How many different manmade chemicals have you encountered today? Hundreds, maybe thousands. They’re in our food, our clothes, our furniture, our buildings, our vehicles. In our cell phones and computers. In the air we breathe, and almost everything we touch. They enrich our lives and make them more convenient in countless ways.

Most of us take for granted that the chemicals in our lives have been tested and deemed safe. But in the United States, by law, a company does not have to prove that a chemical is safe before introducing it in the commercial market. Rather, the burden of proof is on the U.S. Environmental Protection Agency (EPA) to prove that a chemical “presents or will present an unreasonable risk” to human health or the environment in order to require a company to produce safety data on it.

Dr. Tina Bahadori is Director of EPA’s Chemical Safety for Sustainability (CSS) Research division, where she is helping EPA transform its chemical safety screening tools. She holds a doctorate in environmental science and engineering from Harvard School of Public Health and master’s and bachelor’s degrees from MIT.

Can you give us some background on your work?
In the U.S., certain types of chemicals are carefully reviewed for safety: chemicals like pharmaceuticals, food additives, fertilizers, and insecticides—chemicals that we know humans are directly exposed to. But by law, most other chemicals are not required to be approved for safety. There are more than 80,000 such manmade chemicals currently registered for use in the U.S., and at least 1,000 more are introduced every year. And only a few hundred of these have been thoroughly evaluated for their potential risks to human health, wildlife, and the environment.

The law that governs chemical safety regulation for most chemicals, the Toxic Substances Control Act (TSCA), does not require companies to do safety testing or to provide safety data. Instead, if the EPA is concerned about the safety of a chemical, it must do its own testing, putting a significant burden of proof on the Agency.
When TSCA was passed in 1976, legislators may have imagined that human exposure to industrial chemicals was very limited and hence not a concern. But studies by the Centers for Disease Control and others have found that the majority of Americans now have hundreds of industrial chemicals in their bodies. We are incidentally exposed to chemicals whenever we interact with our chemical environment—when we bathe, or eat, or ride in a car, or breathe.

In most situations, these incidental exposures are not large enough to be acutely dangerous. However, we now know that exposure to even very low amounts over time—particularly during critical developmental periods, like pregnancy or adolescence—can affect health. Scientists who do human epidemiological and genetic susceptibility studies are beginning to see that many, if not all, diseases have environmental components, whether a health problem is triggered by exposure to a chemical or merely exacerbated by it. But there is often a long time between the exposure and the medical consequences, which has made it difficult to prove—or even study—such causal effects.

Most of the testing EPA has done has primarily been on laboratory animals like rats or mice for scenarios of acute (short-term) exposure. This doesn’t model in any way what happens with these day-to-day, low-level exposures.

**How will these data be used to assess chemical safety?**

EPA’s scientists are studying many important areas of chemical safety, expanding our understanding of the important biochemical networks and processes that are disrupted by chemicals, and at what doses. We study the effects of chemicals at multiple levels of biological organization: not just how a chemical interacts with specific cellular molecules such as enzymes or receptors, but also to understand the consequences of those interactions at the level of biochemical pathways, the cell, the organ, and the whole organism. This kind of detailed, multi-level analysis is what makes it possible for our models to have predictive power.

One of EPA’s major research initiatives in this area is the Toxicity Forecaster (ToxCast), which uses automated chemical screening technologies called high-throughput screening assays to expose living human cells or isolated proteins to chemicals. The cells or proteins are then screened for changes in biological activity that may suggest toxic effects. This technology has the potential to quickly and efficiently screen large numbers of chemicals.

In the first phase of ToxCast, called proof of concept, 300 well-studied chemicals were evaluated using more than 500 high-throughput screening assays. Those chemicals had already undergone extensive toxicity testing in animals, so EPA researchers were able to compare ToxCast results with those of traditional animal tests and verify the effectiveness of ToxCast’s predictive capacity. ToxCast continues to be refined—it now includes 700 high-throughput screening assays—as we learn more about how chemicals interact with biological systems. EPA will initially use ToxCast as a cost-effective way to prioritize the chemicals that need more extensive toxicity testing. In December, EPA publicly released data on an additional 1,800 chemicals and is now working with its federal partners and stakeholder communities to explore ways in which these data can be used to improve chemical safety.

