

# **Pollution from Personal Actions, Activities, and Behaviors: Pharmaceuticals and Personal Care Products in the Environment**

**= Multidimensional Science Issues Relevant to Regulatory Considerations <**

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**Pollution from Personal Actions, Activities, and Behaviors:  
Pharmaceuticals and Personal Care Products in the Environment  
= Multidimensional Science Issues Relevant to Regulatory Considerations <**

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Perhaps more so than with any other class of anthropogenic chemicals, the occurrence of pharmaceuticals and personal care products (PPCPs) in the environment highlights the immediate, intimate, and inseparable connection between the personal activities of individual citizens and their environment. PPCPs, in contrast to other types of environmental contaminants, owe their origins in the environment directly to their worldwide, universal, frequent, highly dispersed, and individually small but cumulative usage by multitudes of individuals — as opposed to the larger, highly delineated, and more-controllable industrial manufacturing/usage of most high-volume synthetic chemicals.

PPCPs are a diverse group of chemicals, used internally or externally with the bodies of humans and domestic animals (and agricultural plants), comprising a wide spectrum of chemical classes. In very general terms, PPCPs include: < drugs (available by prescription or over-the-counter; including the new genre of “biologics”), < diagnostic agents (e.g., X-ray contrast media), < “nutraceuticals” (bioactive food supplements such as huperzine A), and < other consumer chemicals, such as fragrances (e.g., synthetic musks) and sun-screen agents (e.g., methylbenzylidene camphor); also included are < “excipients” (so-called “inert” ingredients used in PPCP manufacturing and formulation); the universe of included chemicals is expanded yet further by the numerous environmental transformation products (many of these “daughter” products can also be bioactive) that can be created from each parent compound. In addition to the better known antimicrobials and steroids, over 50 individual PPCPs or metabolites (from more than 10 broad classes of therapeutic agents or personal care products) had been identified [as of 1999; see *Environ. Health Perspect.* 1999, 107(suppl 6), 907-938] in environmental samples (mainly in sewage, surface, and ground waters). It is important to note that although a number of representatives from small subsets of therapeutic classes have been identified in the environment, numerous members of most classes have yet to be searched for. Many of these unreported drugs are among the most widely prescribed in the U.S.

Many PPCPs (as well as their metabolites and transformation products) can enter the environment following ingestion or application by the user or administration to domestic animals. Disposal of unused/expired PPCPs in landfills and to domestic sewage is another route to the environment. The aquatic environment probably serves as the major, ultimate receptacle for these chemicals, for which little is known with respect to actual – or even potential – adverse effects. Domestic sewage treatment facilities were never specifically designed to remove PPCPs, and the efficiencies with which they are removed vary from nearly complete to ineffective. While PPCPs in the environment (or domestic drinking water) are not regulated, and even though their concentrations are extremely low (ng/L-μg/L) and far below “therapeutic thresholds”, the consequences of exposure to multiple compounds having different as well as similar (cumulative) modes of action over multiple generations prompts a plethora of questions, many of which impact discussions regarding regulatory significance. While the environmental issues involved with antibiotics (development of pathogen resistance) and sex steroids (“endocrine

disruption”) are the most widely recognized, numerous other therapeutic and consumer-use classes of PPCPs pose environmental questions.

**“Emerging” Chemical Risks:** One of the “signature science” responsibilities of the U.S. EPA’s Office of Research and Development (ORD) (as well as for other environmental science institutions throughout the world) is to pioneer and nurture new programs for identifying, evaluating, and developing the requisite science for minimizing existing – or preventing future – exposure risks from previously unrecognized and unexpected chemicals. By using various approaches to discovery, “futuring” (e.g., see: <http://www.isye.gatech.edu/isf2001/>), and fast failure analysis, a major objective is to minimize the time required for transferring new science to other parts of the Agency, to other government agencies and research institutions, and to the public. This type of science can eventually guide society away from a reactionary mode of being forced to deal with entrenched environmental problems, and instead orient it more towards proactive, preventative science.

The term “emerging” only reflects one aspect of the overall issue surrounding the need to minimize or prevent exposure risks. Because of this, the term “emerging” can misrepresent and obscure the overall issue. Those risks emanating from chemical pollution can be classified into four main categories: (1) Growing/Developing, (2) Hidden/Latent, (3) Emerging, and (4) Future. Clearly, the term “emerging” only accounts for one of four possible categories of previously unrecognized or unanticipated exposure risks – but this term is nonetheless used to encompass all four categories. For further general discussion of “emerging” risks, see the discussion at: <http://www.epa.gov/nerlesd1/chemistry/pharma/science-issues.htm/>.

