Statement

PhRMA

Statement at the Senate Environment and Public Works Committee
Subcommittee on Transportation Safety, Infrastructure Security, and Water Quality
Pharmaceuticals in the Nation's Drinking Water:
assessing potential risks and actions to address the issue

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Alan Goldhammer, PhD
Deputy Vice President, Regulatory Affairs
Pharmaceutical Research and Manufacturers of America

Thank you Mr. Chairman and members of the Committee. My name is Alan Goldhammer, Ph.D., and I am the Deputy Vice President for Regulatory Affairs at the Pharmaceutical Research and Manufacturers of America (PhRMA), a trade association representing the leading research-based pharmaceutical and biotechnology companies. PhRMA member companies invested an estimated $44.5 billion in 2007 for innovative biomedical research to discover and develop new medicines that meet medical needs.

It is not a new development that drinking water may contain trace levels of pharmaceuticals as well as other household chemicals. What is new is that we now have more sensitive analytical methods to detect these substances at very low levels.

Reports of the presence of trace levels of pharmaceuticals in the water sparked the creation of a Pharmaceuticals in the Environment (PIE) Task Force within PhRMA in the late 1990s. The PIE Task Force is familiar with essentially all of the reports published worldwide of pharmaceuticals in water sources, including testing conducted by the U.S. Geological Survey (USGS), routine municipal water testing, testing by scientists from Europe to Asia, and even high school science students whose projects were on display in school science fairs.

PhRMA and its member companies advocate the safe and effective use of medicines and support the principles of product stewardship. As such, we are committed to applying the same level of scientific rigor to studying pharmaceuticals in the environment (PIE) as we apply to other areas of our business. PhRMA and its member companies have conducted research on a variety of PIE-related issues, including: 1) evaluating if detectable levels of pharmaceuticals in drinking water pose a risk to human health, 2) evaluating methods for the effective disposal of human medicines, and 3) determining the potential effects of human pharmaceuticals and their metabolites in surface waters on aquatic life. This research led to the publication of several research reports. We also continue to have an open dialogue with federal and state government officials and other stakeholders about the scientific findings. My testimony today will focus on the detection of trace amounts of pharmaceuticals, the potential human and environmental impacts, and how collectively we can minimize pharmaceuticals in the environment by proper disposal of unused medicines.

Where do these compounds come from?

Pharmaceuticals are found in the environment primarily because trace amounts of medicines

pass through the human body without being metabolized completely and make their way to surface waters through the municipal wastewater treatment system. These pharmaceuticals along with many other consumer products and household cleaning agents find their way into the wastewater from all households where there are family members who take medicines.

It is important for all of us to recognize that the concentrations of pharmaceuticals in the environment are extremely low. In fact, we probably would not be here today were it not for the development of improved analytical testing technology that has made it possible to detect trace amounts of consumer chemicals, including pharmaceuticals, in surface waters. The concentrations of pharmaceuticals reported in U.S. drinking waters are generally at trace levels of nanograms per liter (ng/l) or part-per-trillion (ppt). To put this in context, one ppt is about one second in 32,000 years or 1 penny in $10 billion. On average, those pharmaceuticals detected in U.S. drinking water are present at only 18 ppt.

It is not currently possible to prevent medicines from entering sewage. Wastewater treatment plants are designed to mimic the natural biodegradation processes that occur when organic compounds enter the environment. These systems are designed to reduce, but not eliminate, pollutants present in domestic wastewater. Therefore, a majority of the compounds used in households are expected to be present at trace levels in the discharges from wastewater treatment plants.

There are other minor sources for pharmaceuticals in the environment. Unused medicines can contribute to pharmaceuticals found in surface waters if they are flushed down toilets or poured down sinks. Recent Federal guidance on disposal recommends that medicines be disposed of in household trash or alternatively taken to local collection programs that accept unused medicine.

Is there an effect on human health?

Many technical experts have contributed to the on-going scientific discussions about pharmaceuticals in the environment. The studies conducted to date suggest that it is highly unlikely that the very small quantities of even potent pharmaceuticals detected in the environment would be harmful to human health. Dietary exposure to hormones such as the estrogen that naturally occurs in milk and soy products is much higher than exposure to residues of any estrogen-like pharmaceutical in water. Trace levels of antibiotics found in surface waters are far below the concentrations necessary to develop antibiotic resistance in microbes. In summary, there appears to be no demonstrable risk to human health from detected concentrations of pharmaceuticals in surface waters.

Active pharmaceutical ingredients (APIs) are the most thoroughly studied substances in the world for their effects on human health. Billions of dollars are spent every year to discover and evaluate the efficacy and safety of new pharmaceuticals that can combat the effects of human diseases. Government agencies such as the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMEA) have rigorous regulations that guide the collection and evaluation of information required to support the safety and efficacy of new pharmaceutical compounds. The FDA creates summaries of its evaluations of new APIs and makes them available to the public when the molecule is approved for use as a new medicine in the U.S.

