Pharmaceuticals in the Environment: What we know, and need to know

Herbert T. Buxton, U.S. Geological Survey, 609-771-3944, hbuxton@usgs.gov

Pharmaceuticals are key ingredients to public health and to quality of life. Rapid advances in drug therapies to meet health challenges and their timely availability are essential for a healthy society. Veterinary pharmaceuticals protect animal health, treat disease, and increase the efficiency of food production. Pharmaceutically active compounds are designed to act upon the function of living organisms; therefore it also is essential to assess the potential health effects of inadvertent exposure of nontarget organisms, particularly sensitive species and subpopulations, via environmental exposure pathways.

Recent studies of pharmaceuticals and other chemicals of emerging environmental concern have demonstrated that (1) the manner in which we handle and dispose of our wastes can concentrate these chemicals in some environmental settings, (2) pharmaceuticals likely have been entering the environment, albeit at extremely low levels, for as long as we have used them, and (3) as we lower the levels at which chemicals can be detected in environmental samples, we will continue to detect more and more chemicals in the environment.

Fundamental Questions

Research on pharmaceuticals in the environment can be framed by six fundamental questions that will help direct research—if and where it is needed—and provide information to guide decisions by industry, government, and the public. These questions are:

1. *Are pharmaceuticals entering the environment?*
2. *What are the most significant sources of pharmaceuticals to the environment?*
3. *Are there environmental settings that are sensitive to pharmaceutical occurrence?*
4. *Do pharmaceuticals have adverse ecological health effects?*
5. *Do pharmaceuticals in the environment persist to source waters and finished drinking water; and if so, are they a human health concern?*
6. *How do we minimize the entry of pharmaceuticals to the environment and remove them if they enter?*

The following provides a brief description of how well these questions have been answered and identifies some remaining science gaps.

Are pharmaceuticals entering the environment?

Pharmaceuticals were first identified as potential environmental contaminants in the 1970s. However, the observed presence of pharmaceutical compounds in large European water bodies in the late 1990s raised awareness that chemicals that are manufactured in relatively small volumes compared to industrial chemicals, and used in homes in

relatively small amounts, could be entering the environment at detectable levels. In 2002, a U.S. Geological Survey (USGS) study documented the presence of pharmaceuticals and other waste-associated chemicals at trace levels in streams across the United States.

More recently, pharmaceuticals have been measured in stream water, stream sediment ground water, soils, and plant and animal tissue. Most of these studies investigated locations near suspected sources, such as waters affected by large urban centers and downstream of wastewater treatment plants. Some studies, recognizing animals as a source of veterinary pharmaceuticals, targeted areas downstream of intensive animal agriculture. The continued improvement of analytical capabilities has enabled detection of an ever broadening range of pharmaceutical classes in the environment, including cytostatics, glucocorticoids, beta-blockers, psychoactive drugs, fibrates, barbiturates, antiphlogistics, and anti-depressants. Most concentrations detected in the environment are well below a part-per-billion level. Pharmaceuticals commonly occur in mixtures with other chemicals that enter the environment via similar pathways.

Development of analytical methods to measure pharmaceuticals, their metabolites, and environmental degradation byproducts in various environmental media remains a priority. Prioritization of pharmaceuticals and associated chemicals for methods development, based on their potential to occur in the environment at levels that could have adverse health effects, will enable research to focus where it is most needed. Such a prioritization of pharmaceuticals will require preliminary evaluation of potential health risks using all available information and tools.

What are the most significant sources of pharmaceuticals to the environment?

Pharmaceuticals can enter the environment via a myriad of source pathways. In the simplest terms, they can be released to the environment after being consumed and excreted (either by animals or humans), discarded (unused or as residual in packaging), or accidentally released during manufacturing, handling, storage, or use. The pathway to the environment typically is with the waste stream – domestic wastewater (via septic systems or wastewater treatment plants), domestic solid wastes (via landfill leachate), commercial-industrial discharges (such as from hospitals, other healthcare facilities, and manufacturing facilities), and animal agriculture (such as animal feeding operations (AFOs), aquaculture facilities, and food production facilities). Biosolids and liquid wastes from wastewater treatment facilities and solid and liquid wastes from animal agriculture can be applied to the land as a soil amendment, thereby generating a terrestrial release pathway to the environment.

Some sources have been characterized. Wastewater treatment plant discharges have been measured at numerous locations across the nation. Antibiotics licensed for use in aquaculture have been detected in and near raceway hatcheries. Pharmaceuticals also have been detected in septic system leachate. In addition, pharmaceuticals have been detected in soils where reclaimed water, biosolids, and manure have been applied to the land and concentrations in the soil were found to be significantly higher than water

concentrations. Some of these sources remain in need of initial or further study, including healthcare facilities, manufacturing facilities, landfill leachate, and various animal agriculture facilities. Additional characterization is needed in terms of selected pharmaceuticals that may be released via one or more of these sources. For example, the range of veterinary pharmaceuticals used in animal production is limited.

Are there environmental settings that are sensitive to pharmaceutical occurrence?

Environmental settings exhibiting the highest environmental concentrations of pharmaceuticals likely occur near sources; however, hydrologic conditions may determine times or other circumstances when pharmaceutical levels are elevated in some environmental settings. Sites adjacent to wastewater treatment plants are receiving significant attention for this reason. Climate and the dilution of wastewater discharges by existing streamflow are important factors in determining the range of levels found in streams near these sources. The number of upstream discharges and other sources is also pertinent. AFOs may affect sensitive environmental settings; however, research on adjacent environmental settings is limited. Settings where pharmaceuticals may accumulate on soils or sediments, particularly where biosolids or manure is applied to land, also require additional attention.

