Pharmaceuticals in the Environment

U.S. Environmental Protection Agency Workshop on

Pharmaceuticals in the Environment

August 22 -25, 2005

Pharmaceutical Research and Manufacturers of America

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Issue

- Pharmaceutical compounds are being detected in the environment
- There is concern that human health and aquatic life impacts may result from environmental exposure to pharmaceutical compounds

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Industry Perspective

- A science-based approach:
  - is required to understand and address concerns resulting from detection of pharmaceutical compounds in the environment
  - will identify gaps in existing knowledge that require further investigation regarding the potential for impacts

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Benefits of a Science Based Approach to PIE

- **This type of approach will:**
  - provide confidence to the industry, communities and governments that safety of pharmaceuticals in the environment is well understood
  - provide data needed to prioritize issues requiring further investigation regarding existence and significance of potential impacts

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P*h*RMA Activities

- Publications
  - P*h*ATE™ publication in ES&T (2004)
  - Letters to Editors on PIE publications
  - Publications by P*h*RMA members and associates
  - Human health risk assessment in Regulatory Toxicology and Pharmacology (2005)

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PhRMA Activities

- Publications - in progress
  - *"Pharmaceuticals in the Environment: Implications for Potential Aquatic Life Impacts",* in review at ES&T
  - Human and environmental risk assessments – in preparation
    - Carbamazepine
    - Analgesics
- Reproductive hormones being investigated by PhRMA member companies

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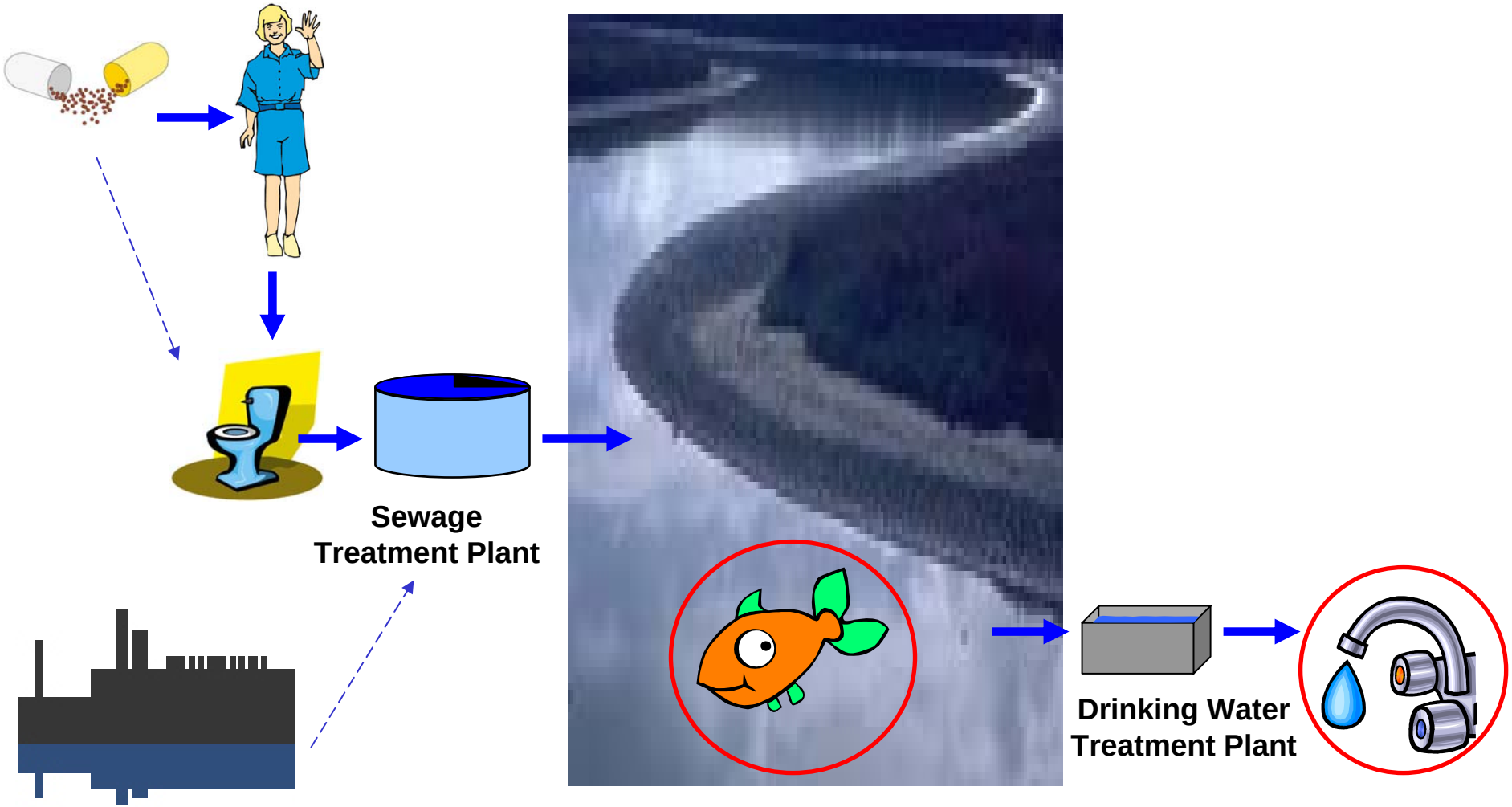
Pharmaceuticals in the Environment



