Pharmaceuticals in The Water Environment: Is The Problem Here or is it Just Around The Corner?

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By

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Presentation Outline

- How Long – PIEs
- The Early Reports
- Why Are We Just Hearing About It?
- The Universe of Sources
- What Do We Really Know?
- Are We at Significant Risk?
- Is The Problem Here?
- What Do The Experts Think?

Definition of Pharmaceuticals

For the purposes of this presentation, pharmaceuticals are defined as: Active pharmaceutical ingredients (API) in FDA-approved products for use in the diagnosis, cure, mitigation, treatment, or prevention of disease, or intended to affect the structure or any function of the body of humans or animals. This definition excludes ingredients that do not provide pharmacological activity, such as excipients and additives. This definition is also consistent with the FDA definition of API.

How Long Pharmaceuticals?

- Ever Since Humans Have Been medicated
- Since/Before Bayer's Aspirin
- Since/Before Dr. Fleming's Penicillin

What Has Changed?

- Increased Population Density
- Increased Use of Pharmaceuticals
- Increased Diversity of Pharmaceuticals
- Improved Analytical Methods Sensitivity
- Increased Discharge of Treated Sewage to Water Bodies
- A More Drug Oriented Society

The Early Reports

Monitoring Studies

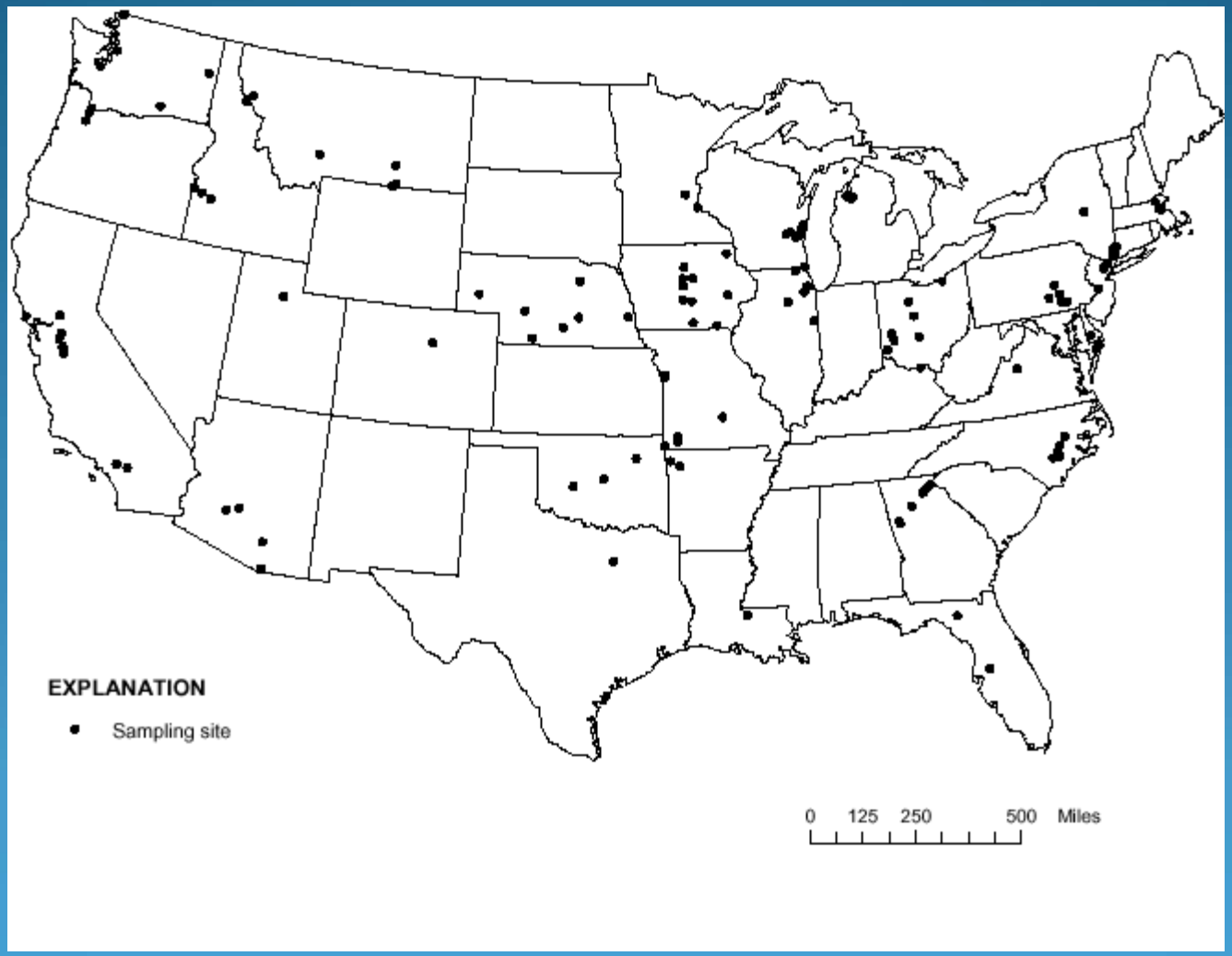
- Dominated by European Scientists
- Dominated by UK Scientists (Garrison, et al. 1976)
- Then the USGS (1990s)
- Some from S. Korea
- Then the USEPA