### **The “Risk Paradigm” as a Framework for Regulatory Considerations:**

This presentation summarizes the wide range of issues associated with this overall topic, touching on some areas of potential regulatory issue and possible actions regarding future direction for pollution prevention.

To understand the regulatory issues that might be involved with PPCPs (or any other classes of “emerging pollutants”), it is first necessary to understand the specific science issues relevant to each of the aspects of the “risk paradigm”, which spans the science involved with their sources/origins in the environment to remediation technology (see the illustration: “[Origins and Fate of PPCPs in the Environment](#),” which shows the major sources of PPCPs in the environment).

Using the “risk assessment paradigm” as an organizing framework, we can consider the factors of pollutant source, occurrence/exposure, effects, and pollution prevention, and encapsulate the overall issue of PPCPs in the environment as follows.

**SOURCES/ORIGINS:** All chemicals applied externally or ingested (and their bioactive transformation products) have the potential to be excreted/washed into sewage systems and from there discharged to the aquatic/terrestrial environments. Input to the environment is a function of the efficiency of human/animal absorption/metabolism and the efficiency of any sewage treatment technologies employed (if any). Efficiencies vary from chemical to chemical and between sewage treatment facilities. Obviously, discharge of untreated sewage serves to maximize the occurrence of PPCPs in the environment.

Consumer use of PPCPs originates not just from medical prescriptions, physician samples, and pharmacy OTC (over-the-counter) sales, but also increasingly via the black market (e.g., Internet sale of legal drugs,

and trafficking of illicit drugs). PPCP use is expected to vastly increase with the accelerating discovery/design of new drugs coupled with the increased medical demands and expectations of an increasing and aging population. Each environmental source can prompt different concerns. The emphasis here is not on waste streams from manufacturing (an already controlled source), but rather on the dispersed activities of people. Sources include those that are anticipated (the expected part of a process - e.g., manufacturing), purposeful (release/introduction to the environment as a result of disposal), and inadvertent (via metabolism, washing). As evident in the [illustration](#), sources include:

- < **Inadvertent release via excretion** (of parent compound and metabolites) and washing into open waters via municipal sewage treatment works (STWs) effluents, septic systems, leach fields, “straight piping”, and other sources such as cruise ships
- < **Hospital waste** (both pre-treated and untreated sewage and solid wastes)
- < **Escape of untreated STW sewage from excessive precipitation** (when storm drains are tied to domestic waste conveyance systems) and STW failures
- < **Purposeful disposal to domestic sewage** (e.g., unwanted, expired PPCPs). This is relevant not just to individual homes, but also to nursing homes [each state has different laws applying to nursing homes, resulting in a nationwide patchwork of disposal laws]
- < **Purposeful disposal to landfills** (e.g., unwanted, expired PPCPs). This can be a major issue for humanitarian efforts that deal with large quantities of excess, donated drugs
- < **Aquaculture** (primarily antibiotics) release to open waters
- < **Medicated pets** (release of excrement primarily to terrestrial systems, but then subject to runoff events)
- < **CAFOs** (confined animal feeding operations): large quantities of excreted antibiotics and growth hormones; used for disease control and growth promotion
- < **Agriculture** (e.g., spray drift from antibiotics used on fruit trees and other economic crops)
- < **Pest control** (minor, little-known use for certain drugs)
- < Uncontrolled and purposeful dumping of materials from **illicit drug manufacturing and trafficking**
- < [It is important to note that the **spectrum of types of PPCPs consumed can vary greatly** between geographic regions and especially between countries; this affects the environmental impact of the source].

**OCCURRENCE:** The occurrence of PPCPs in the environment highlights the following points: (i) *Non-point Sources:* Importance of dispersed, diffuse, non-point “discharges” of anthropogenic chemicals to the environment has been overshadowed for decades by the more obvious point sources. (ii) *Importance of Individual Action:* Importance and significance of individuals in directly contributing to the combined load of chemicals in environment has been largely overlooked. (iii) *“Connectedness”:* PPCPs illustrate the immediate, intimate, and inseparable connection of the actions/activities of the individual with the environment.

