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# Chemicals from Pharmaceuticals and Personal Care Products

**habitat:** the environment in which a plant or animal grows or lives; the surroundings include physical factors such as temperature, moisture, and light, together with biological factors such as the presence of food and predators

**pollution:** any alteration in the character or quality of the environment, including water in waterbodies or geologic formations, which renders the environmental resource unfit or less suited for certain uses

The use or consumption of natural resources often leads to ecological alteration. These changes can result from exposure of living systems to stressors ranging from physical alteration (such as **habitat** disruption) to chemical **pollution**. Untoward effects on wildlife and humans can range from the aesthetic to increased morbidity and mortality.

This article focuses on a large class of chemicals designed for use by humans and domestic animals; namely, pharmaceuticals and personal care products, or PPCPs. Although the benefits of these chemicals are undisputed

The pharmaceuticals and personal care products found in a single bathroom medicine cabinet, multiplied by untold numbers of medicine cabinets in an urbanized area, hold the potential for substantially affecting environmental quality. The impacts on water quality and aquatic ecology from their mere usage and disposal only now are beginning to be investigated.

and wide-ranging, the consequences of their release or escape to the environment are poorly understood.

## Conventional and Nonconventional Pollutants

As early as the 1950s, environmental chemists had focused on **agrochemicals** (for example, dichlorodiphenyltrichloroethane, commonly called DDT), industrial chemicals (for example, polychlorinated biphenyls, or PCBs), and industrial wastes and byproducts (for example, the polychlorinated dioxins). Agriculture and industry were long considered the major sources of chemical pollutants in the environment. Toxic chemicals from these activities are frequently lipophilic (dissolving in fat), persistent (resisting structural breakdown), and volatile (evaporating, subject to atmospheric transport). By virtue of these properties, such "conventional" pollutants have the ability to concentrate in body fat (thereby bioaccumulating in food chains) and to disperse globally.

**agrochemical:** a synthetic or naturally derived chemical used in agriculture, such as a fertilizer, pesticide, or hormone

Despite the long, concerted attention afforded these conventional pollutants, it is not known what portion of total risk due to chemical exposure they comprise. Indeed, many other classes of synthetic and naturally occurring **toxicants** can and do enter the environment. Some of these "nonconventional" pollutants have been long known, whereas others are newly recognized.

**toxicant:** a chemical substance that has the potential of causing acute or chronic adverse effects in plants, animals, or humans

***PROPERLY DISPOSING OF UNUSED AND OUTDATED DRUGS***

In addition to excretion and washing, another origin of drugs in the environment is disposal of expired or unwanted drugs to domestic sewage. Flushing down the toilet is used not just by the consumer, but also not infrequently by medical practices, such as nursing homes and physicians (unused medications and expired "physician samples").

Nationwide procedures do not exist in the United States for consumer return of unused drugs to pharmacies, manufacturers, or hazardous waste disposers. In the absence of recommended practices, in the interim it is best for the consumer to dispose of drugs in domestic trash (ensuring that liquids do not leak) targeted for engineered landfills or to save them for periodic curbside or community hazardous waste pickups. The extremely complex topic of lifecycle stewardship of PPCPs has been covered for the first time by Daughton (in press), as cited in the bibliography.

Until the 1990s, nonconventional pollutants were largely ignored because their higher water solubility relative to conventional pollutants complicated their chemical analysis, made them more easily degraded, prevented their escape to the atmosphere, and constrained their environmental dispersal to local waters. A significant portion of these chemicals includes PPCPs—a broad, diverse collection of thousands of chemicals, including prescription and over-the-counter therapeutic drugs, diagnostic agents, fragrances, cosmetics, and numerous others, many of which possess profound biochemical activity.

## PPCPs in the Environment

PPCPs are applied externally or ingested by humans, and are used for pets and other domestic animals (especially as feed additives). The chemically unaltered, original ("parent") compound together with sometimes many associated transformation ("daughter") products (such as metabolites) have the potential to be excreted (in urine and feces), discharged directly to open waters or into sewage systems, or applied as biosolids (sludge from treated sewage) or washed onto land. Another source is disposal of expired or unwanted PPCPs directly to domestic sewage systems (see sidebar). The potential always exists for migration of PPCPs to, or purposeful introduction to, **groundwaters** (e.g., via septic systems or recharge), where **degradation** is greatly retarded. Other sources exist, as shown in the illustration.