The USGS Reports

Monitoring Studies

- Occurrence Only
- Frequency of Occurrence
- Limited Number of Analytes
- Unvalidated Analytical Methodologies
- Questionable Data Reliability
- Recent Recall of Some Databases*

USGS Site Monitoring Map



Location of stream sampling sites, 1999 through 2000

Results of USGS Studies

(USGS) Kolpin (1999) Occurrence Data Only

No Data to be Presented Here

Nothing Exciting!!!

The US EPA Reports – (2009)*

- Occurrence Only – Influent & Effluent
- Analyzed for >100 Chemicals
- EPA Method 1694 for Pharmaceuticals
- EPA Method 1698 for Steroids & Hormones
- Improved EPA 1699 & EPA 1614
- Analytical Problems Delayed Project

*"Occurrence of Contaminants of Emerging Concern in Wastewater From Nine Publicly Owned Treatment Works." August, 2009.

Some Results of European Studies – (Ternes, 1998)

Influent/Effluent Data

Nothing Exciting!!!

No Data to be Presented Here!!!

The Universe of Sources

- All Pharmaceuticals Originate at the Production Facility
- Hospitals* ~ 6,000
- Extended Care Facilities* ~45,000
- Patients*
- Veterinary Medicine
- CAFOs/Farm Animals

Some Specific Source/Activities (1)

Manufacturing

- WW Discharge >POTWs
- Air Emissions
- Packaged Medicine to Distributors

Hospitals/Extended Care Facilities

- Patient Excretions >WW Discharge >POTWs
- Unused/Expired >Incinerators >Air Emissions
- Unused/Expired >Landfills >POTWs >Groundwater

Some Specific Source/Activities (2)