Each source for PPCPs can impact various physical environmental “compartments”; for the environmental chemist, this means that analytical tools are required to detect and quantify a given chemical in various environmental “matrices” (e.g., water, sediment, suspended solids, tissues, etc.) – usually at very low, trace concentrations. The immediate environmental deposition for PPCPs is primarily either to the terrestrial or aquatic environment. Because of the polar nature of most PPCPs, however, the ultimate sink tends to be the aquatic environment. Some of the major environmental compartments in which PPCPs can occur include:

- < **Surface waters:** streams, rivers, lakes, estuaries receiving treated sewage; the concentrations in untreated sewage should be highest, and then fall off temporally and spatially

- < **Groundwaters:** the two major issues are (i) leaching from grazing/feeding areas and from faulty landfills, and (ii) purposeful introduction via groundwater recharge using tertiary treated sewage. Groundwater contamination is of particular concern since the half-lives of all chemicals can be much longer in groundwater, being that microbial activity is lower
- < **Terrestrial:** result of deposition of excrement from medicated pets and domestic animals (e.g., CAFOs); drugs/metabolites are then susceptible to leaching to groundwater or washing off to surface waters during rainfall events
- < **Tissues:** certain drugs could pose concerns as trace residues in domestic animals intended for human consumption. Few PPCPs are susceptible to biomagnification in foodchains (e.g., the pervasive synthetic musk fragrances, being less polar than many drugs, can be concentrated in aquatic organisms)
- < **Drinking water:** residues remaining in natural waters from treated (and untreated) sewage are further diminished in treatment plants for upgrading (finishing) domestic drinking water. The frequency and spectrum of occurrence is greatly reduced and concentrations can be one or more magnitudes lower
- < [Note that **establishing trends** in occurrence and concentration for individual PPCPs is important for determining priorities for monitoring].

**FATE and TRANSPORT:** In general, PPCPs are not unique from conventional pollutants with respect to their potential environmental physicochemical or biochemical transformations or ultimate fates. They are distinguished primarily from conventional pollutants in that far less is known about the specifics of these processes because their structures differ greatly from those of all conventional pollutants.

- < **Aquatic aqueous environment** is probably the ultimate environmental compartment for most PPCPs since the parent compounds (and especially their metabolites) tend to be more polar.
- < **Atmospheric transport** for most PPCPs is not an issue because of their much lower volatility compared with conventional pollutants (anesthetic gases, gaseous “carriers” or propellants for inhalables such as from metered-dose inhalers, and synthetic fragrances are some exceptions)
- < The **long-established transformation processes** such as precipitation (e.g., with ions), sequestration by or sorption onto suspended particles in waters or sediments, hydrolysis, direct and indirect photolysis via sunlight, and microbial metabolism are all pertinent to PPCPs, but much less is known than for conventional pollutants
- < Each PPCP is susceptible to **various degrees of degradation** in STWs and in the environment (ranging from complete to little)
- < **Bioconcentration/Bioaccumulation** are factors only for lipid-soluble PPCPs (e.g., certain synthetic fragrances), and there are far fewer hydrophobic than water-soluble PPCPs.

**EXPOSURE:** Because the aquatic environment tends to be the ultimate repository for most PPCPs, the primary focus devolves largely to that of exposure of aquatic organisms. But specific concerns may exist for human health. Some of the many aspects that are important with regard to exposure to PPCPs include:

- < Environmental science’s scope of what constitutes environmental “**persistence**” perhaps needs to be modified or expanded for any chemical (such as PPCPs) that routinely emanates from sewage. The key for sewage is not necessarily whether the pollutant has high inherent chemical stability, but that it is continually introduced to the environment. Any diminution by transformation processes can be immediately replenished by fresh effluent, resulting in the ever-presence of compounds that might otherwise rapidly disappear

- < **Aquatic concentrations** of PPCPs range from sub-ng/L (ppt) to µg/L (ppb) and higher. It has only been the advent of more powerful chemical analysis methodologies that has allowed what have undoubtedly been long-present trace levels of these compounds to be detected and quantified
- < **Aquatic exposure is unique** in that for many organisms (esp. those that are sessile), exposure can be continual and multigenerational
- < **Continual, life-long exposure to trace levels** is a largely unexplored domain of toxicology
- < Effects are a function of not just concentration but also the **duration and the timing of exposure**. Timing of exposure with developmental stage can be critical. Response thresholds (no-effect concentrations) can be continually reduced as exposure times increase
- < **Domestic drinking water** concentrations seem to be much less frequent/prevalent and are at least an order of magnitude lower than for the aquatic environment because of additional treatment
- < Concern regarding drinking water exposure pertains mainly to **at-risk populations** (health-impaired, fetuses, children)
- < Exposure is greatly complicated by the fact that metabolites can also be bioactive in their own right and certain metabolites (e.g., conjugates) have the potential to be converted back into their parent forms
- < The “**Risk Cup**”† raises many questions regarding simultaneous exposure and many unanswered questions regarding the different permutations of exposure [see [Figure](#): “The Risk Cup”]. These include exposure from: (i) the same compound from different sources (“aggregate exposure”), leading to additive concentrations, (ii) multiple compounds having the same mode of action (MOA leading to “cumulative exposure”), and (iii) compounds having different MOAs but yielding the same end effect (“complementary exposure”). These exposure scenarios are important to consider as they can all theoretically result from simultaneous exposure to trace concentrations of multitudes of chemicals.

