

## Risky Business: EPA Builds List of Potentially Dangerous Chemicals

RESEARCH TRIANGLE PARK, N.C. -- As the rates of learning disabilities, autism and related conditions rise, the Environmental Protection Agency is preparing to release [a roster of the pollutants](#) likely to contribute to these or other neurological disorders. In an ongoing, three-year effort, an EPA team has determined which developmental neurotoxicants -- chemicals that damage a fetal and infant brain -- may pose the biggest risk to the American public.

Some compounds on the EPA's list are ubiquitous in household products, drinking water, medicine, and within the environment. They range from cadmium, used to etch colorful cartoons onto children's glasses, to flame retardants used to fireproof upholstered furniture. The [Investigative Reporting Workshop at American University](#) visited the scientists in North Carolina and obtained a draft of the first chemicals expected to be on the list. Its release, expected early next year, is awaited eagerly by public health activists, who lack government confirmation that many chemicals they suspect are dangerous, and warily by manufacturers.

"It legitimizes the public health concerns," said Elise Miller, who serves on [EPA's advisory committee on children's health protection](#). "So many consumers hear contradictory reports from different scientific studies highlighted in the media, so having an EPA list more or less 'settles' the question of whether or not these are chemicals of concern."

In addition to naming specific chemicals, solvents and other pollutants that turn up in everything from light bulbs to flea-and-tick products for pets, the compendium will be used to develop new, automated testing of cells in vitro, to supplement and in some cases replace testing on animals, said EPA research toxicologist Kevin Crofton.

"There are too many chemicals and not enough data," Crofton said. "There are literally thousands and thousands of chemicals in use for which we really don't have much information at all." Many experts praised Crofton and his colleague William Mundy, part of a 12-member [research group](#), for their enterprise, but said EPA should have done this years ago -- and warned that the in vitro screen has some sizable holes.

"We need to do this, and we need to do it fast," said R. Thomas Zoeller, an endocrinologist and professor of biology at the University of Massachusetts, who has served on numerous federal advisory committees. "Right now, one in six children in this country is diagnosed with a neurobehavioral disorder. The impact on our society and on our economy is really dependent on Kevin and Bill to come up with something that is workable, and it's not going to be simple, and it's not going to be fast."

Experts spar over the precise numbers, but most agree that data on learning and developmental disabilities indicate a rise -- and that those numbers go well beyond the amount attributable to increased diagnoses.

The [Collaborative on Health and the Environment](#), a partnership of public health researchers and environmental advocates, puts the rate of learning and developmental disabilities at between 5 percent and 15 percent -- or more than 12 million children. The National Parkinson Foundation estimates that 1 million Americans suffer from Parkinson's disease, with between 50,000 and 60,000 new cases diagnosed each year. That number is expected to skyrocket as the population ages.

Many scientists believe a significant number of these cases are related to exposure to toxic chemicals. The National Research Council, a division of the National Academy of Sciences, has reported that only 3 percent of developmental disabilities can be traced to environmental pollutants, but that another 25 percent are caused by interactions between what's in the environment and an individual's genes.

"The dose makes the poison" was a longstanding principle of risk assessment. In the past few years this maxim has been replaced by "the timing makes the poison," reflecting evidence that exposure to pollutants during critical windows of development can wreak havoc on the growing nervous system.

Theodore Slotkin, a pharmacology professor at Duke University Medical Center, likened the developing brain, with its sequences of synchronized growth, to a pianist playing a sonata.

"Imagine that the assembly of the brain is you sitting at the piano, playing the Beethoven sonata," Slotkin said. "Certain keys have to be struck at the right intensity at the right pattern. Now, imagine that someone comes along with a chunk of 2-by-4 and presses down a dozen keys." Different chemicals, Slotkin said, whack the brain the same way the 2-by-4 whacks your piano -- with the result being a far different tune than what was intended.

"The worst outcome of all," he said, "is when you press down the keys, and you can't tell what piece is being played."

From the standpoint of science protecting the public health, Slotkin said, "What we've been doing the past 30 years is a failure. They [industry] can produce these chemicals faster than we can test them."

A group of prominent scientists said in a consensus statement two years ago that the evidence was convincing that 200 chemicals, manufactured in large quantities each year, can cause developmental disorders, defined as deficits in learning and memory, reduced IQ, attention-deficit disorder, autism spectrum disorder, behavioral problems and developmental delays.