Patient Use is the Primary Pathway by which Human Pharmaceutical Compounds Enter the Environment

P*h*ATE™ Model Development (2001)

- Watershed (drainage basin of receiving waterbody)
  - a geographic area in which water, sediments and dissolved materials drain to a common outlet
- Approach allows better understanding of the cumulative impact of human activities
- Many regions moving toward watershed based water quality management

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P*h*RMA – P*h*ATE™ Model

- Model predicts concentrations of pharmaceuticals in the environment due to patient use
- Model was developed by P*h*RMA PIE Task Force and AMEC Earth and Environmental
- Third party reviewers:
  - Dr. Josh Cohen, Harvard School of Public Health
  - Dr. Steve Chapra, Tufts University

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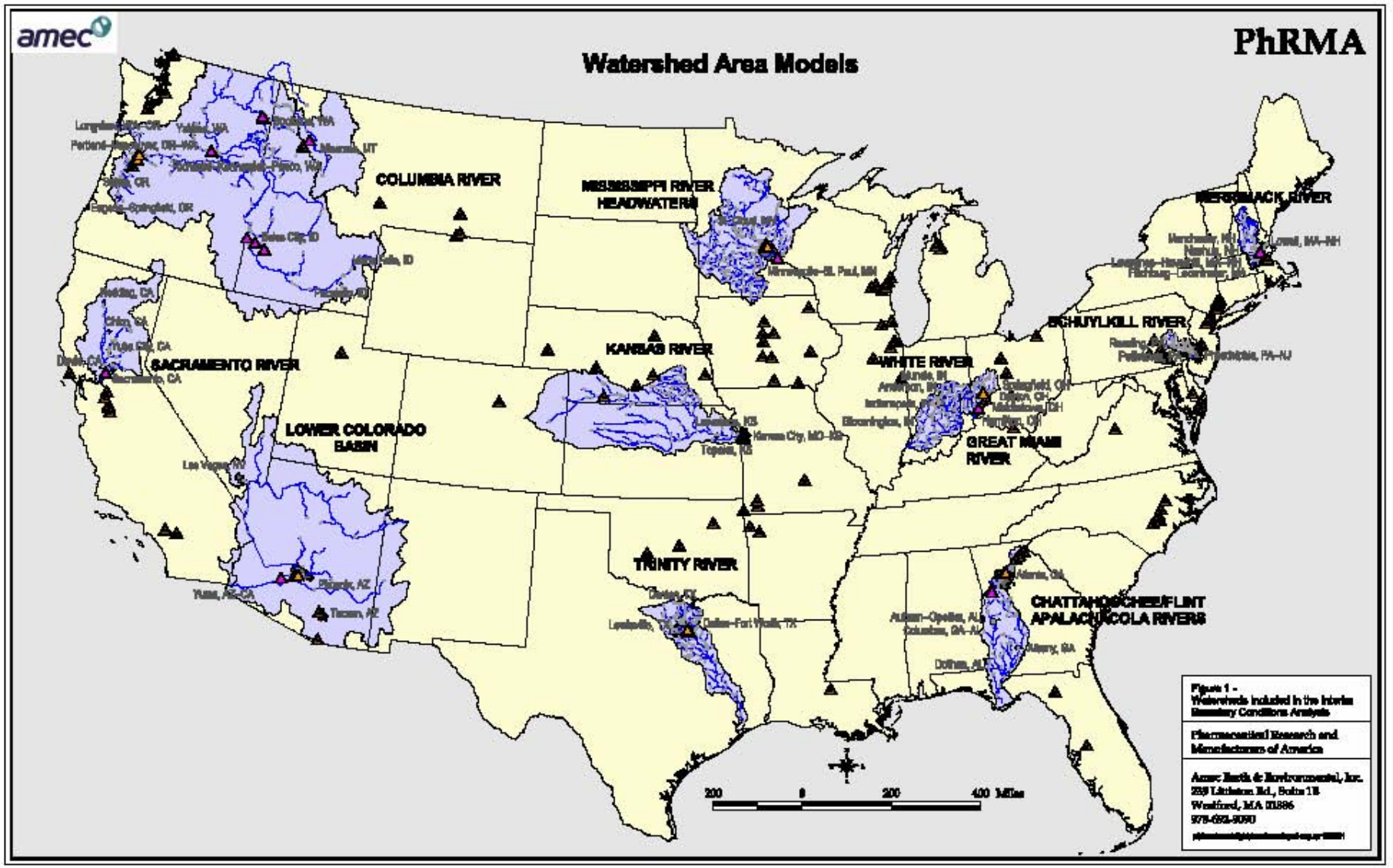
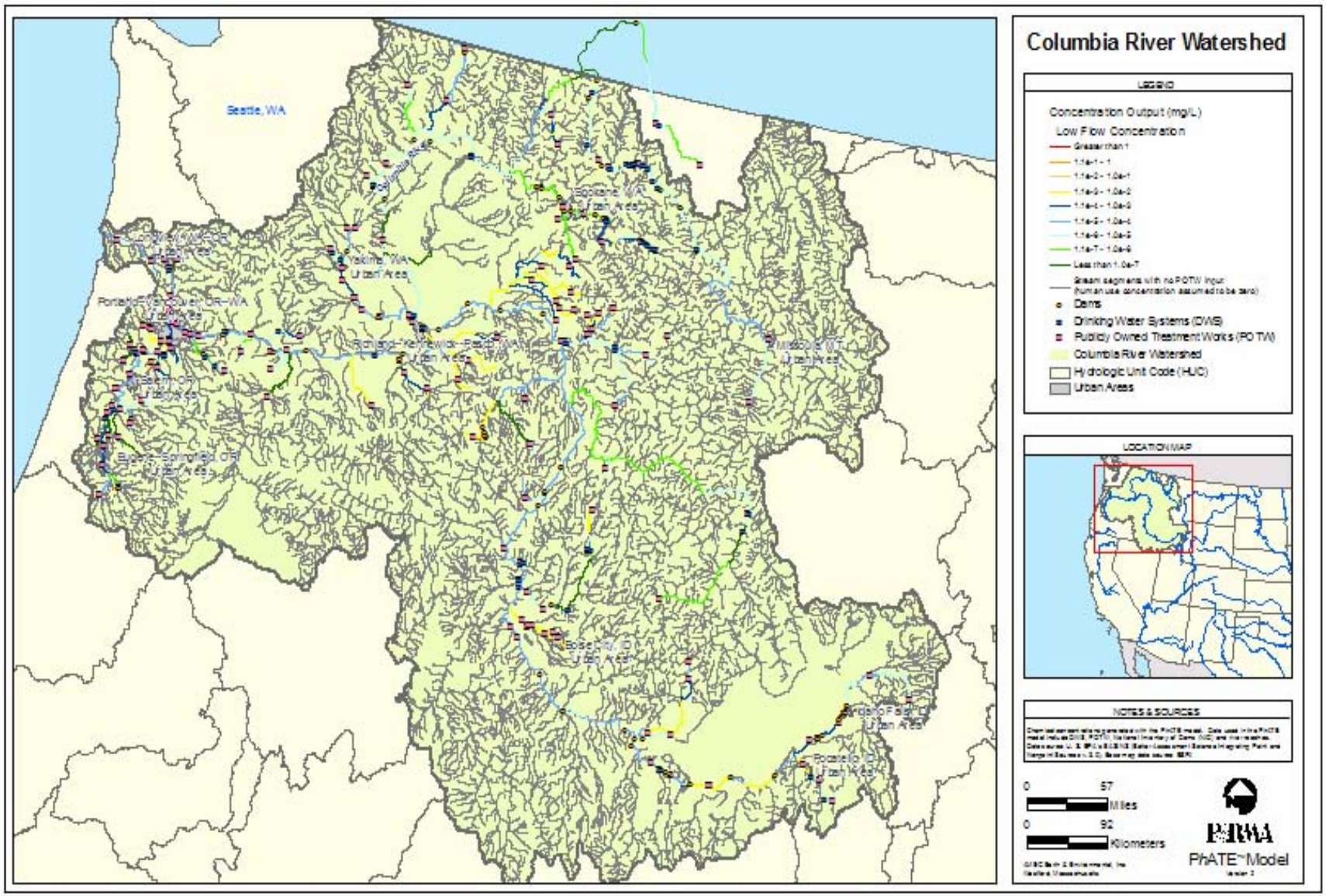
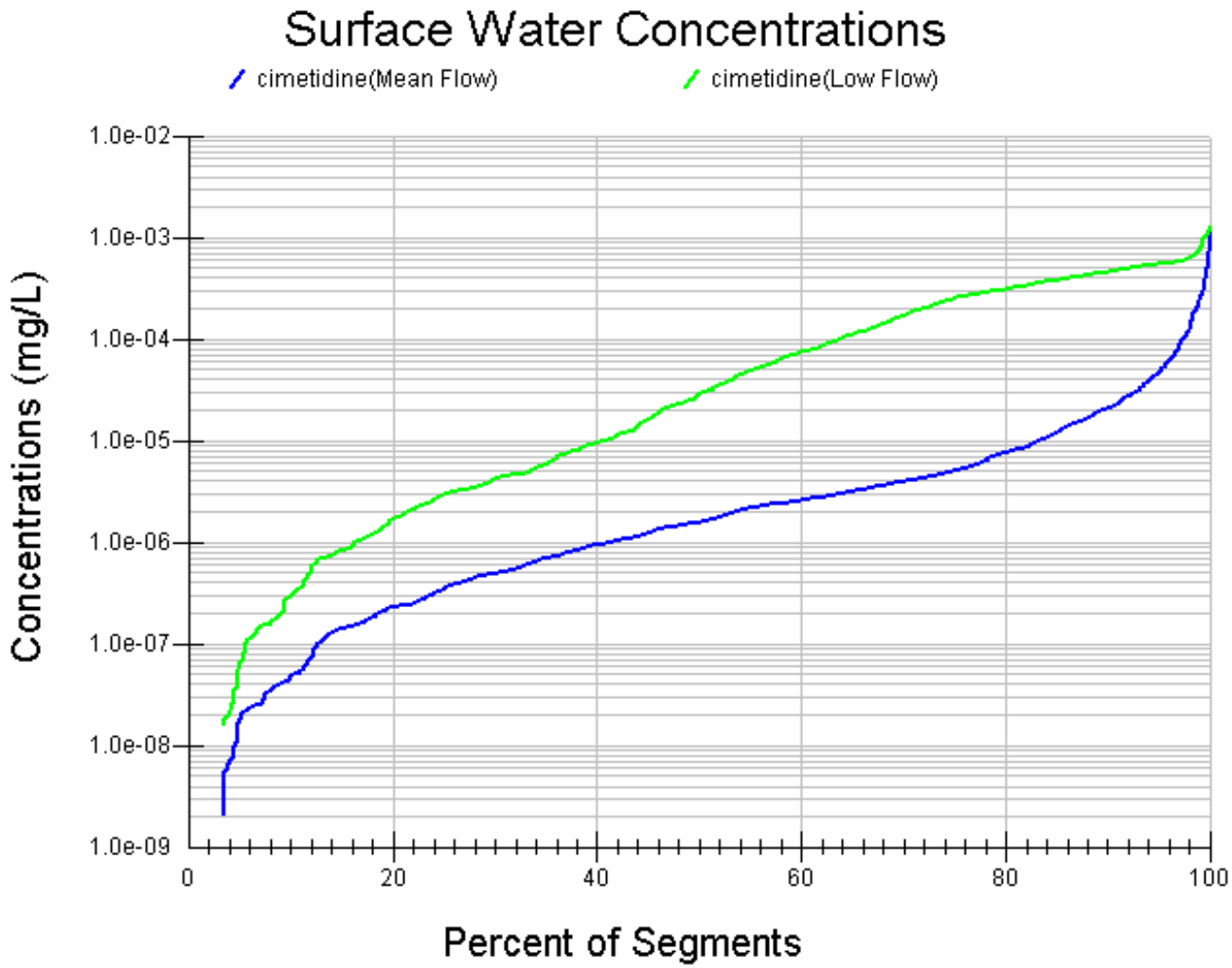