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**How is the EPA improving its chemical safety review processes?**

I’m in the EPA’s Office of Research and Development, so I’m not in the part of EPA that has to regulate the chemicals. In my department, the Chemical Safety for Sustainability (CSS) research program, our goal is to develop better tools and approaches to understand and assess the impacts of chemicals and materials. Computational sciences now allow us not only to generate an incredible amount of data but also to integrate information from many different sources and begin to study the complexity of their interactions.

We know that there’s public consternation about the fact that we don’t know much about many of the chemicals on the market right now. We are trying to incorporate information from many different sources, to fill in the information landscape, and then use our new tools to expedite the process of identifying existing chemicals that should be examined more closely.

We are collaborating with other research partners to integrate information from many scientific disciplines and agencies: chemical risk data from the EPA; genetic susceptibility data from NIEHS; chemical exposure data from the CDC; toxicology and pharmacology data from the FDA; and genomics data from the NIH. These integrated databases are now publicly available for others to use in their chemical safety research and assessments.
Do these tools allow you to look at the effects of exposure to multiple chemicals, too?

In some cases, yes. We are also developing even more advanced tools to model more complex interactions. In collaboration with the FDA, NIH, and other agencies, we’re developing virtual biological systems: a virtual liver and a virtual embryo. These model “organ on a chip” systems will include bioassays as well as multi-level computer analyses and simulations. They will be fantastically complex, but they will begin to allow us to model the sorts of effects a given chemical—or combination of chemicals—might have on an organ or an embryo. Drug companies are very interested in this; they want our predictive models to work so they can use them in their drug discovery business, to reduce the number of drugs that fail in clinical trials.

A vital component of this work will be creating tools to visualize complex relationships—finding ways to communicate big, complex data packages and to separate the signal from the noise. We need to find patterns in these vast amounts of data, to unravel the complexities that the human mind by itself can’t fathom.

Will you be able to use these tools proactively?

Yes, that is one of the most exciting goals of our work. The same innovative computational tools we are developing to assess chemical risks can also be used to predict risk, and then to select or design new materials or processes that avoid unwanted attributes. If we can model chemical consequences better, we can start avoiding toxicity instead of just studying the toxic effects that occur after chemical exposure. This approach can minimize the environmental and human health impacts associated with the production, use, and disposal of chemicals. Some call this approach green chemistry; we call it sustainable design.

A major challenge faced by chemists trying to do green chemistry has been that there isn’t a good database of the biological effects of chemicals. The tools we are creating fill that gap. Our initial goal in green chemistry is to inform chemists of the known biology and toxicology of existing chemicals, so when they design new molecules or manufacturing processes, they can at least consider these issues.
Risk is a function not only of the immediate biological effects of a compound, but also of many other factors. To fully assess a chemical's safety, we need to know the critical biological processes and pathways it interacts with, and with what consequences—the basic toxicology or pharmacology. But we also need to know how it enters the body. What are a person's sources of exposure? The kind of exposure can affect its entry into and impact on our system. For example, some chemicals are more dangerous if inhaled than if eaten or touched, because our lungs, digestive tracts, and skin have different abilities to process chemicals. And is the exposure temporary, episodic, or long-term?

Once in the body, how is it changed? Are its metabolites—the chemicals it is changed into by our own enzymes—also biologically active? If so, we need to know what happens to them, too. How does the body inactivate or excrete it, and under what conditions? For example, people with liver or kidney disease are less able to detoxify or excrete many chemicals. Does it disappear from the body quickly, or does it bio-accumulate? Are its effects transient, long lasting, cumulative, delayed?