But under current law, the [Toxic Substances Control Act](#), the EPA permits companies to put many chemicals on the market without first proving they are safe. Then, if evidence mounts that a particular chemical, such as bisphenol A, or metal, such as lead, could harm people who are exposed to the substances in varying situations, the agency has to play catch-up.

"EPA cannot even study the effects of a chemical unless some independent research shows potential harmful effects," said Dana Barr, an Emory University professor who ran the Center for Disease Control's pesticide laboratory for 15 years. "There has to be a reason for EPA to study a chemical. They can't say, 'It is being used. Let's study it.'"

EPA chief Lisa Jackson, other federal officials, and a group of Democratic lawmakers tried earlier this year to revamp the outdated law, switching the burden of proof of chemicals' safety to manufacturers, but were beaten back [by chemical industry lobbyists](#).

### **How work on the list unfolded**

Crofton and Mundy's group started with a list of more than 400 suspect chemicals, taken from various sources, including a landmark article in the medical journal "The Lancet" in 2006. In whittling down their list, their team culled through all available animal and human studies in scientific literature and divided these studies into three groups based on their extent of proof: no evidence, minimal evidence, or substantial evidence. For substantial evidence, confirmation had to come from more than one research laboratory. "When you get into the literature, there is no real agreement on which are the neurotoxicants, and not much have been tested," Crofton said.

He and Mundy hope to change that. They plan to use their high-evidence chemicals to test screening methods that they believe will expedite the testing of thousands of chemicals currently in commerce -- and rank them for further testing.

Crofton said animal testing is too slow. "If you give me a chemical and we go off for one or two years, we can give you answers," he said. But with so many chemicals to be studied, "We can't do it. There aren't enough neurotoxicologists, enough rats or mice." Or, Mundy added, "enough money."

Still, several critics warn that the high-throughput in vitro tests will fail to detect many types of brain damage that can forever alter a person's potential -- tests in which behavioral changes are more subtle or observable only in a living, breathing creature -- and should not replace animal tests, even as a screening tool. They also question why it has taken EPA so many years to finish the list, given the explosion of peer-reviewed studies showing the harmful effects of dozens of pollutants on the developing brain.

"My initial reaction is that I think we should be further along with this," said Steven G. Gilbert, director of the Institute of Neurotoxicology and Neurological Disorders, a nonprofit research center in Seattle. "I think there's no reason [to

take this long.] We've got data on a lot of neurotoxicants that should be ranked. That should have been done. We should have moved forward onto the high-throughput screening."

Although the project is still under way, the Investigative Reporting Workshop discovered an early list of the chemicals, presented on a poster at a toxicology symposium. The poster was then posted on the EPA's site, though prematurely, said Crofton, adding that the list would go through more changes in the coming months before being published.

In concert with Politics Daily, the Investigative Reporters Workshop website is publishing the list of those chemical with high evidence of neurotoxicity based on the studies and, therefore, expected to be part of the EPA's final list.

Some of the compounds, such as lead and methyl mercury, are already widely known for their ability to diminish intellectual potential and impair memory, among other hazards. Other chemicals used in medications, industrial processes and household products are lesser known as developmental neurotoxicants.

Among those is benzene, one of the top 20 chemicals in production in the United States. It is used to make compounds that are then incorporated into plastics, resins, nylon and synthetic fibers. Although benzene is a byproduct of forest fires and volcanoes, people generally come in contact with the chemical by using lubricants, rubbers dyes, detergents, drugs and pesticides, or in the workplace.

Another compound, acrylamide, can form naturally in some foods, especially potatoes during frying, roasting or baking, but it is also found in cigarette smoke. Acrylamide, too, is used in industrial processes to make plastics and cosmetics.

Other chemicals on the draft roster include:

-- **Aspartame, an artificial sweetener found in sodas, and in other foods and drinks;**

- Bisphenol A, a chemical widely used in consumer goods, including the resin lining of most food and beverage cans; products made from polycarbonate plastics, which include water bottles and baby bottles, and some dental sealants;
- Cadmium, a heavy metal that is used in batteries, coatings and pigments, and is plentiful in tobacco smoke;
- PBDEs a class of chemical flame retardants;
- Pesticides and insect repellents, including aldicarb, DEET, lindane, (used for lice and scabies), maneb, and paraquat;
- Trichloroethylene, formerly used in dry cleaning but still available as a cleaning and degreasing agent and a contaminant in drinking water.