Acceptable use of an API in patients is judged by comparing the benefits from therapy with the risk of potential side effects. Approval of a new API routinely requires testing the efficacy and safety of the molecule in animal studies and directly in human clinical studies. Depending on the targeted use of an API, this testing normally includes evaluation of the molecule for properties of therapeutic efficacy, of acute, chronic and reproductive toxicity, and of genotoxicity and carcinogenicity. Additional evaluations of therapeutic efficacy and side effects are determined for patients in clinical settings. In order to understand systemic exposure from administration of an API, animal and human studies are conducted to measure the time course of absorption into the body, distribution into the blood and throughout the body, metabolism by organs and tissues, and excretion of the molecule and its metabolites via the liver and kidney into feces and urine. APIs and the metabolites eliminated from humans are piped to sewage treatment systems and then to surface waters. Detection of these chemicals has raised questions among some scientists about their safety to humans who might be exposed through drinking water.

Questions about the safety of drinking water have been addressed over several years by authors from the pharmaceutical industry, academia, government and the non-government sector. To date, no published investigation has found that exposure to these detectable residues creates a demonstrable risk to human health. A report for the Drinking Water Inspectorate of the United Kingdom concluded that even worst-case exposure for most major pharmaceuticals provided a high margin of safety.[1] Similarly, a study of human health risk assessments for 26 pharmaceuticals representing 14 general classes found in U.S. waters by the USGS was carried out.[2,3] The safety of drinking water and fish consumption was conducted using methods equivalent to those used by the U.S. Environmental Protection Agency (U.S. EPA) for drinking water under worst-case exposure conditions. The evaluation demonstrated that those detectable residues of pharmaceuticals in surface waters, and concentrations modeled under worst-case conditions, were safe and presented no demonstrable risk to human health.

An evaluation of the safety of drinking water in Germany concluded that risk is likely to be low from exposure to trace levels of pharmaceutical residues.[4] Another study evaluating the safety of potential residues of representative anti-cancer, lipid-regulating, anti-inflammatory, or analgesic drugs in drinking water found no demonstrable risk to human health.[5] A scientific paper published about a decade ago concluded that there was negligible human health risk from environmental exposure to an antibiotic that can be an allergen (phenoxymethylpenicillin), a potent estrogen agonist (17-alpha ethinylestradiol) or an anti-cancer drug (cyclophosphamide).[6]

For some perspective, researchers calculated that more than 90% of the 64 pharmaceuticals they evaluated would have a safety margin of at least 150,000 to reach a single therapeutic dose from water.[7] Put another way, over a 70-year lifetime, less than 20 percent of a single therapeutic dose would be ingested in drinking water. All of the APIs that they evaluated had a safety margin of 1000 or more to reach a single therapeutic dose from water. These safety margins should not be a surprise even for potent pharmaceuticals, since total use and excretion by patients are lower with higher potency pharmaceuticals.

Even though questions about the safety of detectable residues of pharmaceuticals in surface waters to human health have been evaluated in published articles for at least a decade, there are still understandable questions raised by the public about the possible impacts from the

presence of these molecules. PhRMA and its member companies are committed to working with experts to openly consider and help answer these questions.

What is the Potential Impact on Aquatic Life?

PhRMA believes that environmental impacts are already addressed through current regulations. The FDA requires an environmental assessment (EA) as part of the drug registration process in order to evaluate the potential for impacts to the environment (wildlife) as a result of patient use of a pharmaceutical. Substances that may enter the environment at less than 1 part per billion are typically excluded, although the FDA can require an EA for these substances based on extraordinary circumstances. Data on environmental fate (i.e., biodegradation, photolysis), transport (i.e., sorption, solubility), and potential effects (i.e., algae, invertebrates, fish) may be developed and submitted as part of the EA or as part of the drug registration process in other countries. The core finding of an EA is the relationship between the Predicted Exposure Concentration (PEC) and the Predicted No Effect Concentration (PNEC).

The presence of pharmaceuticals in surface waters has captured the attention of scientists, some of whom have speculated that the potential might exist for pharmaceuticals to impact wildlife. However, the scientific community and published literature believe that pharmaceuticals will not result in short term (acute) toxicity. This consensus is based on the documented low concentration of pharmaceuticals in the environment and a substantial quantity of acute toxicity data. PhRMA supports this view.

The results of acute and chronic toxicity testing demonstrate that a significant majority of pharmaceuticals do not present a significant risk from chronic exposure to the concentrations that exist in the environment (i.e., the PEC is well below the PNEC). Some compounds may, however, present extraordinary circumstances based on their potency or exposure scenarios. Compounds such as hormones are being investigated to determine whether extraordinary circumstances are warranted.

