

## Opening the “green pharmacy”

**Can drugs be developed to be ecotoxicologically benign while retaining their desired medicinal properties? Many observers in the field say no, but some academic researchers—and big drug companies—are pushing the question.**

**Naomi Lubick**

Recent news reports in the U.S. of detectable levels of pharmaceuticals in treated drinking water [took many Americans and Congress by surprise](#). But the problem is an old one, one utility companies have been aware of for years.



*MIGUEL TREMBLAY, WIKIMEDIA COMMONS*

**Mixtures of human drugs flow into the Po River in Italy, sometimes at levels that might affect human health, researchers have found, with unknown environmental impacts.**

levels and to scientific meetings where environmental chemists, toxicologists, policy makers, and drug company executives have discussed the possible toxicity of human drugs in the environment and to humans—along with possible solutions.

One of those solutions may be “benign-by-design” drugs. Some scientists argue that the time has come to build from scratch drugs that degrade in the environment, as well as to revisit old drugs

Drugs that flow from humans into the environment may include the lingering analgesic diclofenac, the long-lasting antiepileptic carbamazepine, the omnipresent antibiotic ciprofloxacin, and even seemingly mundane painkillers like ibuprofen, gemfibrozil, and naproxen, not to mention synthetic estrogens. The problem has led to government hearings at the state and federal

unintentionally made that way. The prospect remains difficult, but some evidence shows that pharmaceutical companies are beginning to tackle the problem.

So far, experts have focused on [human-health threats](#). At the [Society of Toxicology](#) annual meeting held in March, academic and industrial chemists presented information at a roundtable session on human-health risk assessments for pharmaceuticals in the environment. But several new meetings, including the first International Conference on Sustainable Pharmacy held in Osnabrück (Germany) in April, are examining pharmaceuticals' entire life cycles, with a special emphasis on how to make benign-by-design drugs.

Later this year, a [new product](#) is scheduled for animal and human drug trials that is similar to an older version of a birth control pill from drugmaker Schering-Plough. The new-old drug uses natural estrogens paired with a biodegradable progesterone.

Scientists outside the company say this may be a much more environmentally friendly drug—one that will both serve its purpose in humans and present less of a threat to ecosystems. Recent research has established the negative impact of synthetic estrogens on [fish populations](#): the sex ratios of the fish are skewed, and their endocrine systems are disrupted. Unfortunately, removal of synthetic estrogens from wastewater remains difficult.

### **Searching for friendlier substitutes**

Finding new drugs that work is difficult enough for researchers at pharmaceutical companies, without adding concerns about pharmaceuticals' environmental impacts, notes David Taylor, the director of environment and sustainability for AstraZeneca, one of the major global pharmaceutical producers. Drug companies spend [tens of billions of dollars every year](#) on medical research, according to the nonprofit trade society Pharmaceutical Research and Manufacturers of America, and that accounts only for the costs before a product gets to the animal- or human-testing stages.

Taylor notes that the idea of revisiting established drug formulas to make them more benign to the environment is not new. Currently, the main focus is on the manufacturing process: drug companies are rejiggering their production steps, if not their final products, to fit green chemistry principles. This approach allows manufacturers to save money by using fewer chemicals and less water, which may lead to better public perception of the companies. But creating a drug that biodegrades while ensuring its stability on the pharmacy shelf remains a conundrum, Taylor says.

For certain drugs, it can be done, says [Klaus Kümmerer](#), a professor in the department of environmental health sciences of the University Medical Center Freiburg (Germany). “Stability and efficiency is not a contradiction by itself—it depends on circumstance,” comments Kümmerer, a leading voice in [the call for developing](#) environmentally benign pharmaceuticals.

Some characteristics, such as photodegradability, could be harnessed during wastewater treatment, he says. Some drugs that have been on the market for 40 years are “very, very biodegradable,” such as valproic acid, Kümmerer notes. This antiepileptic drug may have a toxic

effect in humans at low concentrations, but it is easily degraded. “More examples [will come], and people will learn,” he says.

Thomas Ternes, a professor at the German Federal Institute of Hydrology, notes that the old pain-reliever standby ibuprofen crops up in the environment at incredibly high concentrations, yet it degrades quickly, sometimes mineralizing in the environment. “Good [wastewater] treatment takes care of it,” adds Ternes.

## **End of the line**

Some preventive measures by people who take medications or prescribe them could help avoid environmental exposure. Hospitals that administer drugs known to be extremely environmentally hazardous or that have such potential, such as [chemotherapy drugs](#), are logical locations for preventive measures, Kümmerer says. These drugs could be collected and removed from hospital wastewater through in-house treatment programs that are separate from the municipal waste infrastructure.

Several water utilities and communities across the U.S. have begun [collection drives](#) for unused drugs, which are typically flushed down the drain or thrown into landfills. One program in Sweden, [JanusInfo](#), includes a database to help doctors choose drugs that might have less of an impact on the environment (or that might have fewer human side effects). The program was created with the intent to influence the consumer market. Another program in Sweden, [MistraPharma](#), collects [genetic data](#) that would help drugmakers, environmental researchers, and policy makers predict the potential impacts of human drugs on species that share similar pathways for drug activity.

Other steps aimed at keeping drugs out of the ecosystem include improvements in wastewater treatment. [Ozonation](#) (injecting ozone or OH radicals into wastewater to oxidize contaminants) is one treatment that [has shown some promise](#) for destroying or degrading synthetic estrogens and other drugs before they leave a treatment plant—but the process can be expensive, which might put it beyond the reach of some utilities. Another solution is to improve the information flow between water-utility engineers and pharmaceutical makers so that the engineers can design new water treatments that might remove the drugs. Many observers agree that little communication occurs now between these two groups before drugs are released into the market.

Preventative measures taken by pharmaceutical companies could make some of these end-of-pipeline treatments unnecessary, but those measures may be needed soon. The EU is moving closer to evaluating drugs’ environmental impacts before they enter the treatment system or the environment, Ternes notes. Because of [relatively new guidelines](#) from the EU’s European Medicines Agency (EMA), European companies will have to consider environmental impacts and provide data, “especially for new drugs,” he says. But even if a drug considered to be hazardous to the environment is under EMA review, Ternes cautions, it will most likely be approved in any case: “Human health is priority number one, two, and three. Number four may be the environment.”

Kümmerer argues that even though the impact of low-level exposures to pharmaceuticals in mixtures over long periods of time—for humans or ecosystems—remains an open question, preventing those exposures from happening to begin with means there is no need to find out what those impacts are. “For me, it’s changing a paradigm,” he adds, “changing the education of medicinal chemists.”

In the end, argues AstraZeneca’s Taylor, “you have to start from the question, are [human drugs] environmentally hazardous anyway?” Although pharmaceuticals detected at extremely low levels have been shown to be biologically active, he says, “at the moment, there is staggeringly little evidence that they are a problem. But we have to be careful about that.” In the meantime, he says, benign-by-design pharmacology “is a large, complex, and fascinating subject area” and one that industry will have to address soon.



*WESTERN LAKE SUPERIOR SANITARY DISTRICT*

**Collection programs, such as the first event held by the Western Lake Superior Sanitary District in Minnesota in April (pictured above), attempt to remove human pharmaceuticals from the waste stream before they get into the environment.**