**†The “Risk Cup”: Complex and Currently Unresolvable Issues Affecting Regulatory Approaches Aimed at Multiple Exposure / Multiple Effects**

Multiple effects (combined endpoints): Exposure to one chemical having multiple mechanisms/modes of action (MOAs)

Synergism/Antagonism: Unanticipated endpoints (deviating from additive) from interactions of multiple chemicals [e.g., one drug can reduce the metabolism of another (e.g., via inhibition of any of the microsomal superfamily of cytochrome P450 isoenzymes), and consequently lead to increased excretion of the parent drug; or two drugs can work in concert to create an imbalance in metabolites (e.g., MAOIs and SSRIs leading to “serotonin syndrome”); efflux pump inhibitors can drastically increase exposure to all toxicants]

Aggregate Exposure: Factoring additive exposure via all pathways and sources for one chemical (cumulation of individually smaller risks); e.g., antibiotics via medications, food residues, and drinking water

Complementary Exposure: Co-exposure from chemicals acting by different MOAs but yielding similar ultimate endpoints; e.g., all therapeutic classes of antidepressants, or all antibiotics

Cumulative Exposure: Factoring exposure to multiple chemicals sharing a common MOA; e.g., the multiple members of anticholinergics, selective serotonin reuptake inhibitors, or calcium channel blockers

Biological Effects of Low Level Exposure (BELLE): For example, Hormesis – paradoxical or unanticipated effect at low doses of a chemical (see: <http://www.belleonline.com/>)

**EFFECTS:** Drugs are purposefully designed to interact with cellular receptors at low concentrations and to elicit specific biological effects. In addition to target (intended) effects, however, unintended “adverse” effects can also occur from interaction with non-target receptors. Perhaps the most important consideration with regard to potential effects is that each of the numerous therapeutic classes of drugs and the many types of personal care products can have completely different potential effects because of the wide variety of receptors. A broad constellation of distinct modes (mechanisms) of action (MOAs) requires that risk be assessed on each class separately (while recognizing that complex interactions must also be considered).

As is the case for all toxicants, the potential for interactive effects (between classes) cannot be discounted. For example, the concerns regarding antibiotics differ completely from those for synthetic hormones, which differ from calcium channel blockers, and so on. The current regulatory approach (used by the U.S. Food and Drug Administration [FDA] and by the European Union) is based on hypothesized environmental occurrence (concentration) coupled with traditional ecotoxicological data as opposed to documented occurrence and known effects (see **Learning Resources** at end for references regarding current regulations). Some of the many aspects that are important with regard to **potential** effects from PPCP exposure include:

- < **Toxicity versus Therapeutic Effect.** “All substances are poisons; there is none which is not a poison. The right dose differentiates a poison from a remedy” (Paracelsus 1493-1541). “The dose makes the poison.” Embodied in the concept of “therapeutic index” or therapeutic window, range, or ratio (selectivity) — ratio of the drug dose producing an undesired effect to the dose causing the desired effects
- < Toxicological significance for **non-target organisms** (esp. aquatic) is poorly understood
- < Current knowledge extends mainly to what is known about human metabolism – **little is known about aquatic toxicology** except for aquaculture antibiotics
- < PPCPs can be metabolized via the same Phase I and II enzymatic processes available in different renditions in all organisms. Because of profound variety and differences in their chemical structures (compared with conventional pollutants), **much remains unknown with respect to effects in non-target organisms**
- < **Receptors in non-target species could differ from those in humans.** Just as animal models are frequently called into question for their relevance to human health, likewise, human and other **mammalian toxicity data** (e.g., from PPCPs) **are not necessarily transferable to aquatic organisms**
- < Intended/unintended **receptors of exposure and effects can differ greatly** from those of currently regulated pollutants
- < Up to recently, the historical primary endpoints of interest in risk assessment have been acute toxicity and carcinogenesis — **little attention has been paid to the universe of other endpoints** through which toxicants can exert their action. Other endpoints, such as neurobehavioral, immunological, and endocrine homeostasis alterations, can be very subtle but nonetheless lead to unanticipated, profound outcomes. Subtle endpoints could also be effected by extremely low concentrations of a toxicant (difficult to empirically test). Effects mediated (e.g., via hormone-like compounds) do not necessarily follow the monotonic sigmoid dose-response curve (U- and inverted-U-shaped curves can occur). Of possible tangential importance is the realm of Biological Effects of Low Level Exposure “BELLE”‡