Input of a drug to the environment is a function of the efficiency of human and animal absorption and metabolism coupled with the effectiveness of the technologies employed by municipal sewage treatment works (STWs); furthermore, sewage is often introduced directly to the environment without any treatment by STWs (such as inadvertent "overflow" events or purposeful "straight-piping"). STWs are not specifically engineered to remove PPCPs. The focus of STWs, as historically stipulated by law, is solely on a small number of "criteria" pollutants. While many unregulated pollutants are coincidentally removed during treatment, STW-treated effluents (discharges) can contain a wide spectrum of other chemicals, PPCPs being but one large group.

**Occurrence, Fate, and Risk.** Compared with the "conventional" pollutants, little is known about PPCPs with regard to potential environmental effects. Even though PPCPs are a more recently recognized group of pollutants, it is reasonable to surmise that the occurrence of PPCPs in waters is not a new phenomenon: many PPCPs probably have existed in the environment for as long as they have been used commercially.

Because of the higher **polarity** of PPCPs, their environmental disposition gravitates to waterbodies hydraulically connected to their origin. This includes all surface waters and groundwaters. Toxicological risks from inadvertent exposure of nontarget organisms in the environment are therefore probably highest for aquatic organisms, especially those occupying locations closest to PPCP discharges. The risks are lower for humans because drinking water usually receives further treatment to remove pollutants.

Furthermore, the risks posed to populations of aquatic organisms accrue from continual lifelong multigenerational exposure, whereas for humans, exposure is via long-term but intermittent consumption of much lower

**groundwater:** generally, all subsurface (underground) water, as distinct from surface water, that supplies natural springs, contributes to permanent streams, and can be tapped by wells

**degradation:** breakdown of a chemical to yield usually simpler chemical products (molecules) by way of biocatalysis (e.g., metabolism), photolysis (e.g., sunlight), or physicochemical processes (e.g., hydrolysis)

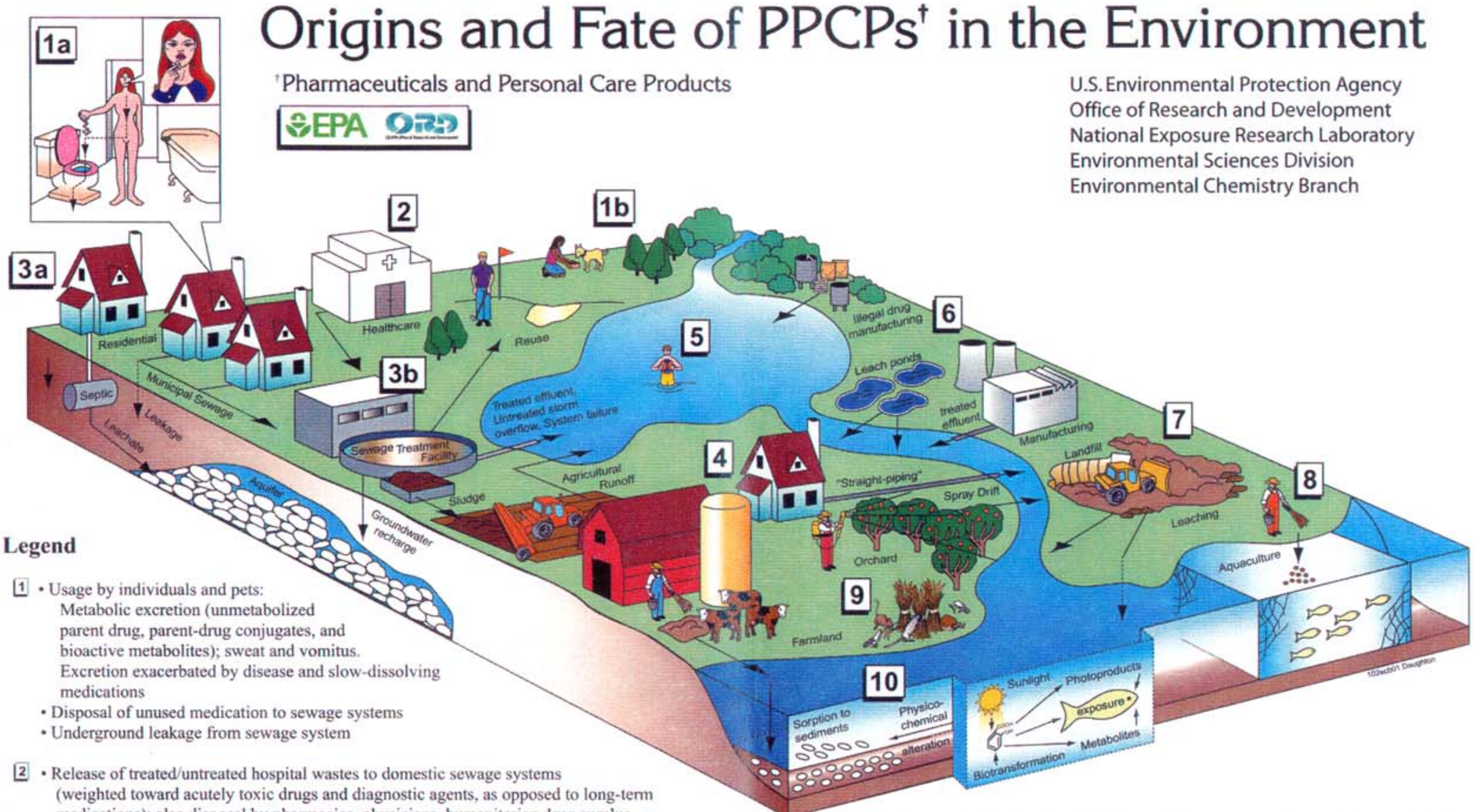
**polarity:** a relative measure of the distribution of electron density for a molecule; its significance for environmental chemistry is that it determines whether a chemical prefers to associate with water (polar, or hydrophilic) or fat/lipid (nonpolar, or hydrophobic or lipophilic)