Columbia River Watershed
LEGEND
Concentration Output (mg/L)
Low Flow Concentration
Greater than 1
1.1e-1 - 1
1.1e-2 - 1.0e-1
1.1e-3 - 1.0e-2
1.1e-4 - 1.0e-3
1.1e-5 - 1.0e-4
1.1e-6 - 1.0e-5
1.1e-7 - 1.0e-6
Less than 1.0e-7
Stream segments with no POTW input (human use concentration assumed to be zero)
Dams
Drinking Water Systems (DWS)
Publicly Owned Treatment Works (POTW)
Columbia River Watershed
Hydrologic Unit Code (HUC)
Urban Areas
LOCATION MAP
NOTES & SOURCES
0 57 Miles
0 92 Kilometers
PhATE™ Model
Seattle, WA
Spokane, WA Urban Area
Yakima, WA Urban Area
Portland-Vancouver, OR-WA Urban Area
Richland-Kennewick-Pasco, WA Urban Area
Missoula, MT Urban Area
Salem, OR Urban Area
Eugene-Springfield, OR Urban Area
Boise City, ID Urban Area
Idaho Falls, ID Urban Area
Pocatello, ID Urban Area

Example P*h*ATE™ Output: cimetidine



Publications

- USGS Paper:

  Kolpin, et al., *Pharmaceuticals, Hormones, & Other Wastewater Contaminants in U.S. Streams, 1999-2000: A National Reconnaissance*, ES&T. 2002, 36, 1202-1211.

- P*h*ATE™ Paper:

  Anderson, et al., *Screening Analysis of Human Pharmaceutical Compounds in US Surface Waters,* ES&T. 2004, 38, 834-849.

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Summary of P*h*ATE™ Manuscript Findings

- P*h*ATE PECs generally had a good fit with USGS measured data.
- Comparing the PECs to the measured data identified some questionable analytical findings.
- P*h*ATE PECs allow the evaluation of potential effects at concentrations below detection limits.
- Comparing PECs to measured data allows the evaluation of the adequacy of POTW and in-stream removal mechanism data.

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Human Health Screening Analysis

Human pharmaceuticals in US surface waters: A human health risk assessment, Schwab, et al. **Regulatory Toxicology and Pharmacology, Volume 42, Issue 3, *Pages 296-312* (August, 2005)**

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Human Health Screening Analysis

- Analysis included 26 USGS human health pharmaceuticals
  - Non-steroidal analgesics, non-steroidal anti-inflammatory
  - Opiate analgesic
  - Bronchodilator
  - H2 receptor antagonists
  - Antimicrobial, antibiotics, antibacterial
  - Calcium blocker, ACE inhibitor, anti-hypertensives
  - Serotonin uptake inhibitors, anti-depressive
  - Hypoglycemic
  - Anti-coagulant
  - Cardiac glycoside
  - Anti-hyperlipidemic
- Compounds studied excluded hormones which are being evaluated separately due to the complexity of that evaluation

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Human Health Screening Analysis

- Identified measured environmental concentrations for compounds reported in published articles (MEC)
- Used P*h*ATE™ in screening mode to predict concentrations in environment

PEC

- Developed predicted no effect concentrations (PNEC)
  - Considered drinking water and fish consumption exposure pathways

PNEC

- Evaluated MEC/PNEC and PEC/PNEC ratios

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Human Health Screening

- Results of human health assessment indicate that residues of these pharmaceuticals in water present no appreciable risk to human health.

