

# PharmEcovigilance & Stewardship: Reducing Human and Ecological Exposure from Pharmaceutical Residues

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## ENVIRONMENTAL ISSUE

Pharmaceuticals can have impacts extending far beyond their intended uses, sometimes with unanticipated consequences for both human health and ecological integrity. The actions and behaviors of those involved in the healthcare system -- from drug manufacturers, physicians, insurers, and pharmacists, to patients themselves -- collectively (and usually unintentionally) contaminate the environment with many of the thousands of active pharmaceutical ingredients (APIs) used in medications. APIs are not always fully destroyed by the body and are then excreted into sewers. APIs applied to the skin have the same fate, as they are washed off during bathing or swimming. Another source for API contaminants is leftover medications, which are often flushed down toilets, tossed into the trash, or stockpiled in the home. Concerns for drug diversion from imprudent disposal in trash or from homes (such as teen recreational use), and accidental poisoning (especially children), have prompted numerous calls (most notably from the White House Office of National Drug Control Policy) for guidance on the prudent disposal of medications.

The work summarized here led to the first conceptualization of a stewardship framework for optimizing the use of pharmaceuticals throughout the healthcare system. Implementing some well-targeted actions in the delivery of health care could have profound, far-reaching benefits for human and ecological health, both of which are intimately linked. By integrating ecological concerns with conventional pharmacovigilance programs that track adverse drug events, a more holistic system for care of both human health and the environment could be created -- one we term *pharmEcovigilance*. Its implementation could reduce the cost of health care, improve therapeutic outcomes, and lessen unintentional acute and chronic exposures of humans and wildlife.

## RESEARCH GOAL

The objectives of this project were to:

- Catalog the diversity of locations where drugs are used and accumulate in society -- eventually requiring disposal.
- Define the processes that control and drive the consumption, accumulation, and disposal of human pharmaceuticals.
- Identify opportunities for pollution prevention and source reduction.
- Develop an approach for accurately identifying the APIs (and their actual quantities) being disposed.