### ‡Biological Effects of Low Level Exposure - BELLE

*Hormesis*: Major aspect of BELLE (<http://www.belleonline.com/>)

Paradoxical or unanticipated effect at low doses of a chemical

Hypothetical, paradoxical phenomenon of seemingly beneficial effects at low doses for chemicals that are otherwise toxic at higher doses

Hormetic: Substance that presents an adverse risk at higher exposure levels but serves to protect at lower exposure levels

Protection purportedly afforded by a variety of mechanisms including: adaptation, damage repair, and stimulation of biochemical processes (e.g., efflux pumps)

In contraposition to the traditional linear/log-linear low-dose extrapolation model

Scientifically controversial (e.g., U- and inverted U-shaped curves)

- < More focus should be applied to the realm of **subtle effects** [see hypothesis proposed by Daughton and Ternes in “Pharmaceuticals and Personal Care Products in the Environment: Agents of Subtle Change?” *Environ. Health Perspect.* 1999, 107(suppl 6), 907-938]
- < **The question exists as to whether immediate biological actions on non-target species can be imperceptible but nonetheless lead to adverse impacts as a result of continual accretion over long periods of time.** For example – latent damage, only surfacing later in life. Could subtle effects accumulate so slowly (perhaps seeming to be part of natural variation) that major outward change cannot be ascribed to the original cause? Effects that are sufficiently subtle that they are undetectable or unnoticed present a challenge to risk assessment (especially ecological) — e.g., subtle shifts in behavior or intelligence. Subtle effects can be slow but still lead to significant change – analogous to aging (with its associated degeneration of biological functions), not noticed on a daily or weekly or even yearly basis, but profoundly obvious over the longer term
- < Must separately consider each class of drugs having **distinct MOAs**. There are many discrete classes of PPCPs, each with distinct modes of action: e.g., antibiotics, efflux pump inhibitors, sex steroids, SSRIs, etc.
- < With respect to human exposure, intake of **multiple drugs** adds to the complexity of additional burden to patients already taking medications having low therapeutic indexes (e.g., combined loading of individual anticholinergics or serotonin modulators)
- < Concerns regarding **at-risk populations** (e.g., compromised health, fetuses, children).

**REMEDICATION/TREATMENT/POLLUTION PREVENTION:** If PPCPs eventually prove to be an environmental concern, it is unknown whether sewage treatment facilities could be cost-effectively modified to reduce emissions. Pollution prevention is preferable to remediation (proactive vs. reactive approaches). Some near-term actions to consider for minimizing the introduction of PPCPs to the environment or their potential effects:

- < **Environmental “Friendliness”:** Factor environmental proclivity into PPCP design/marketing “green” PPCPs: maximize biodegradability/photolability to innocuous end products, minimize therapeutic dose (“calibrated dosing”), more single-enantiomer drugs
- < Develop **alternative, optimal delivery mechanisms:** Reduce dosages with (1) new routes for existing and new drugs (e.g., inhalable, dermal), (2) new formulations (e.g., for insoluble drugs - ca. 30% of

USP drugs and 50% of prospective drugs are poorly water-soluble), and (3) new mechanisms for delivery of drugs to the target (e.g., antibody-linked drugs)

- < **Drug Prescribing and Use:** Better inform physicians (and public) to environmental consequences of over-prescribing medications — minimize misuse/overuse. Engage medical community to develop guidelines. Identify pathogens prior to prescribing antibiotics (“imprudent use”; “misuse” vs. appropriate use).
- < Consider **reducing package sizes** for PPCPs: Some PPCPs are perhaps more prone to being disposed because they are prescribed or purchased in quantities too great to be used before expiration or because they tend to expire more rapidly.
- < **Internet Dispensing:** Educate/encourage the pharmacy community to understand environmental consequences of over-dispensing (and dispensing without a prescription) to minimize unneeded drug use and attendant disposal [see: [www.fda.gov/oc/buyonline](http://www.fda.gov/oc/buyonline)]
- < **Individualization of Therapy:** Encourage drug manufacturers to provide the medical community with the necessary information to tailor drug dosages to the individual (esp. long-term maintenance drugs) on the basis of body weight, age, sex, health status, and known individual drug sensitivities — individualization of therapy. Identify lowest effective dosages (“calibrated dosing”). Genomics offers the future possibility of “personalized pharmaceuticals” (targeted at small, genetically defined communities), thereby reducing widespread use of major drugs and encouraging the use of many minor drugs
- < Expand exploration of **non-chemical alternatives to traditional medications:** Reducing/eliminating drug dosages by use of placebos [e.g., see refs at: “Medicinal Mimicry: Sometimes, placebos work—but how?” D. Christensen, *Science News* 3 Feb. 2001, 159(5), 74-75,78; <http://www.sciencenews.org/20010203/bob1ref.asp>]
- < **Proper Disposal:** Better inform pharmacy industry to provide proper disposal instructions to end-user for unused/expired drugs. Better guidance for disposition of non-controlled substances by disposal companies. Consider implementing Extended Producer Responsibility (EPR)
- < **Importance of Individuals’ Actions:** Educate public on (i) how their individual actions each contributes to burden of PPCPs in the environment, (ii) how PPCPs can possibly affect aquatic biota, and (iii) the advantages accrued by conscientious/responsible disposal and usage of PPCPs
- < Poorly characterized ramifications of PPCPs in the environment (occurrence, fate, transport, effects) warrant a more precautionary view on their environmental disposition. Potential importance of The **Precautionary Principle**<sup>††</sup> – the principle of precautionary action that redistributes the burden of proof (“reverse onus”) because the science required for truly and fully assessing risks lags far behind the requisite supporting science.