Other Human Health Publications

- Christensen, F.M. (1998) **Pharmaceuticals in the environment – A Human Risk?,** Reg. Toxicol. & Pharmacol., 28, 212-221.

- Schulman, et al., (2002) **A human health risk assessment of pharmaceuticals in the aquatic environment***,* Human & Ecological Risk Assessment, 8 (4), pp. 657-680.

- Mons, M.N., (2003) **Pharmaceuticals and drinking water supply in the Netherlands**, Kiwa N.V. Water Research.

- Webb, et al., (2003) **Indirect human exposure to pharmaceuticals via drinking water***,* Toxicology Letters, 142, 157-167.

All concluded that environmental exposure to human pharmaceuticals poses little human health risk.

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Development of Aquatic Life Data Base

- English language peer-reviewed literature
- Being populated with historic data
- Includes:
  - chronic and acute effects in surface water
  - fate and transport in the environment
  - treatment removal

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PhRMA Activities

- Expired/Unused Medicines
  - Evaluate and consider appropriate disposal and management options for expired/unused prescription medicines
    - Continuing to apply science based approach
    - Considering take-back in context of information available through PhATE, human health assessment and aquatic life data base

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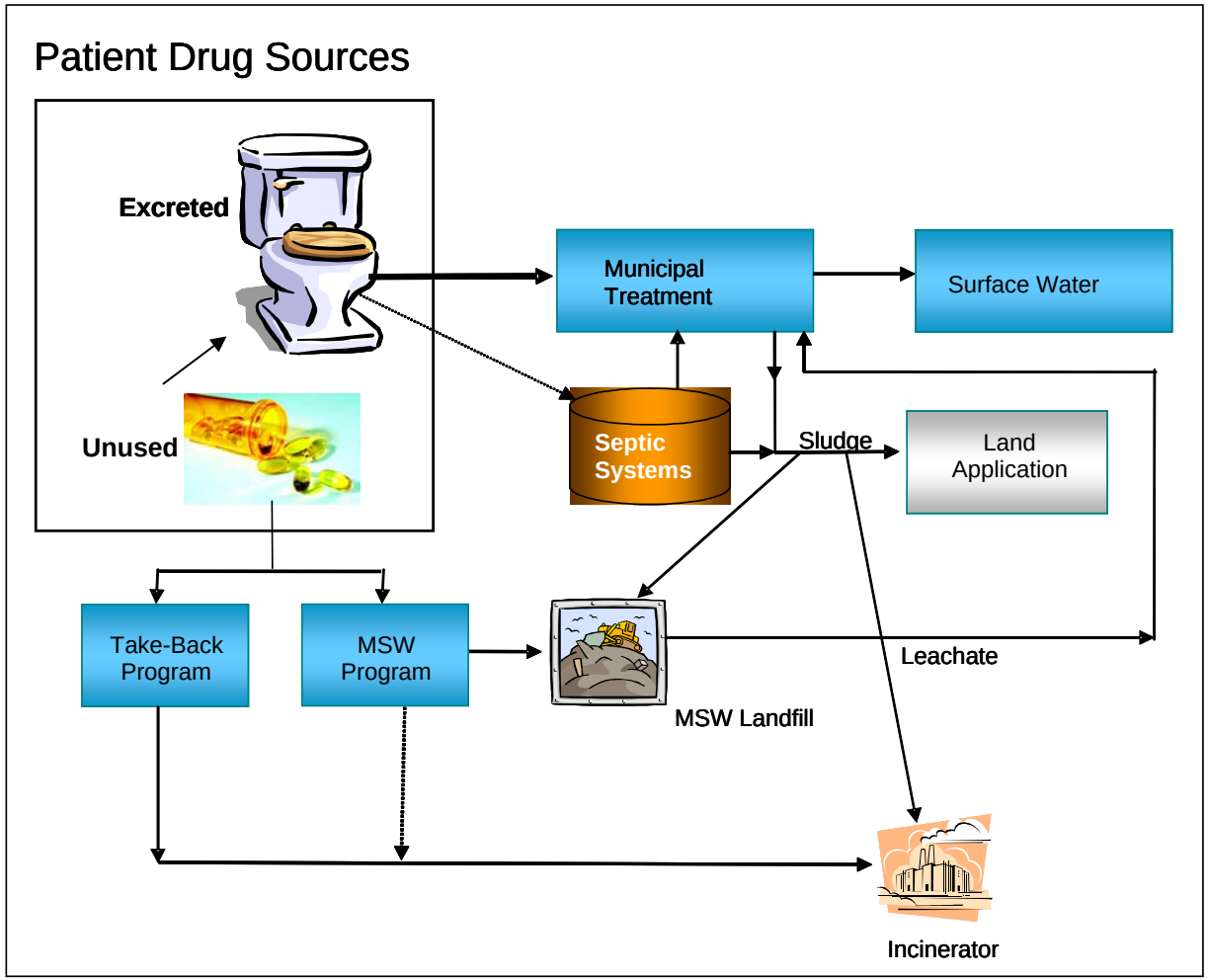
A simplified view of patient contributions to PIE