A high resolution version of this illustration is available at:
http://www.epa.gov/nerlesd1/chemistry/pharma/images/drawing.pdf

# Origins and Fate of PPCPs[†] in the Environment

[†]Pharmaceuticals and Personal Care Products

U.S. Environmental Protection Agency
Office of Research and Development
National Exposure Research Laboratory
Environmental Sciences Division
Environmental Chemistry Branch




## Legend

1 • Usage by individuals and pets:
Metabolic excretion (unmetabolized parent drug, parent-drug conjugates, and bioactive metabolites); sweat and vomitus. Excretion exacerbated by disease and slow-dissolving medications
• Disposal of unused medication to sewage systems
• Underground leakage from sewage system

2 • Release of treated/untreated hospital wastes to domestic sewage systems (weighted toward acutely toxic drugs and diagnostic agents, as opposed to long-term medications); also disposal by pharmacies, physicians, humanitarian drug surplus

3 • Release to private septic/leach fields
• Treated effluent from domestic sewage treatment plants discharged to surface waters or re-injected into aquifers (recharge)
• Overflow of untreated sewage from storm events and system failures directly to surface waters

4 • Transfer of sewage solids to land (e.g., soil amendment/fertilization)
• "Straight-piping" from homes (untreated sewage discharged directly to surface waters)
• Release from agriculture: spray drift from tree crops (e.g., antibiotics)
• Dung from medicated domestic animals (e.g., feed) - CAFOs (confined animal feeding operations)

5 • Direct release to open waters via washing/bathing/swimming

6 • Discharge of regulated/controlled industrial manufacturing waste streams
• Disposal/release from clandestine drug labs

7 • Disposal to landfills via domestic refuse, medical wastes, and other hazardous wastes
• Leaching from defective (poorly engineered) landfills

8 • Release to open waters from aquaculture (medicated feed and resulting excreta)

9 • Release of drugs that serve double duty as pest control agents:
examples: 4-aminopyridine experimental multiple sclerosis drug → used as avicide; warfarin anticoagulant → rat poison; azacholesterol antilipidemics → avian/rodent reproductive inhibitors; certain antibiotics → used for orchard pathogens; acetaminophen analgesic → brown tree snake control

10 Ultimate environmental fate:
• most PPCPs eventually transported from terrestrial domain to aqueous domain
• phototransformation (both direct and indirect reactions via UV light)
• physicochemical alteration, degradation, and ultimate mineralization
• volatilization (mainly certain anesthetics, fragrances)

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For further information on this topic: http://www.epa.gov/nerlesd1/chemistry/pharma/index.htm concentrations of fewer PPCPs in drinking water. These risks are essentially unknown, largely because the documented concentrations in the environment are extremely low—from sub to hundreds of micrograms per liter ($\mu$g/L), or parts per billion (ppb). (One part per billion represents 0.0000001 percent. Detection of a chemical at a concentration of 1 ppb is comparable to searching for one family among the world's entire population.) Moreover, possible effects on nontarget organisms are poorly understood. The occurrence of PPCPs in drinking water is much less frequent and at even lower concentrations than in the environment—nanograms per liter (ng/L), or parts per trillion.

Although these concentrations are very low, they can be perpetual because PPCPs are continually introduced to the aquatic environment. Even PPCPs with short **half-lives** can establish a pseudo-**steady-state** presence because their environmental breakdown is continually balanced by replenishment via fresh sewage effluent. These chemicals are examples of "pseudo-persistent" pollutants.

