Protecting the Great Lakes from Pharmaceutical Pollution

Alliance for the Great Lakes

Ensuring a Living Resource for all Generations

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We gratefully acknowledge the support of
The Searle Funds at The Chicago Community Trust

Photo: Thomas Rohrer

I. Introduction/Background

In a study of source water, finished drinking water and tap water collected during 2006 and 2007 from 19 U.S. water utilities, the 11 most frequently detected compounds were:

- *atenolol — heart medicine*
- *atrazine — Herbicide*
- *carbamazepine — anticonvulsant and mood stabilizing drug*
- *estrone — estrogen*
- *gemfibrozil — lipid reducing drug*
- *meprobamate — anxiety medicine*
- *naproxen — Anti-inflammatory used in pain relievers*
- *phenytoin — antiepileptic*
- *sulfamethoxazole — antibiotic*
- *TCEP — Flame-retardant*
- *trimethoprim — antibiotic*

The Great Lakes provide drinking water, recreation and industry to more than 40 million people in eight states and two Canadian provinces. Recent tests have found very low levels of pharmaceuticals in Lake Michigan at the water intakes for major metropolitan centers like Chicago and Milwaukee. Testing of drinking water outside the Great Lakes region has found similar results. Although at this time there is no known health risk to people at the low levels detected, the presence of pharmaceutical pollution nonetheless represents an emerging concern that should be addressed now to protect public health.

Pharmaceuticals can enter our drinking water when medicines are either disposed of or excreted by individuals after use. It's a mounting problem. Medicines are produced and prescribed in increasing volumes every year.[1] Sales of over the counter medicines have increased by 60% since the 1990s.[2] In 2006, over 3.4 billion prescriptions were written.[3] Once medicines are discarded or excreted, they enter surface waters through many different pathways—effluent from treatment plants, septic systems, runoff and groundwater from uncontrolled landfills, industrial discharges, and commercial animal feeding operations. Wastewater treatment plants and septic systems were not designed to remove these pollutants.

Original reports of pharmaceutical chemicals' presence in drinking water date to the mid-1970s. As analytical techniques became increasingly sensitive and detection limits approached and sometimes surpassed the low nanograms per liter (ng/L) or parts-per-trillion (ppt) level, however, many more pharmaceuticals have been reported in waste water, ambient water and drinking water.

A USGS report in 2002 was the first national-scale examination of emerging contaminants in streams of the United States.[4] In this study, water samples were collected from a network of 139 streams across 30 states during 1999 and 2000. The sampling sites focused on streams considered susceptible to contamination and represented a wide variety of hydrogeologic, climatic, and land-use settings across the United States. The disturbing results showed a broad range of chemicals occurring in mixtures at low concentrations in residential, industrial and agricultural wastewaters. The chemicals detected included human and veterinary drugs, natural and synthetic hormones, detergent metabolites, plasticizers, insecticides and fire retardants. One or more of these chemicals were found in 80% of the streams sampled. Half of the streams contained seven or more of these chemicals, and about one-third contained 10 or more of these chemicals.

[1] This background information is drawn from a toolkit titled "Disposal of Unwanted Medicines: A resource for Action in Your Community" by Sea Grant Illinois-Indiana, updated Feb. 2008. Online at: http://www.iisgcp.org/unwantedmeds/index.html

[2] Ann Pistell, Maine DEP. Presentation at Northeastern Water Science Forum, Aug. 9, 2007. Online at: http://www.neiwpcc.org/ppcpconference/ppcp-docs/AnnPistell.pdf

[3] Id.

[4] Barnes, K.K., Kolpin, D.W., Meyer, M.T., Thurman, E.M., Furlong, E.T., Zaugg, S.D., and Barber, L.B., 2002, Water-quality data for pharmaceuticals, hormones, and other organic wastewater contaminants in U.S. streams, 1999-2000: U.S. Geological Survey Open-File Report 02-94. Available at http://toxics.usgs.gov/pubs/OFR-02-94/

In a study of source water, treated drinking water and tap water collected during 2006 and 2007 from 19 U.S. water utilities, the 11 most frequently detected compounds were atenolol, atrazine, carbamazepine, estrone, gemfibrozil, meprobamate, naproxen, phenytoin, sulfamethoxazole, TCEP, and trimethoprim.[5] The study concluded that the presence of Atenolol, atrazine, DEET, estrone, meprobamate, and trimethoprim can indicate potential contamination from other pharmaceuticals and can be used to gauge the efficacy of water treatment processes.

A. Human Effects

At the levels currently found in surface water, the potential effects of pharmaceutical pollution on humans are not clearly understood. Water pollution can enter the body through ingestion, surface contact and inhalation of water vapor. Pregnant women, infants and children, and people with suppressed immune systems face greater risks from contaminants.

There is little understanding to date of the potentially toxic, interactive effects of pollutants mixing in the environment.[6] In addition, the 2002 USGS study found that several pharmaceutical pollutants may degrade into their constituent compounds over time.[7] The study called for increased research into human health effects of the individual contaminants, mixtures of these compounds, and breakdown products of particular compounds.

The research community is especially concerned about the human health consequences of long-term, low-level exposure to pharmaceuticals as these compounds are deliberately designed to interact with the body at low concentrations in order to bring about a biological change.[8] In particular, hormones and other chemicals that act by signaling and stimulating cell changes can have effects at low levels.

A 1992 study[9] evaluating human sperm quality used 40 years of data gathered from clinics around the world. Researchers found a statistically significant trend toward lower sperm quality that could be linked to estrogen and estrogen-like chemicals in the environment. International efforts to track human sperm quality and to investigate potential causes of significant declines revealed that environmental exposure to some chemicals is strongly associated with low sperm quality.[10]

The EPA is working with the National Academy of Sciences to advise on the potential risk to human health from low levels of pharmaceutical residues in drinking water.[11] EPA's white paper reviewed six studies addressing the issue. Each of the articles presented approaches in which the results showed little to no risk from pharmaceuticals in drinking water. Notably, however:

- None of the approaches considered exposure of different life stages, other than the use of the 22 pound child in the calculations.
- None of the approaches made use of the U.S. Food and Drug Administration's extensive database on adverse drug reactions, data that could be used to modify the uncertainty factor applied to each pharmaceutical.
- Only one of the approaches addressed carcinogenic or chemotherapeutic drugs.

[5] "Pharmaceuticals and Endocrine Disrupting Compounds in U.S. Drinking Water," Mark J. Benotti, Rebecca A. Trenholm, Brett J. Vanderford, Janie C. Holady, Benjamin D. Stanford and Shane A. Snyder, Environ. Sci. Technol., 2009, 43 (3), pp 597–603 (2008) available online at: *http://pubs.acs.org/doi/abs/10.1021/es801845a*

[6] See Suny-Albany 2002 study "Understanding the Human Health Effects of Chemical Mixtures" Environmental Health Perspectives Supplements, 110:25-42, online at: *http://www.ehponline.org/members/2002/suppl-1/25-42carpenter/EHP110s1p25PDF.PDF*.

[7] Kolpin, Dana W., et al. "Pharmaceuticals, Hormones, and other Organic Wastewater Contaminants in U.S. Streams, 1999-2000: A National Reconnaissance." *Environmental Science & Technology* 36.6 (2002): 1202-1211.