Patients

- Urine >POTWs
- Feces >POTWs
- Sweat* >POTWs

Patient's Commonality With Other Discharges

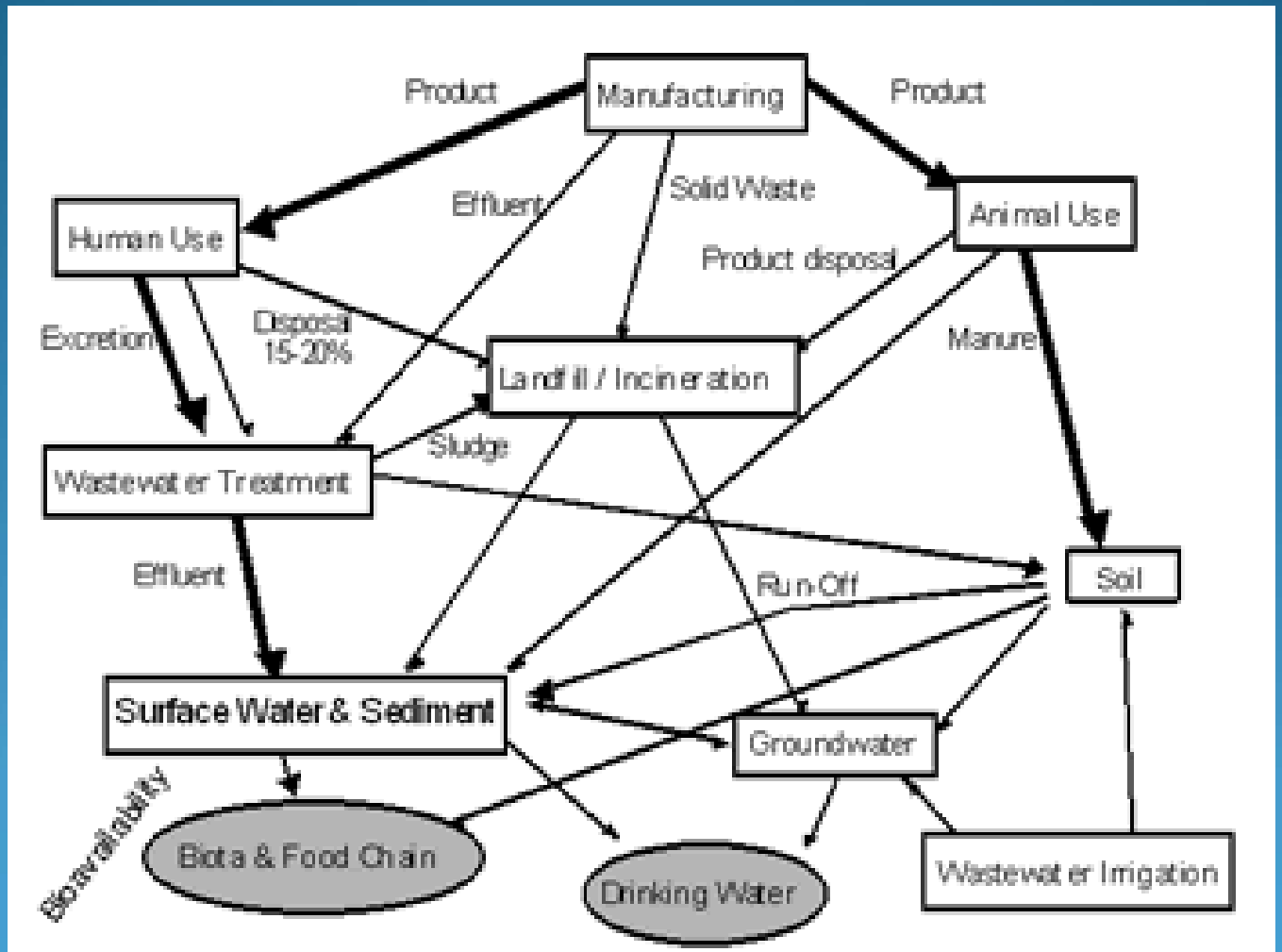
- Hospitals, Extended Care Facilities
- Homes, Churches
- Public Events/Sports

The Advent Of Sweat

(Daughton/Ruhoy, 2009)

- API via Sweat ~1950s
- Sweat-Patch Testing – Forensics
- Cocaine via Sweat – Unchanged Parent Form
- Published Excretion Data – Limited
- Up to 2% of Total Oral Dose Escape via Sweat

Pathway – After Sorensen



Modified from Halling-Sorensen, 1998

Patterns Of Medication Use in US (Slone, 2006)

- People >65 Years = Largest Consumers
- About 82% Take 1+Meds. in a Week
- About 30% Take at Least 5 Meds. in a Week
- About 20% Take at Least 10 Meds. in a Week
- The Use of Multiple Medications 5+ is Increasing

Contributions To PIEs

Human Medicine

- Most Significant source – Medicated Individuals
- More than 80+% to Water Environment
- Via POTWs >Surface Waters
- Via Septic Systems >Groundwater

Animal Medicine – Antimicrobials

- Therapeutic Uses – Low by Comparison
- Non-Therapeutic Uses (UCS, 2001)
  - ~24.6 million pounds in 2001
  - ~70% of Total US Antimicrobial Use (100 mg/lb meat produced)
- Total US Production ~35 million Pounds
- Lagoon/Storage Spills
- Run-Off From Manured Fields

Human Health Effects

- Pharmaceuticals Undergone Extensive Human Clinical Testing
- Example – Penicillin Since the 1940s
- Toxicological Databases are Rich
- Exposure Data are Needed for Risk Assessment
- Acute Risks not Considered Significant
- Chronic Risks ng/L API Lifetime – Not Known???