**half-life:** the time required for the initial concentration of a radioactive element to decrease, through radioactive decay, by 50 percent; in nonradiochemical usage, the time required for a pollutant to lose one-half of its original concentration (e.g., the half-life of DDT in the environment is 15 years)

**steady state:** a state of a system in which reactions are occurring or processes are happening, but the system has reached a state of balance such that all components remain at a constant concentration

## Biochemical Targets and Nontargets

While personal care products are generally consumed in much larger quantities than pharmaceuticals, drugs are designed expressly to be biologically active, with each therapeutic class having different biochemical targets (although many classes can share one or more targets—or "receptors"). Drugs are designed with the safety of the target organism in mind (humans or domestic animals). Little is therefore known regarding the safety of nontarget organisms, such as aquatic life.

Two classes of drugs have received more attention than any others regarding nontarget effects. The first class is **antibiotics**, where the promotion of **pathogen** resistance is a major concern. (Pathogen resistance can be caused by overuse or misuse in the host and possibly by exposure of microorganisms in the environment.) The second class is the sex **steroids**—both the natural, **endogenous** steroids, especially the estrogens, as well as their synthetic counterparts, such as those used for reproductive control.

**antibiotic:** a substance produced by organisms, especially bacteria and fungi, which passes into the surrounding medium and is toxic to other organisms; for example, penicillin from the mold *Penicillin notatum* destroys many kinds of bacteria

**pathogen:** a disease-producing agent, usually a living organism, and commonly a microbe (microorganism)

**steroid:** any of a class of naturally occuring compounds and synthetic analogues, such as sterols, bile acids, sex hormones, or adrenocortical hormones; most have specific physiological action

**endogenous:** originating from within, as opposed to coming from external sources

Steroidal chemicals such as the sex steroids have the capability of disrupting or modulating hormone (endocrine) systems. Certain other PPCPs, together with various other synthetic chemicals, possess endocrine activity. Collectively, these compounds are known by a number of terms, including endocrine disrupting compounds or hormonally active agents. Their aquatic effects include the feminization of male fish and alteration of the behaviors of either sex at part-per-trillion concentrations. A multitude of other aquatic effects are possible because hormone systems are central to the development, functioning, and reproduction of most organisms.

Antibiotic resistance and hormonal effects are only two of numerous possible untoward outcomes. Others, such as neurobehavioral effects, could be so subtle that they escape our immediate attention, accumulating unnoticed until significant outward effects arise but which cannot be ascribed to a cause.

## The Role of Individuals

As of 2002, a growing number of articles were advancing various aspects of the overall issue of PPCPs in the environment. The U.S. Environmental

Protection Agency maintains a web site devoted to the topic (as referenced in the bibliography). Although the issue of PPCPs in the environment has gained more attention by scientists in many fields, the overall topic will probably continue to generate more questions than answers. A larger lesson, however, resides among the unknowns.

Most PPCPs owe their origin in the environment to the combined actions and behaviors of multitudes of individuals. In contrast to the conventional synthetic pollutants, the origin of PPCPs in the environment has no geographic boundaries or climatic-use limitations; that is, PPCPs are discharged to the environment wherever people live or visit, regardless of the time of year.

Perhaps more so than any other class of pollutants, PPCPs illustrate the immediate, intimate, and inseparable connection of the actions and activities of the individual with the environment. Some scientists feel the importance and significance of the individual in directly contributing to the combined load of synthetic chemicals in the environment has been greatly underappreciated. The continuing, escalating advances in design of new drugs will undoubtedly add to the spectrum of questions regarding the environmental significance of these compounds. SEE ALSO CHEMICALS FROM CONSUMERS; ECOLOGY, FRESH-WATER; LAND USE AND WATER QUALITY; POLLUTION OF GROUNDWATER; POLLUTION OF LAKES AND STREAMS; POLLUTION SOURCES: POINT AND NONPOINT; SAFE DRINKING WATER ACT; SUPPLIES, PUBLIC AND DOMESTIC WATER; WASTEWATER TREATMENT AND MANAGEMENT.

*Christian G. Daughton*

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### Internet Resources

"A National Reconnaissance of Pharmaceuticals, Hormones, and Other Organic Wastewater Contaminants in Sources of Drinking Water, 2001." *Emerging Water Quality Issues Investigations Page.* U.S. Geological Survey, Toxic Substances Hydrology Program. <http://toxics.usgs.gov/regional/emc_sourcewater.html>.

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