The quantity of unused medicines depends on the assumptions used.

Number of Prescriptions
3.4 billion

Weight of (Non-Hospital and Clinic) Prescriptions	
Pills:	40.0 MM lbs.
Pills & containers:	143.0 MM lbs.

By weight of pills and containers

% (Non-Hospital or Clinic) Prescriptions Unused			
20 %	10 %	5 %	Best Est. %
28.6 MM lbs	14.3 MM lbs	7.2 MM lbs	4.3 MM lbs

Based on blended individual and LTCF "wastage" rates

Unused medicines management practices vary depending on who holds the unused medicine.

Pharmacies

- Most unused medicines returned for credit

Hospitals

- Use their pharmacies to return for credit
- Unreturnables:
  - Ordinary IV → drain
  - Chemo IV → HW
  - Pills → Medical Waste

Long Term Care Facilities

- Source of 34% (1.5 MM lbs) of unused medicines
- 4% to 10% wastage
- Typical disposal practice is flushing down the drain

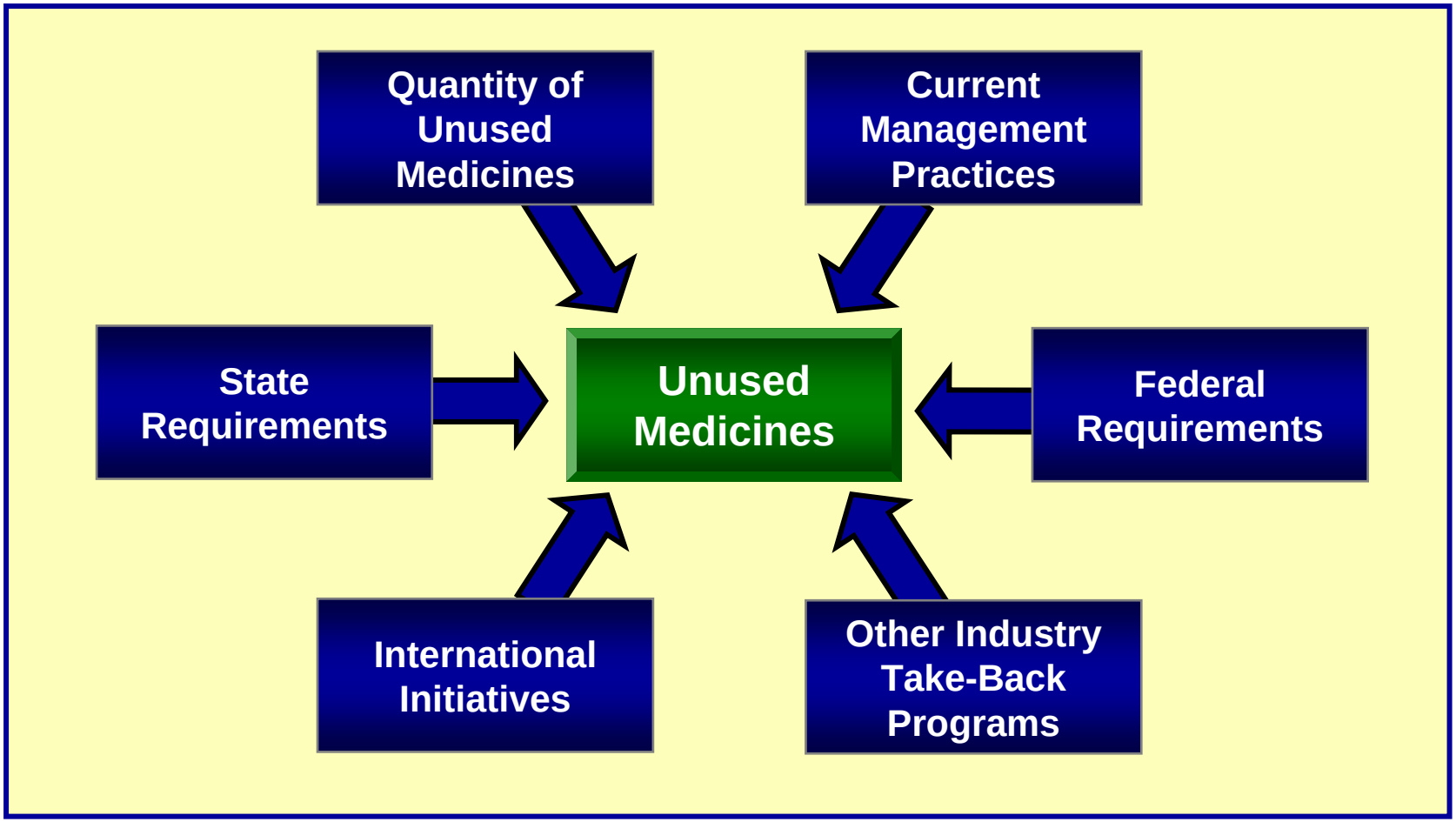
Individuals

- Source of 66% (2.8 MM lbs) of unused medicines

	Pittsburgh	Ontario
Trash	54%	31%
Drain	35%	46%
Keep	7%	
Pharmacy		17%

Expired/Unused Medicines

Factors that influence unused medicines



Review of other Take-Back programs

- Existing Take-Back Programs
  - BCI Lead-Acid Batteries
  - RBRC Rechargeable Batteries
  - CSCND Sharps
  - Eureka Sharps
  - TRC Thermostats
  - Staples Printer Cartridges
  - Collective Good Cell Phones
  - CTIA Cell Phones
  - Dell Computers

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Review of other Take-Back programs

- Program variables
  - Funding
  - Implementation
  - Collection
  - Incentive
  - Fate
  - Results

- Most products recycled or reused
- Most recovery rates < 20%
  - Exception is lead acid and rechargable batteries

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Sources of Expired/Unused Medicines

- Majority of pharmaceuticals in the environment come from patient use.
- Disposal of unused medicines in Subtitle D landfills is an insignificant source of environmental concentrations.
- Disposal of unused medicines by patients is a comparatively minor contributor to environmental concentrations.
- Long term care facilities could generate one-third of unused medicines.