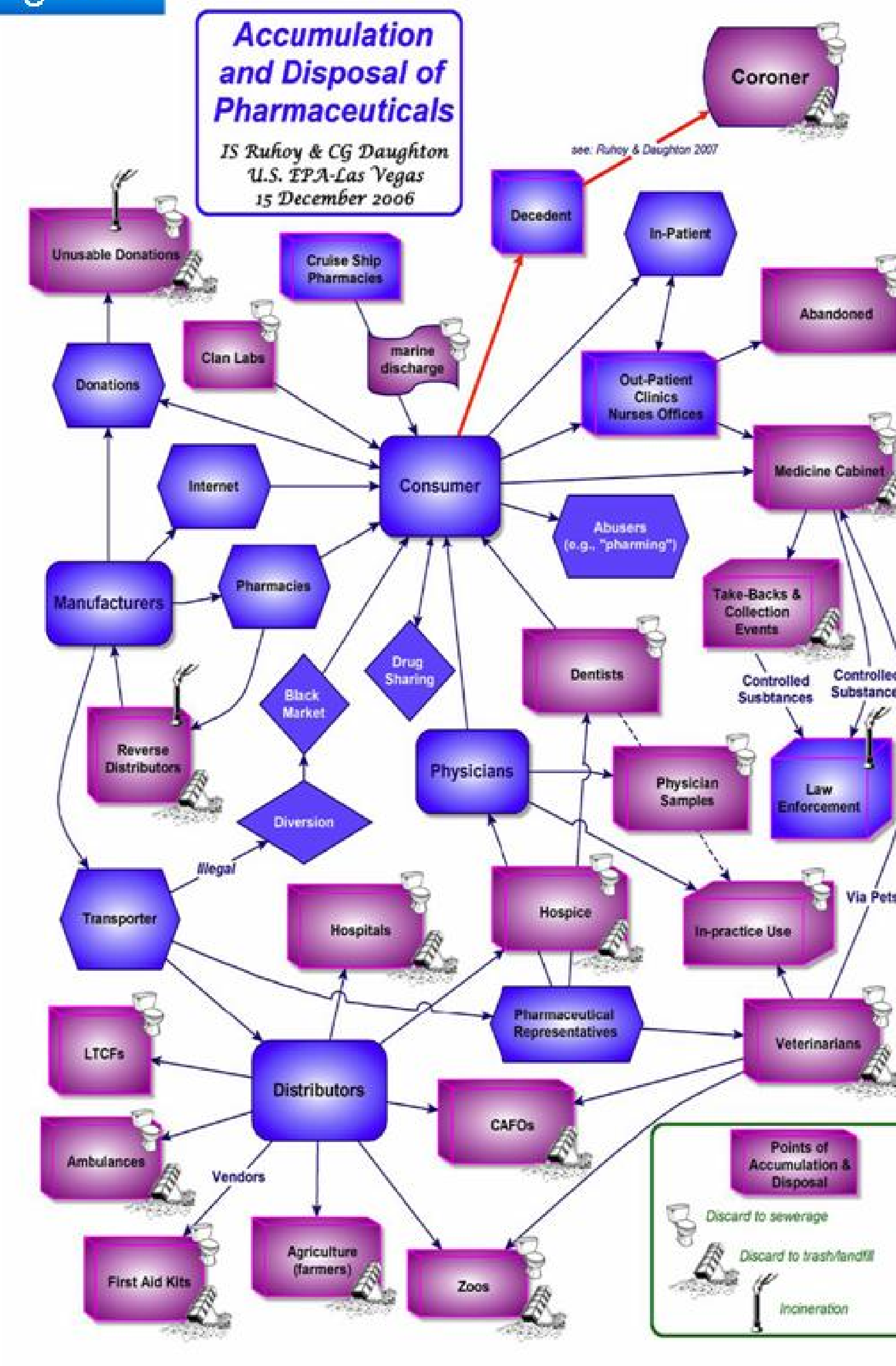
A new methodology was developed for identifying the types, and quantifying the amounts, of individual APIs that are disposed to sewage at the level of the local community. Such a tool had not been previously available. This new approach makes use of the very comprehensive and accurate inventory data collected by coroner offices as shown in Figures 1 & 2. This approach will lead to an eventual assessment of the relative significance or impact of drug disposal versus excretion/bathing on residues of APIs in the environment.

## METHODS/RESULTS

### Identification of Sources

Probably more than for any other perishable, nonfood item consumed by humans, medications are used and stored at a vast array of locations throughout society. These products are frequently purchased in excess or not fully consumed as directed (e.g., patient non-compliance), leading to the accumulation of unwanted, leftover drugs. A broad spectrum of locations at which drugs are used and can accumulate, eventually leading to disposal, are shown in Figure 1. The relative significance of each of these sources with respect to disposal is currently unknown.