[8] See Rapid Health Policy Response Project. 2008. Phamaceuticals are in the Drinking Water: What Does it Mean? George Washington University School of Public Health and Health Services, online at: *http://www.gwumc.edu/sphhs/about/rapidresponse/download/Rapid_H2O_Final.pdf*.

[9] Carlsen E, Giwercman A, Keiding N, and Skakkebaek NE. 1992. Evidence for decreasing quality of semen during past 50 years. British Medical Journal 305:609-613; Sharpe R and Skakkenbaek NE. 1993, abstract online at: *http://www.bmj.com/cgi/content/abstract/305/6854/609*. Are oestrogens involved in falling sperm counts and disorders of the male reproductive tract? Lancet 341:1392-95, abstract online at: *http://www.ncbi.nlm.nih.gov/pubmed/8098802*.

[10] Duty S, Silva M, Barr D, Brock J, Ryan L, Chen Z, Herrick R, Christiani D, and Hauser R. 2003. Phthalate exposure and human semen parameters. Epidemiology 14:269-277, abstract online at: *http://www.ncbi.nlm.nih.gov/pubmed/12859026*.; Hauser R, Chen Z, Pothier L, Ryan L, and Altshul L. 2003. The relationship between human semen parameters and environmental exposure to polychlroinated biphenyls and p,p'-DDE. Environmental Health Perspectives 111:1505-1511.;Swan S, Kruse R, Liu F, Barr D, Drobnis E, Redmon J, Wang C, Brazil C, Overstreet J, and Study for Future Families Research Group. 2003. Semen quality in relation to biomarkers of pesticide exposure. Environmental Health Perspectives 111:1478-1484, abstract online at: *http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=1241650*.

[11] Approaches To Screening For Risk From Pharmaceuticals In Drinking Water And Prioritization For Further Evaluation, Oct. 20, 2008, available online at: *http://dels.nas.edu/best/risk_analysis/Documents/EPA%20Pharmaceuticals%20in%20water%20white%20paper.pdf*

B. Wildlife Effects

For many pharmaceuticals, there is currently little information regarding their potential toxicological significance in ecosystems — particularly effects from long-term, low-level environmental exposures. The 2002 USGS study examining pharmaceuticals, hormones, and other organic wastewater contaminants found that the low concentrations did not appear to cause immediate harmful effects on wildlife, but long term exposure at low levels raised concerns that required additional study. Impacts can include toxicological effects, such as chemical poisoning, or disruption of the organs and body systems that hormones regulate (endocrine disruption).

The 2002 USGS report noted that aquatic species exposed to estrogenic compounds have been shown to alter normal hormonal levels, and that even low levels of hormones can have adverse impacts on aquatic species. The report recommended that additional research on the toxicity of the target compounds should include not only the individual compounds, but also mixtures of these compounds.

Recent USGS research has identified toxicological and endocrine impacts on aquatic and environmental health. For example, studies of endocrine-disrupting chemicals from wastewater treatment effluent on fish resulted in altered (cancerous, reduced size and intersex) reproductive organs.[12] Pharmaceuticals have also been shown to bioaccumulate in earthworms from agricultural soil partially mixed with biosolids.[13]

While examining 20 years of scientific literature dealing with wildlife populations near the Great Lakes, researcher Theo Colborn noticed many physical abnormalities, higher death rates in the young, and decreasing populations in many kinds of animals, especially top-of-the-food-chain predators. After tests confirmed high levels of synthetic chemicals in wildlife tissue samples, she theorized the increasing health problems she saw in the animals were linked to human-made chemicals.[14]

[12] See Hinck, J.E. 2008 "Chemical Contaminants, Health Indicators, and Reproductive Biomarker Responses in Fish from Rivers in the Southeastern United States, abstract online at: *http://www.ncbi.nlm.nih.gov/pubmed/18036634;*" Vajda, A.M., et al., 2008. "Reproductive Disruption in Fish Downstream of an Estrogenic Wastewater Effluent." Environmental Science and Technology, abstract online at: *http://pubs.acs.org/doi/abs/10.1021/es0720661*.

[13] See Kinney, C.A. et al., 2008. "Bioaccumulation of Pharmaceuticals and other Anthropogenic Waste Indicators in Earthworms from Agricultural Soil Amended with Biosolid or Swine Manure." Environmental Science and Technology. 42: 1863-70, abstract online at: *http://pubs.acs.org/doi/abs/10.1021/es702304c*.

[14] Colborn T, vom Saal FS, and Soto AM. 1993. Developmental effects of endocrine-disrupting chemicals in wildlife and humans. Environmental Health Perspectives 101:378-384, abstract online at: *http://www.ehponline.org/docs/1993/101-5/colborn-abs.html*.

Photo: Lloyd DeGrane

II. Sources of pharmaceuticals

A. Metabolic byproducts

The majority of medications patients take are secreted in urine, in unchanged condition or as metabolites. These excreted pharmaceuticals are then flushed, making their way to sewage plants and into rivers and streams and, eventually, the Great Lakes. Animal waste and agricultural runoff also contribute pharmaceuticals to our waters. Medications are often specifically adapted to resist biodegradation and can therefore remain in the environment for a long time. For a few pharmaceuticals, however, only a small percentage of the total amount used makes is way into the environment.[15]

Industry research has concluded that patient use of medicines is the principal source of pharmaceuticals in the water supply.[16] According to one industry estimate: if one assumes 10% of medicine goes unused and all of that unused medicine is flushed, then patient use would account for about 88% of pharmaceuticals in water and the flushed unused medicine would account for about 12%.[17]

B. Residential disposal

According to the EPA, a secondary route of transfer of pharmaceuticals to the environment is from the disposal of medications to sewers and trash. The relative significance of this type of disposal with respect to excretion is poorly understood and subject to speculation. Two major aspects of uncertainty exist. First, it is unknown what percentage of any particular pharmaceutical in the environment originates from disposal, as the individual percentages may vary dramatically among pharmaceuticals. Second, disposal occurs from a variety of sources and the relative contribution from each is unknown.[18]

The Pharmaceutical Research and Manufacturer's of America (PhRMA) estimates that 3 percent (2.8 million pounds) of prescription medicines go unused by U.S. consumers and that 7 percent to 13 percent (1.5 million pounds) goes unused by patients in long-term care facilities.[19] Recent data collection, however, suggests that these percentages may be higher. Based on data collected by the Teleosis Institute in California from July 1 to Dec. 31, 2007, consumers did not use nearly 45 percent of the drugs they were prescribed.[20]

Only a handful of efforts have been made to quantify the amount of unused and unwanted drugs that are disposed into sewers and landfills, however, estimates of disposed drugs suggest that the total is signifi-

[15] See "Disposal as a Source of Pharmaceuticals in the Environment," Ilene S. Ruhoy, MD and Christian G. Daughton, PhD, U.S. EPA, Office of Research and Development, National Exposure Research Laboratory, Environmental Sciences Division, *http://epa.gov/esd/chemistry/images/drug-disposal-1.pdf*

[16] Tischler, Lial, et al. "Landfill Disposal as an Approach to Reduce Discharges of Medicines from POTWs." Proceedings of the Water Environment Federation, WEFTEC 2008: Session 101 through Session 115.18 (2008): 7538-7555.

