Researchers, regulators, industry, and the public remain concerned about the presence of pharmaceuticals in the environment, and regulators and advocates are reacting. The main concerns center on the potential for active pharmaceutical ingredients and metabolites to cause environmental harm and contaminate drinking water sources.

The discarded drugs that end up in surface water or groundwater are generally not detected at concentrations high enough to constitute a therapeutic dose of an individual medication for humans. However, the potential for deleterious effects on the environment can be increased by synergism (toxicity of two or more chemicals being greater than the sum of their individual toxicities), additive

Regulation of Pharmaceutical Disposal Promotes Environmental Protection

by Kathryn Onesios-Barry and Elsie Rivera Palabrica

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individual pharmaceuticals ranging from 0.1 μg/L to 0.73 μg/L, while maximum concentrations for the PFF-influenced WWTPs ranged from greater than 40 μg/L to 3,800 μg/L. Another study examined effluent from a WWTP that receives process water from about 90 pharmaceutical manufacturers near Hyderabad, India. Concentrations were high, with 14 mg/L of ciprofloxacin and 2.1 mg/L cetirizine detected. An earlier study revealed maximum concentrations of ciprofloxacin, losartan, and cetirizine to be 31, 2.5, and 1.4 mg/L, respectively.

Though there are currently no U.S. regulations addressing individual pharmaceutical concentration limits for wastewater, removal of pharmaceuticals from water is an active area of research. Physical, chemical, and biological methods are all being tested for the greatest pharmaceutical removal efficiency involving the least cost. Site- and chemical-specific factors need to be considered when selecting a removal method for a facility. Many options have been successfully demonstrated to remove pharmaceuticals from water and wastewater, including reverse osmosis, granular activated carbon, membrane bioreactors, ozonation, ultrasound, up-flow anaerobic stage reactors, activated sludge, constructed wetlands, and biofiltration.

The disposal of unused, unwanted, or expired pharmaceuticals by households and health care providers is another controllable source of pharmaceuticals to the environment. Household waste is exempt from federal hazardous waste regulation, but government and public/private partnerships have worked to encourage more responsible disposal through drug take-back events. The number of take-back events across the United States has risen dramatically over the past decade. Flushing unwanted pharmaceuticals down a toilet is no longer an effects, and constant exposure of nontarget organisms living in the affected aquatic environment.

Research has shown that animals and plants can be harmed by exposure to pharmaceuticals, with effects ranging from reduced egg fertilization and desmasculinization of males in studied fish to disruption of photosynthesis in plants. Development of microbial resistance to antibiotics and the presence of pharmaceuticals in finished drinking water are also areas of active research and concern. Sources of pharmaceuticals in the environment include nonpoint sources, such as human or animal excretion and disposal of unused medications, as well as point sources, such as effluent from pharmaceutical manufacturing plants. To reduce the potential negative impact of pharmaceuticals on the environment, regulators and advocates are attempting to decrease pharmaceutical input to the environment by focusing on responsible disposal of unused medications.

**Sources of Pharmaceuticals in the Aquatic Environment**

While human and animal excretion of pharmaceuticals and metabolites is not a source to the environment that can be easily controlled, controlling other sources shows more promise. For instance, product manufacturing facility effluent and disposal of unused medications have potential for being successfully controlled as sources of pharmaceuticals in the environment. Drug manufacturers may release active pharmaceutical ingredients into the environment if their processes, such as material handling and tank cleaning and rinsing, do not contain or completely recover all ingredients and products before wastewater effluent leaves the site.

One recent study, for example, investigated effluent from two New York wastewater treatment plants (WWTPs) that received more than 20% of their flow from pharmaceutical formulation facilities (PFFs). Concentrations of pharmaceuticals in the PFF-receiving wastewater were 10 to 100 times greater than concentrations in 24 other WWTPs not receiving flow from PFFs. WWTPs not receiving PFF input showed maximum concentrations of

