

# 1<sup>st</sup> National Survey Revealed Extent of PPCPs in Waterways

- **USGS “Reconnaissance” study in 1999-2000 was 1<sup>st</sup> nationwide investigation of pharmaceuticals, hormones, & other organic contaminants:**
  - 139 streams analyzed in 30 states
  - 82 contaminants identified (many were pharmaceuticals)
  - 80% streams had 1 or more contaminant
  - Average 7 contaminants identified per stream

# Drug Disposal Overview

- Unused medications become pharmaceutical waste
  - Historically, consumers and other institutions have been told to dispose of the drugs via the toilet or the trash
    - Ultimately reside in the environment
  - If not disposed, concern is availability for inappropriate usage of drugs
    - Diversion and poisonings
- Take-back events and programs
- Controlled Substances Act (CSA) 1970
- Stakeholders & Beneficiaries:
  - EPA, DEA, ONDCP, FDA, USFWS, state and local governments, municipal water districts, pharmacy & pharmaceutical industries, healthcare industry, insurance industry

# Environmental Impact of Disposal

- Pharmaceuticals enter the environment by both excretion and disposal of leftover, unwanted medications
  - Excretion comprises continual low-level contributions from multitudes of people
  - Disposal represents acute but transient and episodic contributions from fewer people
    - The only route that is subject most easily to pollution prevention or source control measures is disposal
- **Proper disposal is greatly complicated by the conflict between the need to protect public safety and the need to minimize aquatic (and terrestrial) exposure**

# Environmental Concerns from Pharmaceuticals

- Treatment (palliative, symptomatic and sometimes curative) and prevention of disease, together with improved quality of life, are highly visible aspects of a global industry with sales in 2007 exceeding U S\$700(BN)
- Medicines are designed to have biological effects in small doses
  - Non-target organisms are exposed
  - Possible subtle effects at very low concentrations
- There are 1000s of distinct compounds in medicines
  - Potential for synergistic effects with other medicines and/or other contaminants



# Exposure

- Chronic exposures to very low levels of multiple chemical stressors
  - Ecological: especially aquatic, but also terrestrial (from biosolids)
    - “Pseudo-persistence”
  - Human: via drinking water and foods
- Acute exposures to high levels of single stressors
  - Ecological: (e.g., drug-contaminated carcasses; unanticipated responses from non-target organisms - e.g., vultures and diclofenac)
  - Human: (drug diversion leading to accidental and purposeful human and pet poisonings)
- “Inappropriate” exposures (e.g., ingestion of medications intended for dermal or IV use; fetal exposure to chemotherapeutants)

# Environmental Pollution

- Water treatment
  - Significant percentage of sewage receives minimal or no treatment
    - Septic systems, straight-piping, storm over-flow
  - Conventional
    - Flocculation, coagulation, filtration
  - Advanced
    - Chlorination
    - Ozonation, reverse osmosis, activated carbon, nanofiltration membranes
- Some drugs STILL refractory
  - For example, carbamazepine, ibuprofen, 17 $\alpha$ -ethinylestradiol, meprobamate, dilantin, contrast agents, chemotherapeutics, some  $\beta$ -blockers
  - Not just parent compounds
    - Some metabolites and degradates are more mobile, more persistent, and potentially as toxic

# Effects on Aquatic Organisms: Cause for Concern

- “Pseudo-persistence”
  - Continuous, multigenerational exposure
- May be endocrine disruptors
  - alterations to sexual differentiation
    - Boulder Creek (feminization)
    - Potomac River (intersex)
  - reproduction and growth impairments
    - Antidepressants and frogs
  - behavioral effects
- More questions than answers about effects of pharmaceuticals on aquatic species & human health