[17] Id. at Table 6; Finan, Douglas presentation at PSI Dialogue Meeting December 2-3, 2008.

[18] Ruhoy IS and Daughton CG "Disposal as a Source of Pharmaceuticals in the Environment," U.S. EPA, Las Vegas, NV; illustrated poster, December 2007; NERL-LV-ESD-07-129; available: *http://www.epa.gov/nerlesd1/chemistry/images/drug-disposal-1.pdf*

[19] Buzby, Mary E., Merck & Co., Inc., PhRMA Pharmaceuticals in the Environment (PIE) Task Force. "Pharmaceuticals in the Environment—PhRMA Perspective" May 22, 2007. *http://www.dtsc.ca.gov/AssessingRisk/PPCP/upload/04_Buzby.pdf*.

[20] See Green Pharmacy Preliminary Report, available online at: *http://www.teleosis.org/pdf/GreenPharmacy_FullPreliminaryReport.pdf*

cant. One research study that looked at the disposal of drugs from coroner offices in Clark County, Nevada estimated that a minimum of 17.9 metric tons of pharmaceuticals are disposed into sewer systems annually from deceased people.[21]

FDA may consider environmental issues during the drug approval process, such as toxicity to organisms or increased levels in the environment due to use and disposal of the drug product. These considerations can warrant analysis of factors including the expected environmental fate of the product. Under FDA's regulations, however, drug approvals generally can qualify for a categorical exclusion if the estimated concentration at the point of entry to the aquatic environment will be below 1 part per billion. Strengthening this regulatory process could allow additional scrutiny of pharmaceuticals before they are approved for manufacture.

C. Commercial disposal

1. Pharmaceutical manufacturers

Large quantities of residual waste are generated by the manufacturing processes of the pharmaceutical industry, especially in fermentation and natural product extraction. Chemical synthesis processes generate wastes containing hazardous spent solvents and reactants, combined with residual wastes such as reaction residues. Equipment cleaning water and residue, often containing hazardous chemicals, is a major waste stream.[22]

The Clean Water Act gives EPA the authority to regulate effluents from industrial sources like pharmaceutical manufacturers into waters. The act sets "best available" technology standards for treatment of wastes for both direct and indirect discharges. In 1983, EPA proposed effluent guidelines for the pharmaceutical manufacturing point source category.[23] The implementation of the guidelines is left to the states who issue National Pollutant Discharge Elimination System (NPDES) permits for each facility. Because monitoring and effluent standards are required for all wastewater discharges from the manufacturing process, it is generally not believed that manufacturing wastewater discharges make a significant contribution to the presence of pharmaceuticals in the water system.[24]

Pharmaceutical manufacturers must also comply with regulations governing hazardous waste and FDA regulations. Pharmaceutical manufacturers are regulated by the Center for Drug Evaluation and Research and comply with Good Manufacturing Practices designed to help assure the quality of drug products.

Recently, pharmaceutical companies have engaged in "Green chemistry" projects in an effort to reduce the environmental toxicity and volume of waste created during the manufacturing process.

2. Health care facilities

Health care facilities generate pharmaceutical waste through a wide variety of activities, including but not limited to intravenous (IV) preparation, general compounding, spills/breakage, partially used vials, syringes, and IVs, unused preparations, and outdated pharmaceuticals.

In hospitals, pharmaceutical waste is generally discarded down the drain or landfilled, except chemotherapy agents, which are often sent to a regulated medical waste incinerator. A hospital pharmacy generally stocks between 2,000 and 4,000 different items, each of which must be evaluated against state and federal hazardous waste regulations.[25] Pharmacists and nurses generally do not receive training on hazardous waste management during their academic studies and safety and environmental services managers may not be familiar with the active ingredients and formulations of pharmaceutical products. This offers an opportunity for education efforts.

Some frequently used pharmaceuticals, such as physostigmine, warfarin, and nine chemotherapeutic agents are regulated as hazardous waste under the Resource Conservation and Recovery Act (RCRA).[26]

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[21] Ruhoy, Ilene Sue, and Christian G. Daughton. "Types and Quantities of Leftover Drugs Entering the Environment via Disposal to Sewage-Revealed by Coroner Records." *Science of the Total Environment* 388.1-3 (2007): 137-148.

[22] U.S. EPA, 1991.

[23] 40 CFR Part 439.

[24] Under these guidelines, "Permit compliance monitoring is required for each regulated pollutant generated or used at a pharmaceutical manufacturing facility, except where the regulated pollutant is monitored as a surrogate parameter." 40 CFR 439.2.

[25] Managing Pharmaceutical Waste, "A 10-Step Blueprint for Healthcare Facilities In the United States," Practice Greenhealth Aug. 2008.

[26] Id.

Through its outreach on the issue of disposal of unused pharmaceuticals, USEPA identified that there is near universal interest from stakeholders to better manage unused pharmaceuticals at health care facilities and there is general interest in more quickly advancing the use of best practices for managing unused pharmaceuticals at health care facilities. Therefore, USEPA is developing best practices for unused pharmaceutical management at health care facilities and expects to complete its work during 2010.[27]

D. Others

USGS is currently doing a source characterization study that is to provide a refined estimate of the relative potential environmental contributions in water and sediment of selected emerging contaminants from a variety of urban and agricultural waste sources. Initial studies by the USGS have found that large-scale animal feeding operations,[28] as well as landfill leachate, may also serve as sources of pharmaceutical pollution in ground and surface waters.[29] The study began in 2004 and is expected to have a full report in 2010; however, the study did not include any sampling from the Great Lakes area.[30]

[27] 74 Fed. Reg. 68599, 68611 (Dec. 28, 2009).
[28] Campagnolo, Enzo R., et al. "Antimicrobial Residues in Animal Waste and Water Resources Proximal to Large-scale Swine and Poultry Feeding Operations." *The Science of the Total Environment* 229.1-2 (2002): 89-95.
[29] Barnes, Kimberlee K., et al. "Pharmaceuticals and Other Organic Waste Water Contaminants Within a Leachate Plume Downgradient of Municipal Landfill." *Ground Water Monitoring & Remediation* 24. 2 (2004): 119-126.
[30] See *http://toxics.usgs.gov/regional/emc/source_characterization.html*; Email communications from Dana Kolpin to Lyman Welch, Oct. 8, 2008, Aug. 10, 2009 and Feb. 11, 2010.