That's just looking at a single chemical. What happens when we are exposed (as we all are) to an assortment of chemicals? Are the effects of those exposures independent, additive, synergistic? Trying to study the effects of this chemical soup gets exponentially more complex very quickly.

Yet another confounding issue is that people differ in their vulnerability. Genetic differences make some individuals more vulnerable than others to particular chemicals. And all living creatures are much more vulnerable to chemical assaults during development than as adults. A developing fetus or a child is vulnerable to many chemicals that an adult can safely consume, thalidomide being the most infamous example of this.

Another factor is the persistence of the chemical in the environment. A recent study found that DDT exposure was linked to higher risk of Alzheimer's disease. Even though DDT use was banned in the U.S. in 1972, the molecule takes decades to break down in the environment, so it is still present in U.S. soil and water. It's also still in use in other countries, so consumers can be exposed to it in imported products. A consequence of that persistence is that even 40 years after it was banned, the CDC still finds DDT in 75-80 percent of the blood samples it collects from Americans.

—Carol Blackburn

Is industry embracing this approach?

It varies, but most companies are exploring the economic advantages of these new sustainable approaches. For example, Nike is a leader in the world of green chemistry as applied to athletic apparel. They are trying to make new materials that can meet their performance criteria without having unnecessary adverse effects on the environment. The same chemical innovations pioneered by Nike for a high performance fabric or rubber may be used by Boeing in designing the coating of the surface of their next aircraft. Key to embracing green chemistry is a robust environment of open innovation.

This approach can apply to any and all materials, inorganic or organic, and individual chemicals or mixtures of chemicals. Advances resulting from this research could replace rare, toxic, and expensive chemicals with earth-abundant, benign, renewable alternatives. This paves the way for the design of safer chemicals and more sustainable processes and pathways that consume less fresh water, generate less waste, and use less energy. It can minimize hazards that arise not only from a chemical's structure and intended use, but also from its production and disposal.

That touches on another dimension of the challenge: the “life cycle” of a chemical.

There are potential safety issues in every phase of a chemical's life cycle: in obtaining (mining, etc.) the raw materials, in the production and processing by chemical manufacturers, in the chemical wastes those processes create, in their effects on us when we use them, in what happens to them after we dispose of them, and even if we recycle them.

Part of what we're trying to do, instead of obsessing over what happens in a particular exposure scenario, is to take a life-cycle approach and identify the areas that we absolutely cannot afford not to worry about.

The electronics industry, whose products we all use daily, has notorious life-cycle problems. Can green chemistry help?

Absolutely. That's a sector where we think green chemistry can have significant impact. Because right now, we mine rare earth elements—gold, silver, and platinum—to use in cell phones and other electronic devices to enhance their performance. So first there is the environmental impact of the mining. Then there's the impact of the e-waste from devices that most people throw away after a year or so. And what happens to that e-waste? It's often exported out of the country where environmentally toxic chemicals are then used to extract those precious metals from the salvage. The rest of the materials used in electronics don't have the same market value, so they add to the mountains of plastic waste.

The U.S. State Department released a report last year stating that most of these rare earth materials are no longer mined in the U.S. They're mined in Africa or China, which is also where our e-waste is exported, so we're transferring the toxic impact of our consumerism elsewhere in the world.

But that's only part of the State Department's concern; the other is that we're relying on those countries to provide raw materials that are critical to our economic sustainability. So there is a strong economic incentive to develop alternative materials that are not rare earth but have the same performance properties—materials that we can safely manufacture in this country and not extract out of the earth somewhere else. That's a low-hanging fruit in the world of green chemistry.

What advice do you have for students interested in these challenges?

We look at the issue this way: no matter what our fears about chemical pollution and safety, it's almost impossible to do anything constructive without improving the chemistry we use. And the opportunities to do that have never been more exciting.

Converging advances in biology, biotechnology, informatics, computational chemistry, and exposure science are transforming this field, enabling innovations in sustainable chemistry and providing new tools to model and understand how chemicals interact with biological systems. We are optimistic that our work will enable future innovation while also helping to protect our environment for future generations.