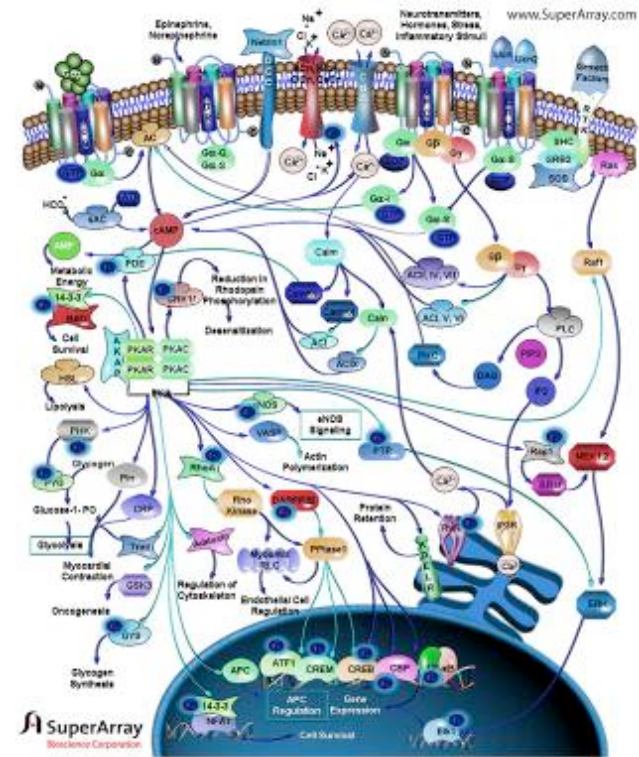


# Effects

- Ecological
  - Sex ratios
  - Feminization
  - Behavioral/Social
  - Neurological
  - Growth
- Human Effects
  - Largely unknown
  - Food chain
  - Antibiotic resistance
- Unintended Exposure in Vulnerable Populations
  - Faeroe Island Statement

FDA – environmental risk assessment

- Short term tests that measure how much of a compound is required to kill an organism outright or stunt its growth in a matter of days