Photo: U.S. Fish and Wildlife Service

III. Research on pharmaceuticals at the end of pipe in Great Lakes

A. Impact of Wastewater Treatment Methods

The links between sewage treatment methods and water quality are presently reducible to five general conclusions: (1) aerobic rather than anaerobic treatments result in lower median concentrations of pharmaceuticals;[31] (2) plants employing activated sludge treatment remove more pharmaceuticals than plants using a trickling filter process;[32] (3) the treatment method employed at the biological phase (sludge vs. filter) is much more important than the treatment method employed at the disinfectant stage (ultraviolet vs. chlorination);[33] (4) ultraviolet treatment at the disinfectant stage is more effective at removing caffeine, but chlorine treatment is more effective at removing steroidal compounds;[34] and (5) increasing sludge retention time from five days to ten days makes the activated sludge method more effective.[35]

Powerful as activated sludge treatment may be, there is still one glaring problem: it produces sludge. The question then becomes whether the efficiency of activated sludge in removing waste from the water is cancelled out by the production of chemically contaminated sludge? The answer is yet to come, but researchers have begun to push for a more complete evaluation of each treatment method's efficiency. This wider approach to a given method's efficiency will go beyond simply measuring the immediate benefits to water quality; it will measure the negative impacts felt elsewhere down the line.[36]

Another area being studied is the impact of storm water on the treatment process. While many used to consider it a foregone conclusion that contamination of receiving waters by untreated storm water would be offset by dilution, a recent study has shown that this is often not the case. The fact that the water bypassed treatment usually cancels any effect of dilution, making the elimination of storm water bypasses an important step in increasing the effectiveness of waste water treatment methods.[37]

Presently there are studies being done on the impact of more advanced treatment systems using newer oxidation processes (AOPs). These processes include advanced treatment techniques such as photocatalysis and nonthermal plasma treatments (NTP). Photocatalysis and NTP are treatments of interest because of their

[31] Conn, Kathleen E., et al. "Occurrence and Fate of Organic Contaminants during Onsite Wastewater Treatment." *Environmental Science & Technology* 40.23 (2006): 7358-7366.
[32] See "A Multi-Disciplinary Approach to the Removal of Emerging Contaminants in Municipal Wastewater Treatment Plants in New York State (2003-2004)," Water Environment Federation's WEFTEC 78th Annual Technical Exhibition and Conference, Conference Proceedings, Washington DC, November 2005, pages 5095-5124.
[33] Id.
[34] "The Occurrence and Fate of Pharmaceuticals, Personal Care Products and Endocrine Disrupting Compounds in a Municipal Water Use Cycle: A Case Study in the Cities of Ann Arbor, Grand Rapids, and Monroe." September 2006.
[35] See "A Multi-Disciplinary Approach to the Removal of Emerging Contaminants in Municipal Wastewater Treatment Plants in New York State (2003-2004), Water Environment Federation's WEFTEC 78th Annual Technical Exhibition and Conference, Conference Proceedings, Washington DC, November 2005, pages 5095-5124.
[36] Kinney, Chad A., et al. "Survey of Organic Wastewater Contaminants in Biosolids Destined for Land Application." *Environmental Science & Technology* 40.23 (2006): 7207-7215.
[37] Phillips, P., and A. Chalmers. "Wastewater Effluent, Combined Sewer Overflows, and Other Sources of Organic Compounds to Lake Champlain." *Journal of the American Water Resources Association* 45.1 (2009):45-57.

ability to reduce contaminants in the water without adding new chemical contaminants.[38] They also expend less energy than other treatment alternatives.[39] Some studies of the effectiveness of AOPs have also tested the impact of reverse osmosis on wastewater effluent.[40]

While the conclusions above are supported by carefully collected scientific data, researchers were often at a loss to explain differences in the levels of contaminants at different areas employing similar processes. In the face of such irreconcilable test results, researchers often reached the same conclusion: "the reason for this difference is not clear."[41] This is because each test site was unique, with its own communities, industries, water uses, methods of treatments, and a whole slew of other variables that may or may not have affected the ultimate level of water quality detected. The research summarized above is a step in the right direction, but much more research into this complex and emerging issue is needed.

B. USEPA's Regional Applied Research Effort study, which includes collaboration of the United States Geological Survey (USGS)

EPA and USGS are investigating endocrine disrupting compounds in the Metropolitan Water Reclamation District of Greater Chicago (MWRD) Calumet plant's service area as part of a joint study. This study started in 2005 and includes a suite of pollutants. There were two sampling events in 2005 and one in 2006. EPA and MWRD did discrete sampling at the plant and channel. The study also looked at mercury and PCBs. USGS is acting as a partner to help with hormone analysis and some personal care products. EPA also took samples at each treatment stage and sludge samples. They will use the samples to see if any changes occur and will set them up for more detailed samples. This will show how well the plant is removing these chemicals. EPA took samples both above the outfall and below the outfall.[42] Preliminary data suggests that the MWRD system is removing upwards of 90% of the compounds, but some chemicals are still being detected in the effluent and downstream. Publication of the report is not expected until 2010.[43]

C. North Shore Channel Study

Chicago has been involved with some research on the presence of pharmaceuticals in the effluent from sewage treatment plants undertaken by the MWRD. The MWRD laboratories do not have the sophisticated instrumentation required to detect and quantify many of the important endocrine disrupting compounds. To monitor these compounds, MWRD has worked with other agencies to help collect and evaluate data.

This study examined the effect of endocrine disrupting components on fish. Fish were analyzed in Fall 2006 and Spring 2007 for pharmaceuticals and personal care products (PPCPs). EPA collected a reference fish in the fall from Monroe Harbor and fish from Braidwood to get fish of the same sexual age. EPA then correlated the concentrations of PPCPs found in the North Shore fish with the results of a national tissue study. The larger national study was run out of Washington DC at five sites across the country, focusing on a suite of 39 compounds.[44] The other four sites were Orlando, Florida; Dallas, Texas; West Chester, Pennsylvania; and Phoenix, Arizona. Each site was chosen because of its close proximity to a wastewater treatment plant, its large percentage of elderly residents, and its slightly higher median income (indicating access to prescription drugs). Samples collected from the Gila River in New Mexico were used as a point of comparison.

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[38] Benotti, Mark J., et al. "Evaluation of a Photocatalytic Reactor Membrane Pilot System for the Removal of Pharmaceuticals and Endocrine Disrupting Compounds from Water." *Water Research* 43.6 (2009): 1513-1522.

[39] Synopsis of presentation "Innovative Advanced Oxidation Processes for the Treatment of Pharmaceuticals and EDCs" at *http://ngwa.confex.com/ngwa/pharm09/webprogram/Paper6454.html*

[40] Synopsis of presentation "Advanced Oxidation Processes and Reverse Osmosis Treatment of Pharmaceutical in a Municipal Watewater-Treatment-Plant Effluent at *http://ngwa.confex.com/ngwa/pharm09/webprogram/Paper6416.html*

[41] See "A Multi-Disciplinary Approach to the Removal of Emerging Contaminants in Municipal Wastewater Treatment Plants in New York State (2003-2004)," Water Environment Federation's WEFTEC 78th Annual Technical Exhibition and Conference, Conference Proceedings, Washington DC, November 2005, page 5104.

[42] Call with Todd Nettesheim, EPA Region 5, Nov. 6, 2007.

[43] Call with Todd Nettesheim, March 2, 2010.

[44] Calls with Todd Nettesheim, Feb. 13, 2008 & Mar. 2, 2010; Alejandro J. Ramirez et al., "Occurrence of pharmaceuticals and personal care products in fish: Results of a national pilot study in the United States." *Environmental Toxicology and Chemistry*, 28.12 (2009): 2587-2597, online at: *http://www3.interscience.wiley.com/cgi-bin/fulltext/123234144/PDFSTART*

The researchers followed uniform procedures at each site: first, harvest 18-24 individual fish of similar size; second, blend the flesh of each fish into a composite sample using a high speed blender; and third, apply liquid mass chromatography-tandem mass spectrometry to detect the presence of pharmaceutical compounds and personal care products. The same was done separately for each fish liver.

