Introduction to Pharmaceuticals and Personal Care Products (PPCPs)

Christian G. Daughton, Ph.D.
Chief, Environmental Chemistry Branch, Environmental Sciences Division,
National Exposure Research Laboratory, Office of Research and Development
U.S. Environmental Protection Agency, Las Vegas, Nevada 89119
daughton.christian@epa.gov

Those chemical pollutants that are regulated under various international, federal, and state programs represent but a small fraction of the universe of chemicals that occur in the environment as a result of both natural processes and human influence. Although this galaxy of targeted chemicals might be minuscule compared with the universe of both known and yet-to-be identified chemicals, an implicit assumption could be that these selective lists of chemicals are responsible for the most significant share of risk with respect to environmental or economic impairment or to human health.

Pharmaceuticals and personal care products (PPCPs) comprise a particularly large and diverse array of unregulated pollutants whose individual environmental residues often occur at the µg-ng/L range in surface or ground waters (total, combined levels in aqueous environments can be 1-2 orders of magnitude higher) or up to the sub-mg/kg level in sewage sludge biosolids. PPCPs comprise thousands of distinct chemical entities, some manufactured in very large quantities. Residues of PPCPs in the environment result from the diffuse and individually minuscule contributions from the combined activities and actions of multitudes of individual consumers as well as from veterinary and agricultural use. The wide spectrum of issues surrounding PPCPs as environmental pollutants is covered in the resources available from the U.S. EPA's PPCPs web site: http://epa.gov/nerlesd1/chemistry/pharma/.

Numerous sources or origins for environmental residues exist but the primary ones emanate from end use (e.g., introduction to sewerage as a result of bathing or excretion) and direct disposal of unwanted, leftover PPCPs to toilets and domestic trash. Likewise, numerous avenues exist for introduction to the environment, ranging from major, pervasive routes such as municipal sewage discharges to surface waters, to minor, localized ones such as discarded carcasses from euthanized animals and leaching from private septic systems. Although the concentration of any individual PPCP rarely ever exceeds the sub-ppm level (if present in drinking water, concentrations of individual PPCPs are generally less than the ppt-ppb level), evidence is accumulating that many of these trace-level pollutants are ubiquitous; they can have a continuous presence regardless of short environmental half-lives (e.g., via constant replenishment where domestic wastewaters enter the environment); and the numbers of distinct and varied chemical entities (including parent chemicals and metabolites) could be extremely large, given that thousands are in commercial use. To date, however, roughly only 100 or so have been targeted in monitoring studies.

The trace concentrations of individual PPCPs are invariably many orders of magnitude below the levels required to elicit intended therapeutic effects. Rather, what is more germane are concerns regarding the potential for subtle effects (e.g., behavioral changes) or unexpected consequences, primarily in aquatic organisms. Although many of the numerous members of this diverse galaxy of chemicals are designed to interact with a broad spectrum of known biological receptors, many nonetheless possess promiscuous potential for a wide range of previously unrecognized receptors. A number of little-discussed toxicological factors further complicates a realistic assessment of hazard. Examples include cumulative exposure to multiple PPCPs (as well as other toxicants) that share the same mechanism or mode of action, as well as the existence of "paradoxical" responses to low-level exposure (e.g., hormesis). The complexities in hypothetically evaluating risk in a holistic manner (accommodating for "Toxicant Totality Tolerance Trajectory" — the 4Ts) are summarized here: http://epa.gov/nerlesd1/chemistry/ppcp/stressors.htm. The numerous factors involved with the 4Ts pose many challenges for assessing human and ecological risk.

The presence of PPCPs in the environment highlights perhaps better than for any other group of pollutants some of the major challenges facing environmental toxicology. These consumer chemicals epitomize the importance of: assessing cumulative exposure (all chemicals sharing the same mode of action); aggregate exposure (multiple exposure routes for the same chemical); better understanding of low-dose effects (nM-pM and lower) and complex mixture interactions (e.g., synergism and antagonism); the potential significance of hormesis (e.g., paradoxical dose-response at low levels); identifying sensitive sub-populations (e.g., unexpected effects resulting from polymorphisms); and developing more effective ways to communicate risk (critical with respect to consumer acceptance of recycled wastewater). Regarding the last point, while no evidence exists that trace residues in drinking water pose any risk for humans, their mere presence can create a refractory obstacle to public acceptance and trust in recycled wastewater. This important outcome results from the way risk is perceived, which in turn is little affected by factual weight-of-evidence. Essentially, PPCPs in drinking water supplies are "out-of-place" chemicals and as such are considered as "chemical weeds" by the consumer.

Finally, the environmental stewardship of PPCPs defines a new pollution prevention field with the potential to reduce the introduction of PPCPs to the environment. This topic is covered in depth at: http://epa.gov/nerlesd1/chemistry/ppcp/images/green1.pdf and http://epa.gov/nerlesd1/chemistry/ppcp/images/green2.pdf.

NOTICE: Although this work was reviewed by EPA and approved for publication, it may not necessarily reflect official Agency policy.

Prepared for: "Non-Regulated Pollutants Workshop: Brominated Flame Retardants (BFRs) and Pharmaceuticals & Personal Care Products (PPCPs)," U.S. EPA Region 2 Pollutants of Emerging Concern Panel Series, New York, NY, 26 October 2005.