### ††Factors Leading to the Precautionary Principle

Science (objective; data oriented) Y

*quick* and versed at delimiting with certainty what is **unknown**

*slow* but able to define what is **knowable**

*poor* at separating the **unknowable** from the unknown

*incapable* of removing all **uncertainty** (absolute current limitations of knowledge)

Science + Uncertainty Y ~~Scientific Certainty~~

Science + Uncertainty + Policy/Political judgment Y course of further study or action  
(subjective, value-oriented, emotional, but rational nonetheless in its approach)

Fusing science with Judgment is a balancing act designed to avoid:

**actions** based on “type I errors” (false alarms; false positives)

==> improperly taking action based on incorrect or insufficient data

**inactions** based on “type II errors” (failed alarms; overlooked significance)

==> not taking action when it was indeed warranted

For some comprehensive discussions on the Precautionary Principle, refer to:

<http://www.biotech-info.net/uncertainty.html>

**RISK ASSESSMENT:** A final phase of the “risk paradigm” leads to the assessment of risk. In conclusion, numerous questions can be raised with regard to regulation and liability. The salient points regarding risk assessment pertain to the main, distinct issues regarding human health and aquatic health – as the two differ in many respects (as outlined in the above discussion).

Perhaps the main question with respect to risk assessment, is whether the current approaches to risk assessment are sufficiently inclusive of chemical exposure. Questions can be raised as to whether the approaches to environmental risk assessment and epidemiological studies sufficiently consider the “universe” of toxic substances involved in exposure – the corollary being whether the decades-long focus on conventional “priority pollutants” might give too narrow of a perspective.

In light of the complexities of the overall issue (esp. from the perspective of the *Risk Cup*), any regulatory decisions are ultimately NOT solely a matter of science – as they must also factor in a broad spectrum of complex, interacting societal values.

#### ***Environmental Health via Public Education?***

The Government Performance and Results Act of 1993 (GPRA) provides the mandate to Federal agencies to account for program results through the integration of strategic planning, budgeting, and performance measurement – with an emphasis on *outcomes* (e.g., impact) as opposed to *outputs* (e.g., products); a discussion of GPRA as cast for the science community can be found at:

<http://www.nsf.gov/sbe/srs/ostp/assess/nstcafsf.htm/>. A review of one version of EPA's GPRA plan by the House can be read at: [http://www.house.gov/science/epa\\_comments.html/](http://www.house.gov/science/epa_comments.html/).

If one accepts that public education may be the most cost-effective means of ensuring and effecting positive environmental change, in the final analysis, regardless of whether PPCPs in the environment prove to pose any concerns whatsoever, their major worth may well be as an educational tool – for their environmental presence serves as a highly visible signpost marking the doorway connecting humans and their environment. Capitalizing on this phenomenon as a teaching tool could be a significant output from an environmental protection program designed to attain a higher quality environmental outcome.

### ***Where to go from here?***

Even though the focus of this document is on that science that might be relevant to regulatory considerations, it is hard to end without an eye to the future. A number of recommendations have been put forth with regard to future research needs and near-term measures to reduce potential ecological and human health effects. These have been summarized in the references cited below. Future discussion regarding the contrasting views of the Precautionary Principle (<http://www.biotech-info.net/uncertainty.html>) as viewed from the U.S. and as implemented in various European countries might also be worthwhile.