The researchers tested Largemouth Bass from Chicago, Bowfin from Orlando, White Suckers from West Chester, Carp from Phoenix, Smallmouth Buffalo from Dallas, and Sonora Suckers from New Mexico.

Of the twenty-four pharmaceutical compounds targeted by the pilot test, only seven were found among the samples. Only two of the twelve personal care products targeted were detected.

Six of the pharmaceutical compounds targeted by the study were detected in the flesh and/or liver samples taken from the North Shore Channel. Three different antidepressants (fluoxetine, norfluoxetine, sertraline) were detected in amounts generally higher in Chicago than all other testing sites but West Chester. One type of antihistamine (diphenhydramine) was detected at levels higher than Dallas or Orlando. One type of anti-hypertension medication (diltiazem) was detected, the mean higher in Chicago than all other sites but West Chester. Finally, one anti-seizure medication (carbamazepine) showed up in the Chicago samples, but failed to appear in any others.

Both of the personal care products (the synthetic fragrances glaxolide and tonalide) detected among the samples were present in the flesh samples taken from the North Shore Channel. As for the fragrances galaxolide and tonalide, Chicago's galaxolide levels were higher than those detected at Dallas and Orlando. Its tonalide levels were higher than Dallas, Orlando, and West Chester.

While concentrations of pharmaceutical compounds and beauty products are generally higher in Chicago than at other testing sites, it is important to note the mitigating effects of advanced wastewater treatment facilities at other test sites. The two cities with low or undetectable levels — Dallas and Orlando — both employ more advanced waste treatment techniques. For example, both use tertiary treatment technologies that give them one final shot via the use of wetlands or filtration to reduce the levels of contaminants in the effluent. Given that there was no discernible relationship between the levels detected and the age, income, and population of the testing site, it may be that Chicago only lags behind for lack of better treatment facilities.

D. Milwaukee Metropolitan Sewerage District

Milwaukee's sewer authority has not done any testing of its effluent for pharmaceuticals due to the expense and uncertainty of which parameters to test.[45]

[45] Call with Sharon Mertens, Milwaukee Metropolitan Sewerage District.

Photo: Jim Palmer

IV. Research on pharmaceuticals at drinking water intakes in Great Lakes

A. Illinois

Illinois EPA Bureau of Water (Division of Public Water Supplies) staff collected samples of raw and finished drinking water that were analyzed for the presence of pharmaceuticals, in order to evaluate whether detectable amounts are present in sufficient concentration to cause adverse human health effects.[46] Samples were collected starting March 24 and continued through March 27, 2008.

This study identified 16 pharmaceutical chemicals in the untreated or potable water of five public water supplies in Illinois. For Chicago, four pharmaceuticals were detected: cotinine, monensin, nicotine, and gemfibrozil. The report noted that the Chicago sample of raw water suggests that Lake Michigan is a relatively clean source of drinking water, with less total numbers of pharmaceutical chemicals detected (4 chemicals) in comparison with the supplies drawing from river sources (9-14 chemicals).

In consultation with Illinois Department of Public Health (IDPH) toxicologists and other health professionals, the Agency developed screening levels for these pharmaceuticals using a conservative risk assessment approach in an attempt to quantify the public health risk from the detected pharmaceuticals. This approach drew heavily on the procedures used in the Australian Guidelines for Water Recycling (2008) to develop Drinking Water Guidelines to be applied to recycled wastewaters in Australia. The results for the potable water samples were compared against conservative screening levels developed by Agency and IDPH toxicologists, IDPH decided that the levels found did not present a public health hazard at this time.

The report also concluded that agricultural sources may be important contributors to the load of pharmaceuticals in the source water of river water supplies. Several drugs that are primarily or exclusively used in agricultural or veterinary treatments (lincomycin, monensin, sulfadimethoxine, and sulfamethazine) were detected in the river samples.

Finally, the report concluded that routine water treatments are capable of reducing or eliminating the levels of some of the pollutants found in the raw water while other chemicals are only minimally reduced.

The report recommended additional research for two main reasons. First, because the sample collection was done when the rivers involved were at high flow levels, dilution likely contributed to an underestimate of the levels of the pharmaceuticals that might be present in the water at low flow levels. Second, the analytical methods used were not capable of detecting some chemicals/chemical families that have been identified as potential problems because of high use, high levels found in some studies, and/or high toxicity (e.g. codeine, diazepam (Valium), ranitidine (Zantac), chemotherapy drugs cyclophosphamide and isophosphamide, and estrogenic hormones 17 beta-estradiol and 17 alpha-ethinyl estradiol).

[46] Report on "Pharmaceuticals and Personal Care Products in Illinois Drinking Water," Bureau of Water, Illinois EPA (June 2008) available online at: http://www.epa.state.il.us/water/pharmaceuticals-in-drinking-water.pdf

In addition to the Illinois report, Lake County tested their drinking water intake. Their testing in March 2008 found two compounds in the intake from Lake Michigan—DEET and Gemfibrozil.[47] DEET was detected at 6 parts-per-trillion and Gemfibrozil was detected at 8.9 parts-per-trillion. Lake County reported that they did not detect these two compounds in their drinking water after their treatment process.

B. Milwaukee

The Milwaukee Water Works was one of the first utilities in the U.S. to test for endocrine disrupting compounds (2003) and pharmaceuticals and personal care products (2006) in its source water and drinking water. Milwaukee has found small amounts of cotinine (2 ppt) and gemfibrozil (6 ppt) in its Lake Michigan drinking water supply. Continine was also found (2 ppt) in the finished drinking water. The 2008 test results are posted on their web site.[48]

C. Erie, Pennsylvania

Drinking water tests by Erie Water Works in June and July 2008 detected ibuprofen, a common painkiller, at 2.5 ppt; gemfibrozil, a cholesterol-lowering drug, about 2.5 ppt; carbamazepine, an anticonvulsant, 2 ppt; caffeine at 21 and 60 ppt and continine, a nicotine derivative, at 4 ppt and 7.6 ppt.[49] Found in the raw water supply — but not detectable in the treated water — were trace amounts of lincomycin, an antibiotic; sulfadimenthoxine, an animal antibiotic; estrone, a hormone; sulfamethoxazole, an antibiotic; and 4-methylphenol, a household cleaner and disinfectant.

D. The Michigan Case Study: Ann Arbor, Grand Rapids, and Monroe

A 2006 study in Michigan investigated the presence of pharmaceuticals, personal care products, and endocrine disrupting compounds in the municipal water supplies of Ann Arbor, Grand Rapids, and Monroe. Ann Arbor's source water is from the Huron River, Grand Rapids depends on Lake Michigan, and Monroe draws from Lake Erie. The study took samples at three different phases of the water's use cycle: (1) as source water, (2) drinking water, (3) and as influent/effluent wastewater. Depending on which of the twenty-two targeted chemicals the researchers were testing for, they used a combination of gas chromatography, mass spectrometry, and liquid chromatography.

