are protective of public health.

For more information concerning the National Fish Contamination Program or for copies of the above described materials, contact Jeffrey Bigler, National Program Coordinator, phone: 202-260-1305, fax 202-260-9830, e-mail: bigler.jeff@epamail.epa.gov; or write to: U.S. EPA (4305), Fish Contamination Program, 401 M Street SW, Washington, DC 20460.

EPA's Draft Action Plan for Mercury

PBTs

Karen Maher

Mercury, a naturally occurring metal, moves between the water, the air, and soil as a result of natural and human activities. It enters the environment from sources like coal-fired power plants, mining and smelting of various ores, and the disposal of consumer products manufactured with mercury. Because it is a persistent, bioaccumulative and toxic (PBT) pollutant, the amount of mercury in the biosphere has been increasing since the beginning of the industrial age. In its organic form, methylmercury bioaccumulates in fish and becomes more concentrated as it moves up the food chain to humans and other animals who eat the fish. Mercury is the most frequent reason for fish consumption advisories in the U.S., accounting for 60 percent of all advisories in fresh water bodies. To date, 40 states have issued advisories for mercury in one or more water bodies, and 11 states have issued them on a state-wide basis.

The amount of mercury in the biosphere has been increasing since the beginning of the industrial age.

Mercury is a well-known and long-established neurotoxin that slows fetal and child development and causes irreversible deficits in brain function. Scientific debate is ongoing to more precisely determine the level of mercury exposure at which effects begin to occur. Several, but not all, existing studies show adverse human health effects at the level at which many Americans are exposed today from fish consumption. Tens of thousands of babies are born each year after being exposed in the womb to levels of mercury at which some studies have shown adverse health effects.

The draft EPA Action Plan for Mercury is the first of a series of such national action plans. It is a part of EPA's draft Multimedia Strategy for Priority Persistent, Bioaccumulative, and Toxic (PBT) Pollutants. The Agency has reviewed current regulations, initiatives, and programs which manage and control mercury, and has identified a set of cost-effective options to move toward achieving further reductions.

Specifically, EPA proposes the following actions, in consultation with other federal agencies, and with the involvement of states, tribes and other stakeholders.

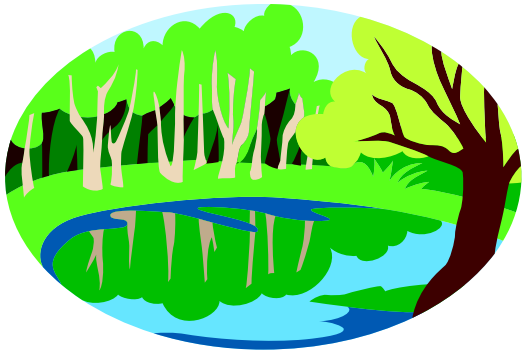
- Control emissions from air point sources.
- Revise the water quality criterion, and improve measurement of mercury in water.
- Seek reductions in uses of mercury and improve information and citizens' right-to-know.
- Develop an environmentally acceptable disposal method for mercury wastes designated as hazardous wastes.
- Seek reduction in exposure to highly exposed populations.
- Decrease further environmental contamination from illegal use/disposal of mercury through focused compliance monitoring and enforcement of mercury restrictions and requirements.
- Continue international efforts to reduce mercury releases.
- Perform and support further research on all aspects of the mercury problem.
- Support regional, state, tribal, and local actions to reduce mercury.

For copies of the draft EPA Action Plan for Mercury and other related documents, contact the Pollution Prevention Information Clearinghouse at (202) 260-1023 or access the EPA Web site at www.epa.gov/pbt/strategy.htm.

Preparing the Mercury Research Strategy

PBTs

Kathryn Mahaffey and Jonathan Herrmann



According to the December 1997 *Mercury Study Report to Congress*, the total annual global input of mercury to the atmosphere from all natural sources and human activity is 5,500 tons. Approximately 150 tons of that amount is emitted by human activity within the United States. Mercury is released into the environment as either an element (e.g., the silvery metal released as a liquid or vapor) or as one of a number of compounds (e.g., mercuric chloride). Depending on a number of factors, including the type of mercury released, its transport/deposition pattern can result in either:

- *Local* scale impacts (e.g., depositing within 30 miles of an emissions source);
- *Regional* scale impacts (e.g., depositing thousands of miles from a source over a wide area); or
- *Global* scale impacts, i.e., becoming part of the global emissions pool, where it can remain for a year before depositing on either land or water.

Deposited mercury, particularly when it resides in lake sediments, transforms to methyl mercury, an organic form of mercury, which is eventually taken up in fish. Such mercury can then accumulate in the tissues of both humans and wildlife (e.g., eagles, otters) if they eat mercury-containing fish. Numerous water bodies in the United States have fish advisories for mercury. There are also mercury "all coastal waters" advisories for those states bordering the Gulf of Mexico.

In response to this situation, EPA's Office of Research and Development is preparing a Mercury Research Strategy with the help of scientists and engineers from other EPA program offices and regions. The strategy will provide a framework to address unanswered research questions on the assessment and management of mercury releases from human activities and natural sources. The Mercury Research Strategy will consider a number of issues related to the following set of research themes:

- Hazards of methyl mercury to human health;
- Ecological effects of mercury/methyl mercury;
- Modeling and monitoring of environmental media for mercury;
- Human and wildlife exposures to methyl mercury through the aquatic foodweb;
- Control technologies for combustion sources of mercury;
- Controls for non-combustion sources of mercury; and
- Risk communications on mercury/methyl mercury;

EPA is currently rewriting the strategy following an internal review this past Fall. It is scheduled to undergo external peer review in the Spring of 1999. Once the strategy has undergone this review, ORD and EPA offices, in cooperation with the greater scientific community, will develop and implement the EPA research plan. The plan will build on ongoing efforts on the research themes listed above and will support EPA's regulatory and court-ordered deadlines for mercury.

Numerous water bodies in the United States have fish advisories for mercury.

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