**Learning Resources:** The U.S. EPA's Office of Research and Development, as well as other national agencies, have begun to consider the many scientific issues involved with this multifaceted environmental concern. An overview of the topic can be gained at the EPA's PPCPs web site [<http://www.epa.gov/nerlesd1/chemistry/pharma/index.htm/>], in the review article by [Daughton and Ternes](#) [[“Pharmaceuticals and Personal Care Products in the Environment: Agents of Subtle Change?”](#) *Environ. Health Perspect.* 1999, 107(suppl 6), 907-938], as well as in an upcoming book [Daughton, C.G.; Jones-Lepp, T. (eds.) **Pharmaceuticals and Personal Care Products in the Environment: Scientific and Regulatory Issues**, *Symposium Series 791*; American Chemical Society: Washington, D.C., 2001, in press].

The materials presented in this current document highlighted some of the many issues that might be involved in regulatory considerations for “emerging” environmental contaminants (such as PPCPs). For an overview of the current regulatory status of drugs in the environment, see [“FDA's Statutory Framework and the Evaluation of Pharmaceuticals for Potential Environmental Impacts”](#) (by Nancy B. Sager, Assoc. Director, Quality Implementation, U.S. FDA, Center for Drug Evaluation and Research; available at: [http://www.epa.gov/nerlesd1/chemistry/ppcp/21st-overview.htm#FDA's Statutory Framework/](http://www.epa.gov/nerlesd1/chemistry/ppcp/21st-overview.htm#FDA's%20Statutory%20Framework/)).

Other sources of current information can be obtained from past and future conferences devoted to the topic of PPCPs (see: <http://www.epa.gov/nerlesd1/chemistry/ppcp/conference-past.htm/> and <http://www.epa.gov/nerlesd1/chemistry/ppcp/conference-upcom.htm/>).

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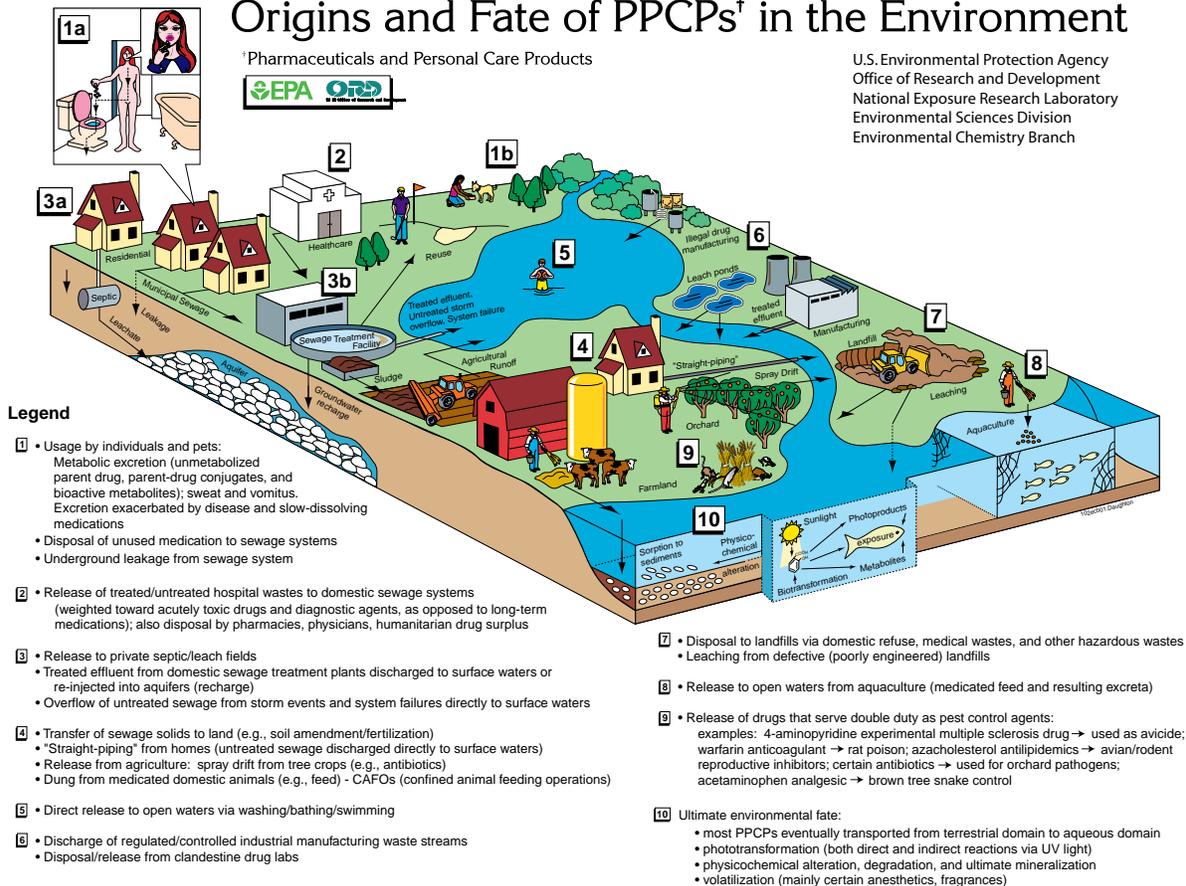
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# Origins and Fate of PPCPs<sup>†</sup> in the Environment