The source water of Ann Arbor contained seventeen of the targeted chemicals, with ten remaining at detectable levels post treatment. In Grand Rapids, the source water flowed into the treatment facility with eighteen, but left containing nine. And in Monroe, the source water had seventeen going in but only seven flowing out.

While each waste treatment plant had its strengths and weaknesses, no single decrease in a contaminant could be "correlated to a particular treatment process since individual components of the process were not analyzed."[50] That said, the researchers were able to make the following important conclusions: (1) chlorine was the most effective treatment option against steroidal compounds, and (2) UV disinfection was the most effective treatment for removing caffeine.

It is important to note that the twenty-two chemicals targeted are only a small portion of the pharmaceuticals most likely present in the source waters of all three cities.

E. Other

A national USGS study of source water intakes examined water samples taken in 2001 from untreated sources of drinking water at 25 ground-water and 49 surface-water sites in 25 states and Puerto Rico. This study found that the most frequently detected chemicals in surface water were cotinine (nicotine metabolite), and 1,7-dimethylxanthine (caffeine metabolite). Detections of pharmaceutical pollutants were more common

[47] See Central Lake County Joint Action Water Agency Report, "Pharmaceutically Active Compounds in Untreated Lake Michigan Water," April 2008.
[48] MMSD source water quality information is at *http://water.mpw.net/files/LakeMichiganTestsReport.pdf*
[49] Miller, George, "Pharmaceuticals found in Erie's drinking water" Dec. 1, 2008, Erie Times News. Online at: *http://www.goerie.com/apps/pbcs.dll/article?AID=/20081201/NEWS02/312019963/-1/ETN*
[50] The Occurrence and Fate of Pharmaceuticals, Personal Care Products and Endocrine Disrupting Compounds in a Municipal Water Use Cycle: A Case Study in the Cities of Ann Arbor, Grand Rapids, and Monroe. September 2006.

in water collected from surface-water sites than from ground-water sites. Sixty percent of the 36 pharmaceuticals (including prescription drugs and antibiotics) analyzed were not detected in any water sample. The maximum concentrations of the measured chemicals were only slightly above detection levels. Mixtures of chemicals were common. Pharmaceuticals, including antibiotics and prescription and non-prescription drugs, generally were detected less frequently in sources of drinking water than they were in the national stream reconnaissance.

V. Existing policy

A. Regulatory regime governing intakes and outputs of contaminated water

The federal government has established regulatory standards on over 100 chemical and microbial contaminants in drinking water through the Safe Drinking Water Act (SDWA), which governs public water systems. Many states have established their own standards, which must be at least as stringent as the federal standards. In general, drinking water standards have not been set for pharmaceutical pollutants.

The U.S. EPA evaluates the need for new drinking water contaminant regulations through a program called the Contaminant Candidate List (CCL) which periodically identifies and lists contaminants that may be present in public water supplies and may adversely impact public health. Occurrence and health effects information for substances on this list are carefully evaluated to determine whether federal regulations are needed. Because of the extremely low concentration levels of detected pharmaceuticals in water and the lack of indication for human health impacts, these substances were generally not listed for regulatory consideration until very recently.

In September 2009, EPA announced that it would add ten new pharmaceutical-related chemicals to the CCL because the contaminants are known or anticipated to occur in public water systems and may require regulation.[51] These new chemicals include one antibiotic (erythromycin) and nine hormones (17 alpha-estradiol, 17 beta-estradiol, equilenin, equilin, estriol, estrone, ethinyl estradiol, mestranol, and norethindrone).[52] Uses of these hormones include hormone replacement therapy and birth control pills. EPA's current schedule is to continue to gather information and evaluate contaminants it has identified on the CCL to make a regulatory determination for at least five new contaminants by 2013. The Agency will also continue to refine the CCL process and gather more data to identify contaminants for the next CCL by 2014.

Wastewater treatment plants are designed to remove conventional pollutants such as suspended solids and easily biodegradable organic material, not other pollutants such as pharmaceuticals. Sewage treatment plants are regulated under the Clean Water Act (CWA) National Pollutant Discharge Elimination System program and similar state laws and generally are not required to monitor for pharmaceutical pollutants.

The CWA also requires EPA to promulgate regulations that restrict discharge of wastewater indirectly through sewers to publicly owned treatment works (POTWs). Industrial users of POTWs must comply with CWA pretreatment standards before introducing pollutants into a POTW. These pretreatment standards must control pollutants that may pass through or interfere with POTW treatment processes or contaminate sewage sludge. Such standards could be interpreted to prevent disposal of pharmaceuticals from industrial sources into the public sewer system, due to the potential that they would pass through treatment. However, most

[51] 74 Fed. Reg. 51850-62 (Oct. 8, 2009), available online at: *http://www.epa.gov/fedrgstr/EPA-WATER/2009/October/Day-08/w24287.pdf*
[52] Id. at 51855.

POTWs have not aggressively enforced these standards against industrial users who may dispose of unused or expired pharmaceuticals.

B. Legal issues that hamper disposal efforts

1. Federal controlled substance laws

Strict application of the federal controlled substance laws prevent acceptance of controlled substances from end-users who would like to dispose of unused and expired medications. The federal controlled substance laws and regulations were not created with pharmaceutical take-back programs in mind. There are hundreds of different medications covered by the controlled substance laws and end-users typically do not know whether their medication is regulated as a "controlled substance." Under the current DEA interpretation of the law, only law enforcement officers can be authorized to accept controlled substances. Law enforcement officers that do accept such controlled substances must carefully follow procedures to ensure destruction.

The goal of the Controlled Substances Act (CSA) and Drug Enforcement Agency's (DEA) regulations[53] collective goal is to provide a closed distribution system so that a controlled substance is at all times under the legal control of a person registered, or specifically exempted from registration, by the DEA until it reaches the ultimate user or is destroyed. When a controlled substance has become outdated or otherwise unusable, the registrant who possesses the substance must dispose of it in a method approved of by the DEA. There are three primary disposal methods for controlled substances which the DEA approves.

The first method is a distributor or dispenser of controlled substances can return the controlled substances to the pharmaceutical manufacturer who, as a service to its customers, may accept returns of outdated or damaged controlled substances. Distributors, dispensers, and manufacturers must all be registered with the DEA.

Second, the distributor, dispenser, or manufacturer can itself dispose of the controlled substances under the procedures outlined in 21 CFR 1307.21. Under 21 CFR 1307.21, any person may request permission to dispose of controlled substances without the benefit of a DEA or State witness. In the majority of cases, blanket permission for disposal of controlled substances is granted to registrants who have an ongoing need to dispose of unwanted controlled substances. Thus, pharmacists wishing to dispose of unwanted controlled substances may contact the DEA for blanket permission if they need to consistently dispose of controlled substances. Pharmacists seeking permission must receive the DEA's authorization for the disposal in writing. The DEA may require that a set schedule be established for any disposals done by registrants. Registrants may also be granted disposal authority on a case-by-case basis. It is typical for the DEA to require that the registrant provide two designated responsible individuals to accompany the drugs to the disposal site and witness the destruction; this process achieves the DEA's goal of ensuring the controlled substances are rendered non-recoverable for future use. Disposal under the authority of 21 CFR 1307.21 maintains the closed distribution system because the controlled substances remain under the legal control of a registrant at all times.