In a recent report the Associated Press (AP) claimed that “Drugs in Water Hurt Fish and Wildlife.” This claim pointed to the potential for some of these situations to be considered extraordinary. Although the AP did not reference specific scientific reports that were the basis of these claims, most of the evidence cited by AP appears to be already known to scientists. In some cases, AP mentions preliminary results from ongoing studies. Without peer review or the ability to examine the methodology used and data produced from these studies, it is impossible to evaluate the science and validity of the AP claims.

The mere presence of a substance in water does not mean harm will result. The crucial factors determining whether a risk to wildlife exists are the concentration present in the water and to which an organism is exposed, as well as whether that concentration is at a high enough level to cause an effect. If the concentration is not high enough, that compound is likely to simply be part of the vast background of inorganic and organic chemicals, both natural and synthetic, present in natural environments such as soil and water.

What is PhRMA Doing?

When this issue first arose, PhRMA committed to understand the environmental significance of

trace concentrations of pharmaceuticals in the environment and since that time has worked to assess the range of concentrations of pharmaceuticals that could be in the environment due to patients taking medicines and their potential effects on human health and aquatic life.

PhRMA developed the P*h*ATE® model to predict the concentrations of human health pharmaceuticals in wastewater treatment plant effluent, surface water, and drinking water throughout twelve watersheds in the U.S.[8] The model was recently upgraded to predict concentrations of APIs in biosolids that are removed from wastewater treatment systems. The P*h*ATE model is being used by researchers in Korea, Japan and more recently in Canada to predict environmental concentrations of APIs in the surface water of those countries.

PhRMA published an assessment of the human health effects of the APIs that were investigated by USGS during the national reconnaissance survey. In addition, PhRMA member companies have published dozens of articles in peer reviewed scientific journals evaluating the fate and effects of APIs in the environment.

PhRMA has developed the P*h*ACT® database to summarize all published English language peer reviewed literature about the effects of pharmaceuticals on aquatic life as well as treatment data for pharmaceuticals in wastewater and drinking water. Over 1,200 scientific papers have been entered into the P*h*ACT database through the end of 2007.

PhRMA representatives have participated in and led numerous scientific conferences over the past five years. PhRMA scientists also have chaired sessions on the PIE issue at several technical conferences, including a recent Water Environment Federation Symposium in Providence and the Society of Toxicology 47th Annual Meeting in Seattle.

With respect to unused medicines, PhRMA scholarship leads to the conclusion that the best action for the patient and the environment is for patients to take all of their medication as prescribed. Although the contribution of unused medicine disposal to the presence of pharmaceuticals in water is small, PhRMA encourages patients not to flush unused medicine and to dispose of them in an environmentally acceptable manner. In March 2008, PhRMA joined the American Pharmacists Association and the U.S. Fish & Wildlife Service in launching the SMARxT DISPOSAL™ program aimed at educating the public about not flushing or pouring any unused medicines down the drain. The SMARxT Disposal program is designed to raise public awareness and promote the use of household trash disposal or local collection programs as alternatives to drain disposal. Following these guidelines will also reduce the potential for abusing unused medicines where this may be a concern.

PhRMA has determined that both household trash disposal and incineration of unused medicines are environmentally acceptable ways to dispose of unused medicines. PhRMA is working with the University of Michigan's Graham Environmental Sustainability Institute to study the environmental impacts of take back for incineration and household trash disposal in order to better understand the overall environmental impacts of both these alternatives.

PhRMA is in the process of publishing a scientific study that finds if all unused medicines were placed in household trash and disposed of in municipal landfills, less than 0.1% of the total amount of medicine found in the environment would be contributed from landfills. In order to verify the conclusion of the landfill study, PhRMA is seeking the opportunity to partner with a researcher that is conducting landfill leachate sampling.

PhRMA is working with U.S. EPA, excelleRx, Inc. and other stakeholders to address the unique disposal issues associated with long-term care facilities (LTCFs). These facilities are required to witness destruction of unused medicines and which have typically relied on flushing down the toilet as the primary disposal method. PhRMA believes that approximately one-third of all unused medicines are generated by LTCFs.

Conclusion

PhRMA and its member companies remain committed to the ongoing study of trace amounts of prescription pharmaceuticals in the environment. Our PIE Task Force will continue to work with interested stakeholders to explore the scientific issues associated with pharmaceuticals in the environment. PhRMA will also partner with interested parties to better communicate the message about responsible disposal of unused medicines. As the available science demonstrates, and PhRMA concurs with, trace amounts of pharmaceuticals in the environment do not pose any human health or environmental risks.

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