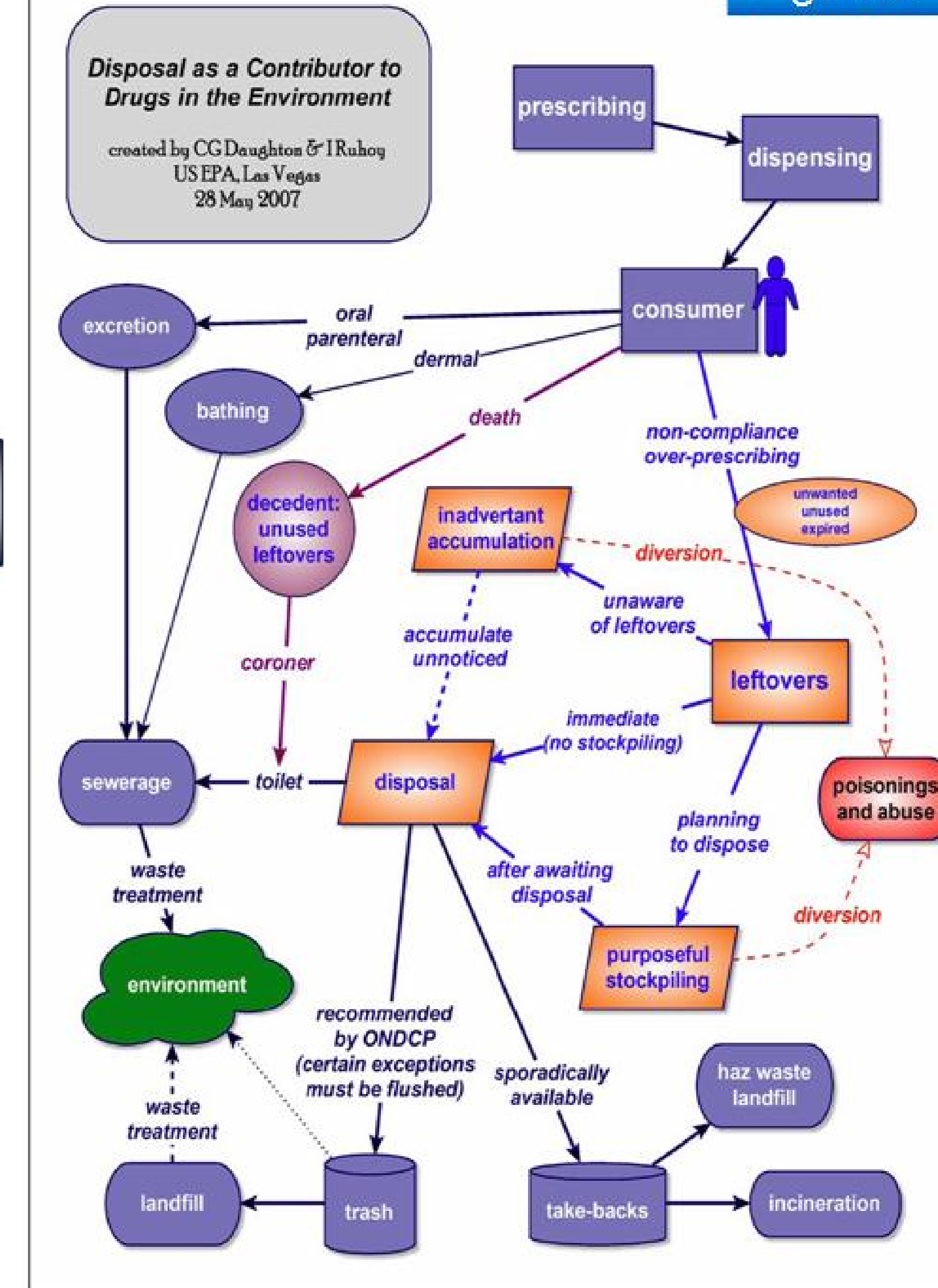
Figure 1



### Factors Governing Disposal

The processes leading to the disposal of drugs by the individual consumer are illustrated in Figure 2. A significant point is that accumulated, leftover medications pose several major problems for human health and safety and for the integrity of the environment. These problems result from the diversion of accumulated drugs to those for whom they were not intended (leading to accidental and purposeful poisonings of infants, children, adults, and pets) and from the disposal of accumulated drugs to trash and sewage. The latter promotes the entry of APIs to the ambient environment.