Third, the distributor, dispenser, or manufacturer can distribute the controlled substances to a reverse distributor to take control of the controlled substances for the purpose of returning them to the manufacturer or, if necessary, disposing of them. For several years the DEA opposed granting DEA registrations to firms engaged in the disposal of controlled substances because they were not considered an essential link in the closed distribution system that the Controlled Substances Act established to control the flow of drugs from the manufacturer to the ultimate user. In recent years, however, increasingly stringent requirements imposed by the U.S. Environmental Protection Agency (EPA) resulted in fewer and fewer approved disposal facilities. As a result, a new type of business developed called a "reverse distributor or returns processors" which is a middle man service that developed to collect controlled substances from registrants and either return them to the manufacturer or arrange for their disposal. The DEA requires that "reverse distributors or return processors" must comply with all requirements under 21 CFR 11, parts 1300-1316.

[53] These DEA regulations are found in Title 21, Code of Federal Regulations (CFR), parts 1300-1316

Currently, DEA regulations do not allow for consumers to return controlled substances, except for delivery to law enforcement.[54] DEA regulations also require that individual pills/containers of controlled substances must be counted and recorded.[55] A DEA waiver/license is needed to send controlled substances for hazardous waste disposal based on DEA requirements that hazardous substances can only be transferred between licensed registrants.[56]

2. RCRA regulations

Currently, certain chemicals found in pharmaceuticals caused them to be classified as hazardous waste under the Resource Conservation and Recovery Act (RCRA), requiring special handling and transportation. In December 2008, the Environmental Protection Agency (EPA) published a proposed rule to reclassify waste pharmaceuticals as "universal waste." If finalized, the new classification of these materials as Universal Waste would make it more feasible for hospitals, pharmacies, and other organizations and businesses to dispose of waste pharmaceuticals. Individual states that list pharmaceuticals as hazardous waste under state law would also need to adopt the Universal Waste provisions. This provides another opportunity for action.

3. State requirements

If a pharmacy conducts a take back program for non-controlled substances their efforts may be complicated by both state and federal pedigree laws. Section 503(e)(1)(A) of the Federal Food, Drug, and Cosmetic Act establishes the pedigree requirement for prescription drugs. By definition, "a drug pedigree is a statement of origin that identifies each prior sale, purchase, or trade of a drug, including the dates of those transactions and the names and addresses of all parties to them." In 1987, the Federal Prescription Drug Marketing Act of 1987 (PDMA), was signed into law mandating that that no person or entity may engage in the wholesale distribution of human prescription drugs in any state unless the person or entity is licensed by that state in accordance with federally prescribed minimum guidelines issued by United States Food and Drug Administration (FDA) regulations.[57]

Illinois pedigree law is called the Whole Sale Distribution Licensing Act.[58] This law exempts "drug returns when conducted by a hospital, health care entity, or charitable institution in accordance with federal regulation."[59]

Illinois also recently signed a new law, the "Safe Pharmaceutical Disposal Act," which prohibits health care institutions from flushing unused medications.[60]

[54] See 21 USC § 802 (definition of "distribute" means to deliver to a federal or state authorized licensed registrant) and 21 CFR 1301.24.
[55] 21 USC § 827(a)(1).
[56] See 21 USC § 802.
[57] The PDMA amended several sections of the Federal Food, Drug, and Cosmetic Act, codified at 21 U.S.C. Sec. 321 et seq.
[58] 225 ICLS 120.
[59] 225 ICLS 120/15(4).
[60] Illinois Public Act 96-221, online at *http://www.ilga.gov/legislation/publicacts/fulltext.asp?Name=096-0221*

VI. Source reduction measures

A wide array of changes to pharmaceutical manufacturing, distribution, prescribing, consumption and disposal have been proposed for reducing the introduction of pharmaceuticals into the environment at the source of the problem.

A. Manufacturers

One method for source reduction is creating new drugs that degrade in the environment, as well as to revisit old drugs unintentionally made that way.[61] This idea of "Sustainable Pharmacy" was addressed at the first International Conference on Sustainable Pharmacy held in Osnabrück, Germany in April 2008.[62]

Some drug characteristics, such as photodegradability, could be harnessed during wastewater treatment. Some drugs that have been on the market for 40 years are "very biodegradable," such as valproic acid, notes Klaus Kümmerer, a professor in the department of environmental health sciences of the University Medical Center Freiburg, Germany. This antiepileptic drug may have a toxic effect in humans at low concentrations, but it is easily degraded.

An example of this technique is a new product now scheduled for animal and human drug trials that is similar to an older version of a birth control pill from drugmaker Schering-Plough. This drug uses natural estrogens paired with a biodegradable progesterone. 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.

A 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).[63] Classification is made of both the medication's inherent ability to affect the environment (environmental hazard) and the environmental risk posed by the pharmaceutical substances. The risk assessments rate substances based on the probability that they will cause adverse effects. The database rates pharmaceutical substances in terms of their toxicity, persistence, and bioaccumulation potential based on data given by pharmaceutical manufacturers.

The environmental hazard assessment was initiated in 2003 by Stockholm's County Council's environmental department and is based on data from pharmaceutical manufacturers. During 2005 the classification was extended to also cover an environmental risk assessment carried out by the Swedish Association of the Pharmaceutical Industry; these assessments are to include all medications by 2010.

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. MistraPharma will use an approach that considers all 1200 Active

[61] Lubick, Naomi. "Opening the 'Green Pharmacy'." *Environmental Science & Technology* 42.23 (2008): 8620-8621.
[62] See Conference registration brochure at: http://www.dbu.de/media/041207025458f128.pdf
[63] JanusInfo information is available online at: http://www.janusinfo.se/imcms/servlet/GetDoc?meta_id=7236

Pharmaceutical Ingredients (APIs) currently available on the Swedish market. For the 30 highest ranked APIs, MistraPharma will evaluate the present loading of APIs and the discharge of these compounds from the different types of Swedish wastewater treatment plants. This evaluation will form the basis for defining, evaluating and development of promising methods for removal of APIs through wastewater treatment.

The EU is moving closer to evaluating drugs' environmental impacts before they enter the treatment system or the environment. Relatively new guidelines from the EU's European Medicines Agency (EMEA) require European companies to consider environmental impacts and provide data, however, environmental impact alone will not prevent approval of a drug.

B. Physicians and Health Care workers

Several measures have been suggested for health care workers to reduce pharmaceutical pollution. The Practicegreenhealth.org website provides an excellent summary of these steps.[64] Potential source reduction measures include: changes to purchasing policy systems, using already opened chemotherapy vials, implementing samples policy, labeling drugs for home use, adjusting packaging sizes to use and patient dosage, and improving inventory policies to minimize expired drugs.

In June 2008, U.S. Environmental Protection Agency's mid-Atlantic region and excelleRx, Inc. co-convened a summit which brought together 60 representatives from government agencies and private companies in Delaware, New Jersey and Pennsylvania to discuss different ways to approach pharmaceutical waste. There was interest after that meeting in pursuing both disposal options and reducing the quantity of pharmaceutical waste.