Pharmaceuticals and Personal Care Products



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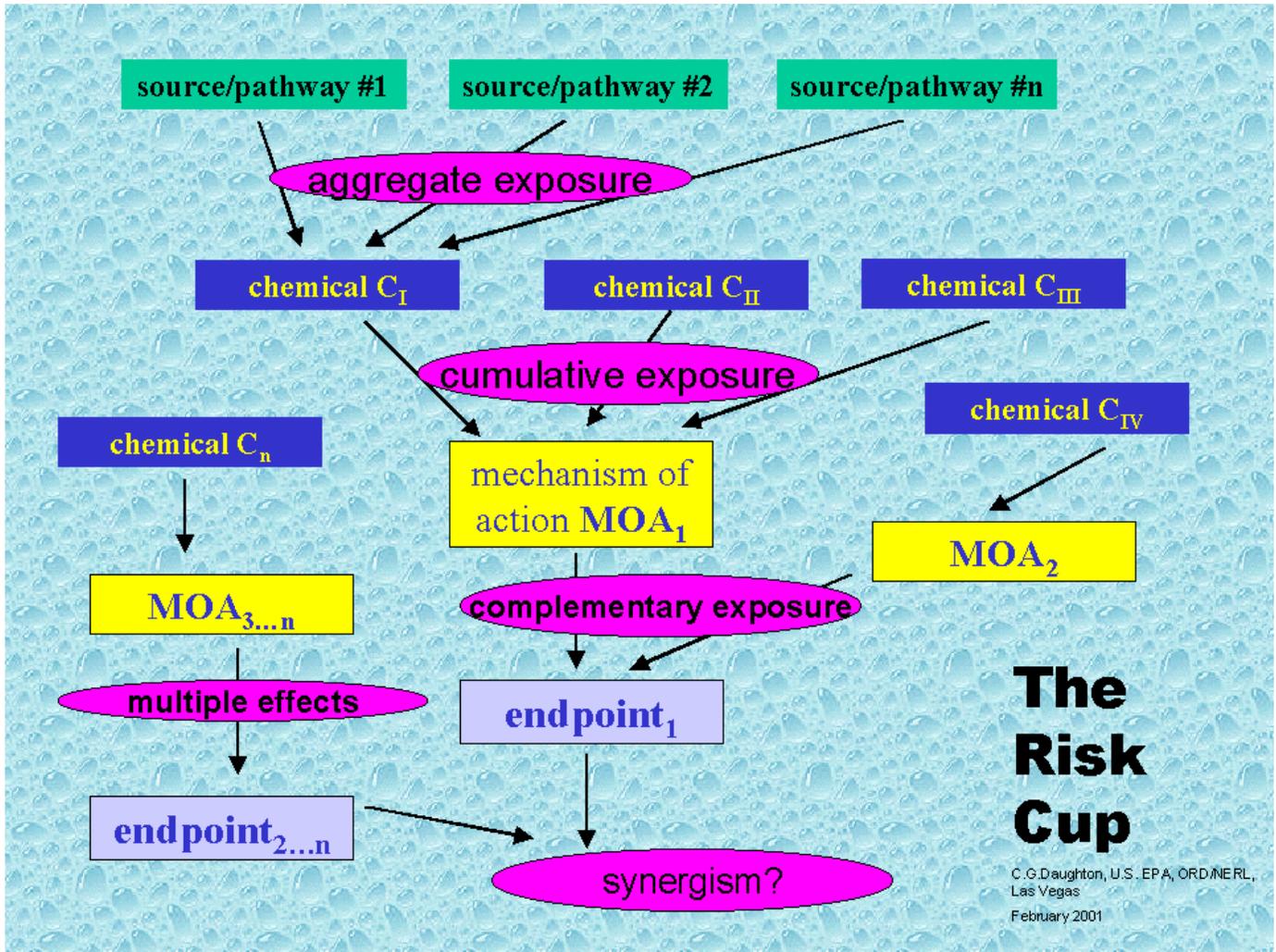
<http://www.epa.gov/esd/chemistry/pharm/index.htm>

## Origins and Fate of PPCPs in the Environment



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