Hydrologic events such as floods, the spring flush, and combined sewer overflows may also warrant additional attention. Combined sewer overflows (CSOs) can produce elevated levels of wastewater contaminants; however, studies on CSOs are limited at this time. One study of the occurrence of corn and soybean herbicides in the Midwest during the spring flush (the first major runoff event during the spring) included measurement of antibiotics in stream water. Only traces of antibiotics were detected. More detailed, site-specific studies are needed to document the potential mechanisms that determine sensitive environmental settings over a range of sources and environmental conditions.

Do pharmaceuticals have adverse ecological health effects?

The scientific literature on potential ecological effects is increasing as research on pharmaceuticals in the environment increases. Some documented cases include fatal effects on vultures exposed to a nonsteroidal anti-inflammatory drug (an effect that was not anticipated), reduced soil microbial activity upon exposure to antibiotics (an effect that was not unanticipated), and shifts in algal community structure upon exposure to a chemical mixture containing an antibiotic (an effect that raises the issue of chemical mixtures). These examples are mentioned only to indicate that existing research has demonstrated the potential for adverse ecological health effects, and this research should proceed and provide a more robust base of scientific knowledge upon which to gage the potential adverse impacts of pharmaceuticals in the environment. A prioritization of pharmaceuticals for such research based on potency and environmental concentrations should improve the efficiency of such research. However, existing research has demonstrated that some adverse effects may be difficult to anticipate.

Endocrine disruption is perhaps the highest research priority as a potential adverse ecological health effect, because despite the low levels of many pharmaceuticals found in the environment, hormonally active chemicals can affect organisms at these low levels. Endocrine disruption is an example of a mode of action that is exacerbated by exposure to mixtures of chemicals. Feminization of fish exposed to estrogenic chemicals has been studied most widely. Chemicals with estrogenic activity include biogenic hormones (naturally occurring estrogens), synthetic hormones (ovulation inhibitors), and industrial chemicals or pesticides that mimic or block normal estrogen function. Research on fish and other aquatic organisms that live in sensitive environmental settings is a priority and may serve as sentinels for potential effects on other organisms.

Do pharmaceuticals in the environment persist to source waters and finished drinking water; and if so, are they a human health concern?

Studies have shown that many pharmaceuticals are found in source waters and at comparably lower concentrations and lower detection frequencies in finished drinking water. However, some compounds, such as carbamazepine, have been found to be quite persistent in the environment and through wastewater and drinking water treatment. The potential human health risk of prolonged exposure to the low-level mixtures that likely occur in finished drinking water has not been evaluated. A priority is assessing the potential health effects of exposure of sensitive subpopulations, such as pregnant women, infants, the elderly, the immuno-compromised, and those inclined to develop chemical sensitivity from exposure. Significant information on the potential for adverse health effects is developed during the drug approval process. That information may be useful to the evaluation of human health risks, as well as to setting priorities for developing methods to measure pharmaceuticals in environmental assessments.

The occurrence of antimicrobials in the environment has been identified as a potential factor in the development and/or maintenance of antimicrobial resistance. The development and spread of antimicrobial resistance is an important human health concern. Research to date has not demonstrated that environmental release of antimicrobials plays an important role in decreasing the effectiveness of antimicrobials used for human therapies or for preventive or therapeutic treatment of animals. Research to evaluate this potential is warranted.

How do we minimize the entry of pharmaceuticals to the environment and remove them if they enter?

The observed presence of pharmaceuticals in the environment has prompted significant public interest regarding potential adverse ecological effects and potential contamination of drinking water. The interest has already increased public awareness of the ways we handle and dispose of our medications, as well as interest by industry in waste treatment technologies and best management practices that are most effective at removing

pharmaceuticals and other trace organic chemicals from surface waters, ground waters, and solid and liquid wastes. Local drug take-back programs are being explored. Guidelines for drug disposal were issued by the White House Office of National Drug Control Policy in February 2007 (http://www.whitehousedrugpolicy.gov/news/press07/022007.html). Research priorities of the Water Environment Research Foundation and other industry organizations include treatment removal of pharmaceuticals (http://www.werf.org//AM/).

Some field studies conducted to date have compared the environmental levels of pharmaceuticals resulting from different best management practices for human- and animal-waste handling and disposal. Others have sampled within wastewater or drinking water treatment plants to provide insights into the most effective treatment processes for pharmaceutical removal. These studies are valuable; however, systematic studies of the performance of treatment technologies and best management practices are needed.

Pharmaceuticals and Other Chemicals of Emerging Environmental Concern

Pharmaceuticals in the environment are often discussed separately as novel or unique environmental contaminants. In fact, pharmaceuticals are just one class of an increasing number of chemicals, referred to here as chemicals of emerging environmental concern or emerging contaminants, which are entering the environment through human and animal waste pathways. It is important to consider these emerging contaminants together for two notable reasons. First, they have been found to enter the environment via similar waste pathways and co-occur as mixtures in sensitive environmental settings. Second, they may develop synergistic, antagonistic, or additive interactions that make assessing their potential health effects inextricable. The case of estrogenic endocrine disruption is an important example, whereby chemicals including biogenic and synthetic hormones, and industrial organic chemicals, pesticides and metals that mimic or block hormone function must be considered together for a complete analysis of the problem.

Conclusions

At this time it is extremely difficult to determine the ultimate level of concern and corresponding efforts that will be made to address environmental contamination from pharmaceuticals and other emerging contaminants. Additional research is warranted and it should be undertaken systematically so as to inform subsequent research and decisionmaking. The understanding gained to date is being used by the public, industry and government to take steps voluntarily to reduce the release of these chemicals to the environment and improve their removal after entry.