A pharmaceutical collection box was placed outside Marshall County Jail in Plymouth, IN. (Photo credit: Mike Good)
waste. Pharmaceuticals on the P-list (acutely hazardous) include arsenic trioxide, epinephrine base, nicotine, nitroglycerin, phentermine, physostigmine, physostigmine salicylate, and warfarin (> 0.3%). The U-list (toxic) contains more than 20 pharmaceuticals, including azaserine, chlorambucil, daunomycin, lindane, melphalan, mercury, paraldehyde, resorcinol, and warfarin (≤ 0.3%). If a waste’s sole active ingredient is the listed compound, then the drug is considered hazardous waste. In addition, wastes that exhibit a characteristic of ignitability, corrosivity, reactivity, or toxicity under RCRA regulation are also regulated as hazardous waste.9

In its 2012 report, entitled “EPA inaction in identifying hazardous waste pharmaceuticals may result in unsafe disposal,” the Office of Inspector General (OIG) found that the U.S. Environmental Protection Agency (EPA) has not kept up with identifying pharmaceuticals that could potentially harm human health or the environment.10 OIG found eight unregulated pharmaceuticals that it contended should be regulated as acute hazardous waste. OIG also identified more than 20 unregulated pharmaceuticals with lethal dosage (LD50) toxicity values on par with those of pharmaceuticals already included on the U-list. In 2008, EPA considered regulating pharmaceutical waste under the RCRA Universal Waste Program, but decided against it due to negative public feedback. EPA is currently continuing this effort for effective management of pharmaceutical hazardous waste from healthcare facilities, and publication of these forthcoming rules is anticipated in 2014.11

Controlled substance pharmaceutical waste is regulated in the United States by the Drug Enforcement Administration (DEA). In December 2012, the DEA proposed new regulations that would implement the Secure and Responsible Drug Disposal Act of 2010. This would provide ultimate users with more disposal options, including take-back events, mail-back programs, and collection boxes. Currently, ultimate users need to dispose of controlled substances to law enforcement, DEA agents, or through other means deemed appropriate by the DEA. The proposed regulation would
also allow manufacturers, distributors, reverse distributors, and retail pharmacies to operate mail-back programs for on-site destruction of the drugs and to maintain collection boxes. Though these programs would be allowed to operate voluntarily under the DEA regulations, some U.S. counties have proposed legislation that would require drug manufacturers selling products into their jurisdictions to finance and operate take-back programs for all drugs.

In California, Alameda County passed an ordinance in July 2012 that requires drug producers selling or distributing pharmaceuticals into the county to participate in and finance a County Department of Environmental Health-approved Product Stewardship Program or to arrange for a “Stewardship Organization” to operate a program on their behalf. Pharmaceutical Research and Manufacturers of America (PhRMA), the Generic Pharmaceutical Association (GPhA), and the Biotechnology Industry Organization (BIO) sued to block this ordinance, but the U.S. District Court for the Northern District of California denied their motion. The court’s written decision stated that Alameda County had “adequately shown that the [o]rdinance serves a legitimate public health and safety interest, and that the relatively modest compliance costs producers will incur should they choose to sell their products in the county do not unduly burden interstate commerce.” The pharmaceutical trade group filed an appeal in September 2013.

King County Board of Public Health in Washington enacted a similar regulation in June 2013 that requires drug producers to participates in a standard stewardship plan or to develop their own Public Health-approved plan. Drug producers will be required to promote the program, report the amount of drugs collected, and survey residents regarding the program’s efficacy. Producers will pay for collection, drug transportation, drug incineration, and reimbursement of Public Health for review and
oversight. PhRMA, GPhA, BIO, and Consumer Healthcare Products Association sued to block this regulation as well.\textsuperscript{17}

New York and California introduced similar drug disposal legislation in 2013.\textsuperscript{18,19} The U.S. federal government has also introduced legislation addressing safe pharmaceutical disposal, such as the Pharmaceutical Stewardship Act of 2011\textsuperscript{20} and the Servicemembers and Veterans Prescription Drug Safety Act of 2013.\textsuperscript{21} In February 2014, a Notice of Data Availability and Request for Comment was published seeking comment on information gathered by EPA about hazardous waste (including pharmaceuticals) management practices in retail stores and RCRA applicability.\textsuperscript{22}

**Conclusion**

With the new legislation from Alameda and King Counties, federal, state, and now local regulation of pharmaceutical waste is here and continues to expand. Concerned stakeholders who proactively engage on this topic, including industry, government, and advocates, can demonstrate their commitment to the prevention of environmental exposure.

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