

## Pharmaceuticals in the Environment (PIE)

Pharmaceuticals have become chemicals of emerging concern to the public because of their potential to reach drinking water. Patient use of medicines is the principal pathway by which pharmaceuticals (prescription and over the counter) find their way into the aquatic environment. Typically, a fraction of the medicines taken by patients is excreted and enters waterways. To a lesser extent, pharmaceuticals can enter the environment through improper disposal of medicines and from manufacturing discharges.

For over a decade, trace concentrations of pharmaceuticals have been detected in the aquatic environment in the U.S. and other countries. The issue has gained increasing attention, in scientific literature and the media, with governments, regulators and with other stakeholders (e.g., socially responsible investors). At the heart of the issue is whether existing controls (regulatory and other) of pharmaceuticals are protective of human health and the environment.

There are no reported adverse human health effects attributed to drugs in the aquatic environment. Data currently fail to show any connection between the concentration of pharmaceuticals detected in the aquatic environment and acute environmental effects with the notable exception of some hormones in certain circumstances. Some studies suggest that in specific situations, chronic environmental exposure of certain species to select classes of pharmaceuticals (e.g., hormones) may be linked with environmental effects.

### Background

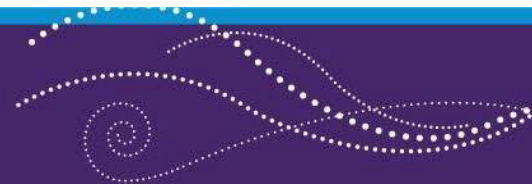
The pathways for pharmaceuticals and over the counter (OTC) medicines entering the environment are well established. Prescribed and normal patient use and excretion is the primary source of pharmaceuticals entering bodies of water, accounting for over 90 percent of the detected concentrations. The remaining sources are a combination of improper disposal of unused medicines (by pouring them down a sink or toilet) and normal manufacturing discharges.<sup>1</sup>

With advances in analytical technology, scientists have been able to detect trace levels of pharmaceuticals in the aquatic environment with several reports appearing in the literature over the past decade. The ability to detect these tiny amounts has increased public awareness and raised new questions about the potential longer-term impact of pharmaceuticals on human health and the aquatic environment. These concerns have sometimes resulted in sensational news stories and headlines despite published studies by many scientists and scholars demonstrating that trace concentrations in water present no appreciable risk to human health.<sup>2</sup>

Current observations suggest that it is very unlikely that exposure to very low levels of pharmaceuticals in drinking water would result in appreciable adverse effects on human health. The concentrations detected in drinking water, typically in the parts per trillion<sup>3</sup> range, are several orders of magnitude—typically more, and often much more, than 1,000-fold—lower than the minimum therapeutic dose.<sup>4</sup>

Since implementation of the E.U. Environmental Risk Assessment (ERA) Guidelines (2006), a comprehensive ERA data package (chronic effects, fate and physical-chemical properties) has been developed on most new chemical entities registered in the past five years. This data package covers global registration requirements for those products registered in the U.S. (New Drug Application), in the E.U. (Marketing Authorization Application) and Canada (New Substances Notification Regulation), as examples. ERAs for established products and generics have been prepared as needed when registered for new indications or registered in new markets.

In addition to mandated ERA requirements as noted above, there is guidance supported by both the private and public sector regarding the safe disposal of unused medications.



One widely referenced study identified significant concentrations of pharmaceuticals downstream from a wastewater treatment plant serving multiple bulk drug manufacturers in India. The results suggested an increased focus on the potential release of active pharmaceutical ingredients from production facilities in different regions.<sup>5</sup>

### Human Health and Aquatic Environment Consideration

There are no reported adverse human health effects attributed to drugs in the aquatic environment; recent studies including those from the World Health Organization (WHO) conclude that trace amounts of pharmaceuticals measured in water should not be of concern to human health even if consumed for many years.<sup>6</sup> Data currently fail to show any connection between the concentration of pharmaceuticals detected in the aquatic environment and acute environmental effects, with the notable exception of some hormones (e.g., estrogens, androgens) in certain circumstances.<sup>7</sup> Some studies suggest that in specific situations, chronic environmental exposure of certain species (e.g., fish) to select classes of pharmaceuticals (e.g., hormones) may be linked with environmental effects.<sup>8</sup> Further studies are needed to determine if there may be environmental effects arising from chronic exposure to pharmaceuticals in the aquatic environment.

### Key Facts and Findings

- On average, all pharmaceuticals detected in U.S. drinking water are below 10 ppt. Caffeine, at 25 ppt, is one exception. A person would have to drink more than 5 million 20 oz bottles of water to get the amount of caffeine in one cup of coffee (~75mg).<sup>9</sup>
- Ibuprofen is one of the drugs most widely detected in water and has been measured at 2.5 ppt. At this concentration, a person would have to drink 2 liters/day of water for over 100,000 years to get the equivalent of a single tablet (200 mg).<sup>9</sup>

### Pfizer's Position

Pfizer is committed to ensuring that manufacture, use and disposal of our medicines does not adversely affect human health or the environment. Pfizer works directly with and in partnership with other member companies on trade associations (e.g., PhRMA, EFPIA)<sup>10</sup> to ensure relevant science is understood and where necessary, further advanced to best ensure these activities do not pose risk to human health and the aquatic environment.

### How the Public Benefits

Effective management and communication of risk based on sound science should ensure a well-informed public, regulatory community and industry. Through this approach, our stakeholders should be better assured that controls are protective of human health and the environment.

### See Related Pfizer Policies at

[http://www.pfizer.com/responsibility/protecting\\_environment/product\\_stewardship.jsp](http://www.pfizer.com/responsibility/protecting_environment/product_stewardship.jsp)

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1 Heberer T, et al (2002). *Occurrence, fate, and removal of pharmaceutical residues in the aquatic environment: a review of recent research data*. Toxicol Letter 131:5-17.

2 WHO (2011). Technical Report on *Pharmaceuticals in drinking water* - WHO/HSE/WSH/11.05.

3 What is 1 ppt? It is one nanogram/liter or 10-9or, second in 32,000 years or 1 penny in \$10 billion.

4 Bruce, GM, et al. (2010). *Toxicological Relevance of Pharmaceuticals in Drinking Water*. Environ. Sci. Tech., 44, 5619–5626.

5 Larsson, J., et al (2007). *Effluent from drug manufacturers contains extremely high levels of pharmaceuticals*. Journal of Hazardous Materials 148, 751–755.

6 WHO (2011).

7 Cunningham, VL, et al (2006). *Effects of Human Pharmaceuticals on Aquatic Life: Next Steps*. Environ. Sci. Tech., 40, 3456–3462.

8 Sanchez, W, et al (2011). *Adverse effects in wild fish living downstream from pharmaceutical manufacture discharges*. Environ Int. Nov; 37(8):1342-8.

9 Rengao, S. *Pharmaceuticals in U.S. Drinking Water and Beyond*, Louisville Water Company, referring to AwwaRF Study project #2758.

10 Pharmaceutical Research and Manufacturers of America. European Federation of Pharmaceutical Industries and Associations.