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Unused Medicines – Considerations

- Drain disposal should be avoided

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Unused Medicine Disposal

- The pharmaceutical industry encourages patients to follow their doctor or pharmacist's instructions when taking prescription medications. However, from time to time it may be necessary to discard unused medications, for example when medications are no longer necessary or have expired.

- When discarding unused medications, it is important to do so in a way that minimizes the potential for harm to people, pets, or the environment. While no single preferred disposal method has been identified for all products and situations, it is generally acceptable to discard unused medications in household trash providing you have made it secure from children and pets. Consider securing any childproof closures and placing the medication in a sealed opaque bag or container to keep it out of sight.

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Unused Medicines – Considerations

- Decisions on take-back of prescription medicines need to consider:
  - ongoing occurrence, fate and effects research
  - effectiveness of the existing municipal solid waste infrastructure
  - local, state and federal regulatory requirements
  - rules and standards of the national and state boards of pharmacy
  - estimated recovery rates and public acceptance

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Summary

- The industry is committed to assessing the significance of pharmaceuticals in the environment using science- based approaches.
- The human health assessment indicates that pharmaceuticals in drinking water for the compounds investigated to date present no appreciable risk to human health.
- The industry is evaluating published data on aquatic life impacts and formulating an approach to assess the potential for impacts to ecosystems.
- The industry is continuing to research sources of unused medicine, to identify options for their disposal and to participate in discussions with stakeholders on these issues.

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