Ultimately, the EPA group expects to name more than 100 chemicals, which will serve as a benchmark to determine whether their in vitro screens pick up the same problem chemicals discovered in human and animal studies.

In an interview, Philippe Grandjean, co-author of "The Lancet" article, an adjunct professor at the Harvard School of Public Health, and a professor at the University of Southern Denmark, called Crofton "brilliant," and said the project is a reasonable place to start. But he is also concerned that this new approach may miss dangerous pollutants.

One of Grandjean's worries is that the chemical being tested might not be toxic, but the metabolite -- the breakdown product that occurs when enzymes change the chemical structure -- might be. He also said the in vitro cells' lack of a blood-brain barrier, which protects the brain from many toxic chemicals, is also a major drawback to the new testing method.

Elise Miller of the EPA, who also is director of the [Collaborative on Health and the Environment](#), said she is pleased to see the new test methods, but wants to ensure that studies on animals and people are not neglected.

"It's easy to get caught up in the new technology and get infatuated," she said. "It needs to be complemented by animal and epidemiological studies, and an overhaul of the risk assessment. The high-throughput test isn't going to tell you how a chemical is going to affect someone in West Harlem." In addition, she said, some chemicals such as lead,

polychlorinated biphenyls (PCBs), many pesticides, manganese, acrylamide and certain solvents, have already been [studied quite enough](#).

But Crofton and Mundy said they have no choice. In several interviews, the scientists stressed that they do not expect their testing program to replace animal studies. Rather, it will simply meet a critical need to test thousands of chemicals that are already ubiquitous in consumer goods, medicines, drinking water and the environment.

### Next steps

It won't be easy to parlay their test results into protective policies. The researchers included manufacturers and chemical industry representatives in numerous meetings over the last five years to discuss their plans, but already there is pushback from industry.

Lorenz Rhomberg, a former EPA employee who now works for Gradient Corp., an environmental risk-consulting firm that often advises businesses, said, "In industry, there are two strains of thought. One, this promises a chance to look at a lot of chemicals more thoroughly, much more cheaply and quickly and could provide us with better answers. And there are other people who say we are worried about how they might be used because there is always the problem that chemicals might make physiologically detectable changes in the body that are not adverse. "

That's precisely the argument that troubles Deborah Rice, an epidemiologist with the state of Maine and recent winner of the prestigious [Heinz award](#) for her neurotoxicology research. Industry is already arguing that adverse affects in the lab don't necessarily mean adverse effects in people, she said. If EPA doesn't accept results of the in vitro tests as evidence that a chemical may be dangerous, Rice said, "Then, that's it, game over... You are doing this for nothing."

Public health experts also worry about which chemicals are being used to replace those found to be hazardous. Barr of Emory said she is especially concerned about [bisphenol A](#), commonly known as BPA, which is used in the resin lining of cans and also in bottles and other products. Canada has moved to ban BPA.

"Now you have BPA-free containers, but nobody asks what the new containers are made of," she said. "It's a new polymer that has phthalate in it, plus two other chemicals. Two of them have no toxicity testing whatever. None has been done."

Other scientists question how seriously the government takes the whole issue of environmental health hazards. Melanie Marty, branch chief of the air toxicology and epidemiology branch of California's Office of Environmental Health Hazard Assessment, said, "People say, 'What are a few IQ points?' That is something we heard in the 1990s on lead," Marty said. "The person will not know the difference. But as a society, do we want to be shifting our IQ lower? I don't think so."

"It's very important to have animal models," adds Edward Levin, professor of psychiatry and behavioral science at the Duke Institute for Brain Sciences. "It's a lot of hubris to think we are anywhere near understanding how the brain works, and all the points of vulnerability in terms of brain function and development."

The reality, says Levin, who conducts research on the behavioral impairments caused by early exposure to pesticides and heavy metals, is that "everything actually is tested on animals. It's a matter of who is first, the lab animal or the first person who uses a shampoo or takes a drug or is exposed to an environmental toxicant. We are animals, too."

Levin, a past president of the [Neurobehavioral Teratology Society](#), many of whose members study developmental neurotoxicity, added, "Behavioral toxicology is a field defined as a race to figure out what's going wrong and how to deal with it before we're too stupid to care."

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