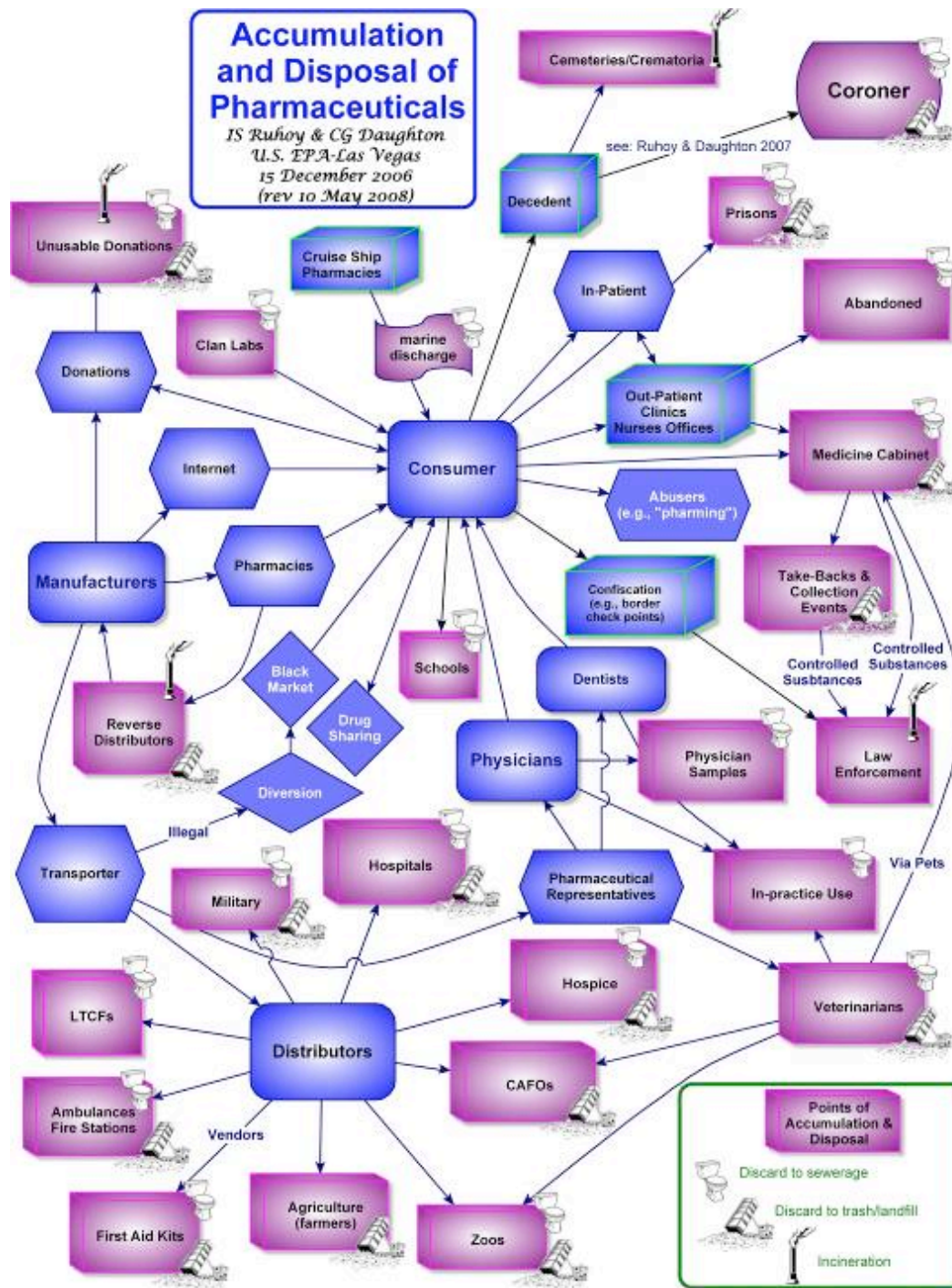


# Factors Leading to the Generation of Leftover, Unwanted Medications

- Promotionals
  - Prescribing
  - Dispensing
- Non-compliance

# Accumulation and Disposal of Pharmaceuticals

IS Ruhoy & CG Daughton  
U.S. EPA-Las Vegas  
15 December 2006  
(rev 10 May 2008)



# Pharmaceutical Accumulation

- Consumer Homes
  - Both human and animal medicine
- Physician Offices and Clinics
  - Samples and in-office procedure use
- Veterinarian Offices
- Animal Shelters
- Dental Offices
- Hospitals
- Long-Term and Chronic Care Facilities
- Decedent Homes
- Donations
- Schools (confiscation and health care offices)
- Military Bases
- Shelters
- Dialysis Centers
- Transfusion Centers
- First Responder Services
- First-Aid Kits
- Border Check Points
- Customs (airline and freight)
- Confined Animal Feeding Operations (CAFOs)
- Agriculture
- Aquaculture
- Zoos
- Clan Labs
- Cemeteries
- Cruise Ships
- Prisons and Jails
- Humanitarian Organizations

# Major Unknown

- **What fractions of drug residues occurring in the ambient environment result from discarding leftover drugs?**
  - No studies exist that provide objective data from well-defined populations to support any type of conclusion
  - Data are needed on the types, quantities, and frequencies with which drugs accumulate as household waste

## New Approach to Mining Data for Types and Quantities of Disposed Drugs

- Medications collected and disposed of by coroner offices are potentially a significant source of drugs in the environment
- Inventories of medications provide information regarding the categories and dosage amounts of medications disposed
- From the inventory data, the mass of each *active pharmaceutical ingredient* (API) can be derived

## New Approach to Mining Data for Types and Quantities of Disposed Drugs

- Understanding the categories and quantities of drugs disposed facilitates assessing potential impacts on both the environment and human health by helping:
  - health care practitioners to address inefficient prescribing practices and patient non-compliance
  - environmental scientists to better target APIs for monitoring purposes
  - assessment of risk to human health from chronic and/or acute exposures
  - policymakers (including those in the insurance industry) to begin to understand and confront the growing issue of wasted and discarded medications.
- **Ultimate Objective: No Leftover Drugs**

Summary of API Masses Disposed to Sewerage by a Coroner Office  
during a 12-Month Period: Categorized by Therapeutic Class

<b>ATC Code</b>	<b>ATC Main Group</b>	<b>Quantity (mg) disposed</b>	<b>#of APIs</b>	<b>% of Total</b>
A	Alimentary Tract	18,685,271	56	34.6
N	Nervous System	16,510,963	95	30.6
C	Cardiovascular System	6,331,976	71	11.7
J	Anti-infectives	5,608,735	45	10.4
M	Musculoskeletal System	3,851,949	21	7.1
R	Respiratory System	984,780	16	1.8
B	Blood	721,450	9	1.3
V	Various	622,800	1	1.2
P	Antiparasitics	236,269	2	0.44
L	Antineoplastics	186,013	14	0.34
G	GU System & Sex Hormones	146,440	23	0.27
H	Hormonal Preparations	50,601	10	0.09
S	Sensory Organs	4,375	1	0.008
D	Dermatologicals	3,420	3	0.006
<b>TOTAL</b>		53,945,042	367	