Figure 2



### Factors Governing Consumption and Accumulation

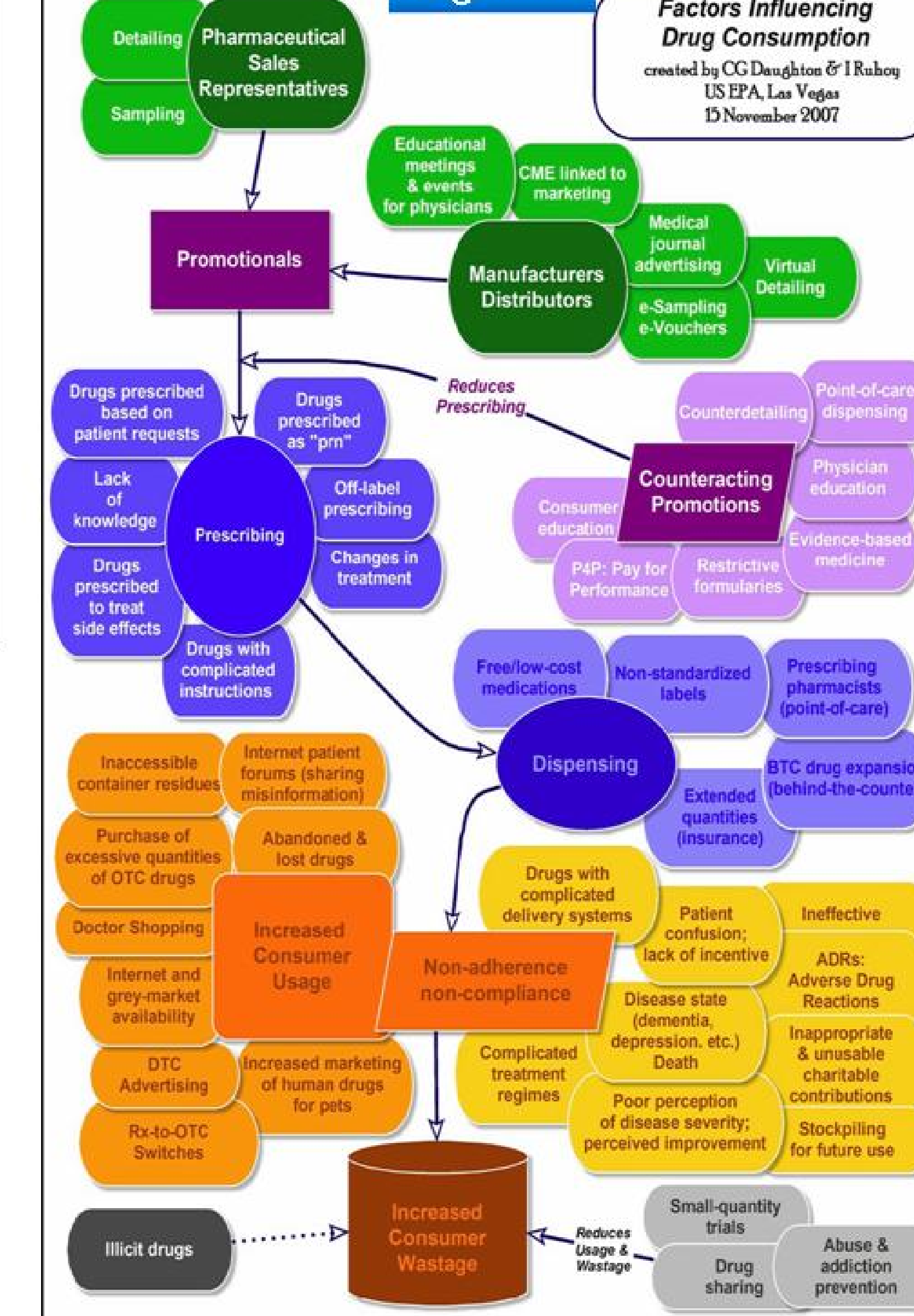
Numerous factors affect the consumption of drugs by consumers (Figure 3). Most serve to increase use, although several are at work to reduce use. Most of these factors are amenable to measures that could be designed to reduce their influence on the consumer. The significance of these factors is that each is amenable to targeting by various actions or activities to actively and substantially reduce the potential for drugs to accumulate on-site prior to their disposal.