Following the mid-Atlantic summit meeting, the Philadelphia Partnership for Pharmaceutical Pollution Prevention (P5) is conducting semi-structured, one-on-one phone interviews of up to 32 individuals under supervision of the Institutional Review Board (IRB) at the University of the Sciences of Philadelphia. The interview questions have been vetted with representatives of the stakeholder groups to be interviewed and reviewed nine times.

These interviews will target four general stakeholder groups: Healthcare practitioners (nurse practitioners, doctors, physicians' assistants), Pharmacists, Insurers, and Consumer advocacy organizations (union groups, AARP). The purpose of the research is to develop and distribute educational modules to use with different constituents and to develop quantitative research techniques that could be used nationwide. The Alliance is exploring how to include Great Lakes regional information in this study, possibly by replicating the Philadelphia survey in the Chicago area.

C. Pharmacists and Consumer Over-the-Counter Purchasing

Practice Greenhealth has suggested several source reduction methods for Pharmacists and consumers.[65] These methods include standardization of naming conventions and substitution of natural alternative medicines. Practice Greenhealth contends that similar looking names, similar-sounding names, similar looking pills, and similar looking packaging contributes to confusion and errors from the consumer as well as for healthcare practitioners. The similarity has direct bearing on the possible overconsumption of drugs and their unnecessary release to the environment.

Natural alternatives can be used in place of possibly unnecessary use of certain medications for treating symptoms that can be frequently controlled simply by proven nutritional measures. One example is the growing medication of young children and teens to treat symptoms of depression and obsessive compulsive disorder. Rather than prescribing medication, natural alternatives such as omega-3 food oils and dietary changes might be used in some cases.

[64] Greenhealth, Practice. "Managing Pharmaceutical Waste: A Ten-Step Blueprint for Healthcare Facilities in the United States." Revised August, 2008: 93.
[65] Christian G. Daughton, Ph.D. "Environmental Stewardship of Pharmaceuticals: The Green Pharmacy." In the Proceedings of the 3rd International Conference on Pharmaceuticals and Endocrine Disrupting Chemicals in Water. Minneapolis, MN: National Ground Water Association, March 2003. 11.

Photo: M. Lansing

VII. Areas where additional research is needed and legislative changes

A. Research Needed

1. Research is needed to determine whether the Centers for Medicare/Medicaid Services and other third party payers can develop tactics for reducing the quantity of waste pharmaceuticals through changes to reimbursement practices or otherwise.

2. Further research is needed to determine whether changes in sample distribution systems or trial prescriptions can make a significant reduction in the amount of waste pharmaceuticals.

3. More research is needed on the effects of combinations of pharmaceuticals in very low dosages on human health.

4. Research is needed to quantify the amount of pharmaceutical pollution contributed through excretion compared with other sources. If research confirms that excretion is responsible for most pharmaceutical pollution in our nation's waters, then source reduction methods become even more important.

5. Manufacturers must continue their research efforts to improve drug development to reduce the toxicity of pharmaceuticals and to minimize waste products created during pharmaceutical use.

6. Industry believes that more data is needed to determine the percentage of medicine that goes unused, the concentration of pharmaceuticals in landfill leachate, participation levels in take back programs and an overall assessment of the environmental impact of takeback and disposal options.[66]

7. Research into effective treatment technologies in sewage plants for pharmaceutical pollutants.

B. Legislative Changes

In September 2009, the Alliance endorsed recommended changes to the federal Controlled Substances Act developed through the Product Stewardship Institute nationwide stakeholder dialogue process.[67] These recommended improvements seek changes along the following guidelines: (1) the broadest possible range of people should be able to access new options created for the secure collection of controlled substances; (2) multiple collection and disposal options should be available to those designing and implementing drug take-back programs; (3) collection efforts should be able to accommodate all pharmaceutical drugs (both controlled substances and other drugs); (4) collection and disposal options should not require law enforcement

[66] See Finan, Douglas, presentation at Dec. 2-3, 2008 PSI national dialogue.

[67] See "Input on Federal Legislation to Amend Statutes Related to Safe Drug Disposal, Product Stewardship Institute Regulations Workgroup," September 14, 2009, available online at: *http://productstewardship.us/associations/6596/files/PSI%20Input%20on%20Amending%20Federal%20Statutes%20Final%20w%20Endorsement%20List.pdf*

for normal operations; (5) no additional enabling legislation at the state or local levels should be needed; (6) federal law should not mandate that drugs collected for disposal be inventoried and (7) new regulations developed under an amended Controlled Substances Act should be developed in consultation with the Environmental Protection Agency (EPA).

The Alliance is also exploring other policy changes such as the following:

1. Pharmaceutical manufacturers could be required to include toxicity information on drugs they produce similar to the Swedish requirements.

2. FDA can improve their drug approval process by requiring manufacturers to provide more information on the toxicity of pharmaceutical waste products and potential issues from combinations with other waste pharmaceuticals.

3. The FDA drug approval process could require a life-cycle analysis at the time a drug is approved and also require a closer look at end-of-cycle waste management.

Photo: GLERL, M. McCormick

VIII. Conclusion

Recent testing of Lake Michigan water near the water intake pipes for such major metropolitan centers as Chicago and Milwaukee has found low levels of pharmaceutical compounds, including cotinine, a nicotine byproduct, and the cholesterol-modifying drug gemfibrozil.

Awareness of the presence of these and other drug-related pollutants in U.S. waters dates back to the 1970s, but their prevalence in our drinking water has come to light as water quality monitoring technology has grown better at detecting lower and lower contaminant levels.

The low levels of these compounds and the limited scientific research available to date has led most experts to determine the water is safe to drink. Yet the rapidly expanding use of pharmaceuticals, coupled with the growing knowledge of the potential health risks these insidious chemicals pose to people and wildlife, make pharmaceutical pollution in the Great Lakes an urgent and emerging concern for the Alliance.

The Alliance's past efforts to reduce pharmaceutical pollution have mirrored those of the federal government's, emphasis on the collection and safe disposal of unneeded and unwanted medications. In light of the growing number of over-the-counter and prescription drugs circulating within the population and our environment, the Alliance is now taking the more aggressive approach of seeking to curb drug pollution at its source: the design and prescription stages. Already many opportunities exist at the design stage to reduce the environmental risks posed by pharmaceuticals, and improving health care practices may reduce the amount of waste from existing drugs as well as new drugs.

The Alliance also supports further research into the dangers these drugs pose once released into the environment, specifically how combinations of pharmaceuticals in very low dosages can affect human health. Finally, the Alliance calls for additional research into how effective sewage treatment systems are at removing pharmaceutical compounds as most treatment plants are ill-suited to address this form of pollution.

ALLIANCE FOR THE GREAT LAKES

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About Alliance for the Great Lakes

Alliance for the Great Lakes serves as the voice of the 40 million people who rely on Great Lakes water for drinking, recreation and commerce. Formed in 1970, it is the oldest independent Great Lakes protection organization in North America. Its mission is to conserve and restore the world's largest freshwater resource using policy, education and local efforts, ensuring a healthy Great Lakes and clean water for generations of people and wildlife. Its headquarters are in Chicago, with offices in Cleveland, Grand Haven, and Milwaukee.

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