## Current Federal Activities

- Research—USEPA, USGS, FDA, CDC, NOAA, FWS, ARS, and others are evaluating environmental occurrence, effects, & treatment options
- Policy—USEPA water & waste programs reviewing applicable regulations
- Disposal guidelines
  - Office of National Drug Control Policy
  - US Fish & Wildlife/APhA/PhRMA SMARxT program



# Consequences of APIs in the environment

- Contamination of the environment
- Acute risks for wildlife
- Widespread, unintended exposure of the general public to 'recycled' APIs
- Diversion of unused, unwanted drugs, exacerbated need for disposal
- Contamination of drinking water
- Development of resistance to antibacterials

# Medical and Environmental Consequences of Accumulated, Leftover Medications

- Wasted healthcare resources
- Lost opportunities to treat
- Risky self—medication
- Unintentional poisonings
- Facilities diversion
- Imprudent disposal contaminates the environment

# PharmEcovigilance

Conventional pharmacovigilance expanded to encompass environmental concerns

Unify the parallel but interconnected needs for protecting both human and ecological health

## **Actions to reduce APIs in the environment and protect human health and safety**

- Unit dosing
- Trial scripts
- Low-quantity packaging of OTC medications
  - Increased monitoring of patient
  - Implement practice of concordance
    - Samples and donations
- Reduce incentives for excessive purchasing
  - Personalized medicine

## **Risk Management- Strategies to Abate the Risk of Transfer of Pharmaceuticals from Households to Inappropriate Locations**

- Morgan (1981) describes four alternatives for risk management:
  1. alter the built (man-made) or human (natural) environment
  2. avoid or modify exposure processes
  3. avoid or modify effects processes
  4. mitigate or compensate for effects

Morgan, M. G. (1981). Probing the question of technology-induced risk." IEEE Spectrum 18(11):58-64.

## **Risk Management- Strategies to Abate the Risk of Transfer of Pharmaceuticals from Households to Inappropriate Locations**

1. Modify likelihood that households will acquire pharmaceuticals that will not eventually be used
  - Develop alternative treatments
  - Tailor treatments
  - Trial scripts
  - Unit dosing
  - Short-term scripts

## **Risk Management- Strategies to Abate the Risk of Transfer of Pharmaceuticals from Households to Inappropriate Locations**

2. Modify likelihood that acquired pharmaceuticals will be used
  - Minimize non-compliance
  - Increased monitoring of patient
  - Concordance

## **Risk Management- Strategies to Abate the Risk of Transfer of Pharmaceuticals from Households to Inappropriate Locations**

3. Modify likelihood of successful transfer of unused pharmaceuticals to an appropriate location
  - Identify and inventory all unused pharmaceuticals
    - Collect in a centralized secure location
  - Facilitate transfer of unused pharmaceuticals to appropriate endpoints
  - Recognize major routes of inappropriate transfer
  - Develop take-back and collection programs
  - Educate patients on appropriate disposal options

## Risk Management- Strategies to Abate the Risk of Transfer of Pharmaceuticals from Households to Inappropriate Locations

4. Modify likelihood that pharmaceuticals transferred to an inappropriate location will have an adverse impact
  - Mitigate impacts of unused pharmaceuticals that have been transferred to an inappropriate location OR compensate for those impacts
  - Develop sewage treatment systems that remove pharmaceuticals
  - Encourage pharmaceutical manufacturer stewardship
  - Reduce environmental toxicity profile of drug without compromising therapeutic efficacy
  - Require environmental risk ratings of all drugs
  - Develop an understanding of treatment for toxin exposure
  - Charge fees to patients, pharmaceutical companies or others for inappropriate transfers
  - Increased law enforcement, addiction services, and social welfare

# Stewardship

- Stewardship involves much more than prudent disposal of leftover drugs
  - Actions taken to reduce PPCPs in the environment will have collateral benefits in also capturing chemicals we are currently not aware of and may improve morbidity and mortality
    - Federal Guidelines
    - Take-Back/Collection events

## Stewardship

- Drug disposal is not just an environmental issue, but also an acute human health concern
  - The very fact that excess drugs accumulate and need disposal points to problems in the way health care is administered
- A major objective should be the design of prescribing /dispensing practices that do not lead to the accumulation of leftover drugs
  - Leftover drugs represent wasted medical care resources and suboptimal therapeutic outcomes

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# **“Discarded Drugs as Environmental Contaminants”**

**SSIT Boston**

**Monthly Meeting**

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