### Possible Outcomes from Pollution Prevention

Pollution reduction/prevention measures aimed at the causes of unwanted, leftover medications could yield substantial benefits, including:

- reductions in the types and quantities of drugs that accumulate, and which then become targets for disposal or diversion,
- reducing healthcare costs (by lessening wastage from unused drugs), and
- improving healthcare outcomes (by ensuring patients are prescribed prudent amounts of medications and that they comply with prescribing directions).

Figure 3



### Products & Collaborators

This work resulted in five journal articles, five invited book chapters, a doctoral dissertation, and 12 invited presentations at local, regional, and national conferences [see list of publications at: *Drug Disposal: Ramifications for the Environment and Human Health*, U.S. Environmental Protection Agency, Las Vegas, NV (web page maintained by CG Daughton); available: <http://www.epa.gov/ppcp/projects/disposal.html>]. Expert consulting was provided to EPA program offices (OSW, OW, and OCHP), Regions, and various stakeholders in the public and private sectors.

## CONCLUSIONS

While the disposal of leftover drugs adds to the environmental burden of drug residues, it is currently not known how significant it might be. By identifying which drugs accumulate (Ruhoy and Daughton 2007), and where they accumulate (Ruhoy and Daughton 2008), measures could be implemented that would not only reduce the consequent need for disposal, but also improve healthcare outcomes and reduce healthcare expenses. This would be done preferably not by focusing on ecologically prudent methods for disposing of leftover medications, but rather by changing the human and healthcare processes that lead to accumulation in the first place -- to eliminate accumulation altogether.

If new approaches to medical care were developed that eliminated leftover drugs, the consequent environmental residues could be eliminated, therapeutic outcomes could improve, healthcare expenses could go down, and human morbidity and mortality (due to addictive usage and poisonings from diverted, leftover drugs) could decline. Reducing, minimizing, or eliminating leftover drugs represents a very significant opportunity to improve both ecological and human health.

## FUTURE DIRECTIONS

A major future focus will be to actively engage the healthcare communities, dispensers, and insurers in a productive dialog and in taking the first steps to address those facets of healthcare contributing to API pollution by adopting a pharmEcovigilance program. *The main focus is on identifying and reducing those sources of APIs that contribute to human and ecological exposure.*

A pharmEcovigilance program would focus on the numerous points along the network spanning from manufacturers to patients -- where medications are designed, packaged, prescribed, dispensed, and consumed, and where numerous processes and procedures could be redesigned to ensure optimal therapeutic outcomes from minimized drug use. The ultimate objective and measure of success would be the degree to which medications are fully consumed (reducing leftovers) while maintaining or improving therapeutic outcomes. Such a program could lead to a more efficient, optimized healthcare system, resulting in a cleaner environment and improved, less-costly treatment outcomes.

Another question needing resolution is determining the overall significance of drug disposal to sewers as a contributing factor for environmental residues of APIs.

## IMPACT

This work has been used as a basis for - or to inform or augment decisions regarding - a wide array of actions and activities, some of which include:

- the Committee on Environment and Natural Resources [CENR] Interagency Task Group on Pharmaceuticals in the Environment [PIE],
- Drug Enforcement Administration's policy on drug disposal and the Controlled Substances Act,
- White House Office of National Drug Control Policy's guidance on drug disposal,
- first statewide legislation for the disposal of unwanted drugs (State of Maine),
- EPA's first Drug Disposal Pilot Project grants (OCHP: Office of Children's Health Protection),
- extension of EPA's Universal Waste Rule to pharmaceutical waste,
- OW's Health Services Industry Study for the Effluent Guidelines Program,
- expanding the EPA's PPCPs Literature Database (<http://www.epa.gov/ppcp/lit.html>),
- the doctoral dissertation for Ilene Ruhoy (MD, PhD) at UNLV,
- several US Senate hearings on PPCPs,
- creation by Touro University of a new Institute of Environmental Medicine,
- responding to numerous inquiries and interviews from regulators, legislators, scientists, public, and press regarding the disposition of unwanted pharmaceuticals.