Lets Do The Math For Benicar

- Benicar @40mg/day = Therapeutic Dose
- Drinking Water <10ng/L or 100L to Ingest 1.0 µg of API, or
  100x1000L to Ingest 1.0 mg API, or
  40x100x1000L to Ingest 40 mg API
  = 4,000,000 Liters to Ingest 40mg API
- Drink 2L/day =4,000,000/2=2,000,000 days
  = 2,000,000/365= 5,479 Years to Ingest 40 mg of Benicar

What We Think We Know

Human Health Effects*

Compound	Finished Water Max. Conc. (ng/L)	Defined Daily Dose (mg)	Volume to Consume Single Dose (L)	Time to consume Single Dose (years)
atenolol	18	75	4,166,667	5,708
carbamazepine	18	**1,000**	55,555,556	**76,104**
Diazepam	0.33	10	30,303,030	41,511
fluoxetine	0.82	20	24,390,244	33,411
gemfibrozil	2.1	**1,200**	571,428,571	**782,779**
sulfamethoxazole	3	**2,000**	666,666,667	**913,242**

*Benotti et al. *ES&T* 2009

Some Characteristics Of Pharmaceuticals

- Complex Chemical Structures – Digestion
- Some Designed to be Toxic
- Some Designed to be Radioactive
- Some are Antimicrobials
- Some are Endocrine Modifiers

Water/Wastewater Treatment

- Existing POTW Bio. Systems are Inadequate Research With:
  - Extended SRTs
  - MBRs, Microfiltration
  - Activated Carbon, Fine Filtration
  - Reverse Osmosis
  - Thermal Hydrolysis
  - Ozonation

Industrial Waste Treatment – Wyeth, Ireland

Technologies Tested (Helmig, 2009, p, 273):

- GAC
- Thermal Destruction 90-100°C
- Acid & Alkaline Hydrolysis
- Advanced Oxidation – (O_3)
- Ultrasound

Industrial Waste Treatment – Wyeth, Ireland

Technologies Adopted:

- Membrane Bio-Reactor, Followed by
  - High-Level Ozonation (Helmig, 2009, p. 273)
- Flow ~650 m3/day ~170,000 G/d
- Some Operation Parameters – (Ozone)

Ozone System Operating Parameters

- Applied dosage: ~70 mg/L
- Contact Time: 1.2-1.5 hours
- Contact Pressure: 2.3 Bar (Atmo)
- WW Temp: 22.5°C
- Number of O_3 Injectors: 1of 3
- Ave. Ozone Mass Transfer Efficiency ~94.9%
- Process Parameters at End of Presentation (Helmig p.272-3)

So Is The Problem Here?

- Are We at Significant Risk
- What is the Extent or Level of Risk

General Consensus:

- The Human Health Assessment Indicates that Pharmaceuticals in Drinking Water for the Compounds Investigated to Date Pose No Appreciable Risk to Human Health

What Do The WHO Experts Think

(The June 2009 Singapore Meeting)

Occurrence:

- Available studies show traces of a few pharmaceuticals in water in the low ng/L range, typically more than 1,000 times less than the therapeutic doses
- Treatment effectiveness is reasonably predictable based upon the physical and chemical properties of the compounds

What Do The WHO Experts Think
(The June 2009 Singapore Meeting)

Human Health risk:

- Based upon current evidence on margins of exposure to individual compounds, the development of global drinking water quality guideline values for pharmaceuticals is not warranted
- Screening values can be developed. Various methodologies have been developed and they are typically based upon human data and modeled exposure data
- Currently risk assessment methods do not explicitly address human health effects at low-level chronic exposure to chemical mixtures, including pharmaceuticals

What Do The WHO Experts Think
(The June 2009 Singapore Meeting)

Human Health risk (contd.):

- Appreciable adverse impacts on human health are unlikely at current levels of exposure from drinking water
- Concerns over pharmaceuticals should not divert water suppliers and regulators from pathogenic microbial water quality issues

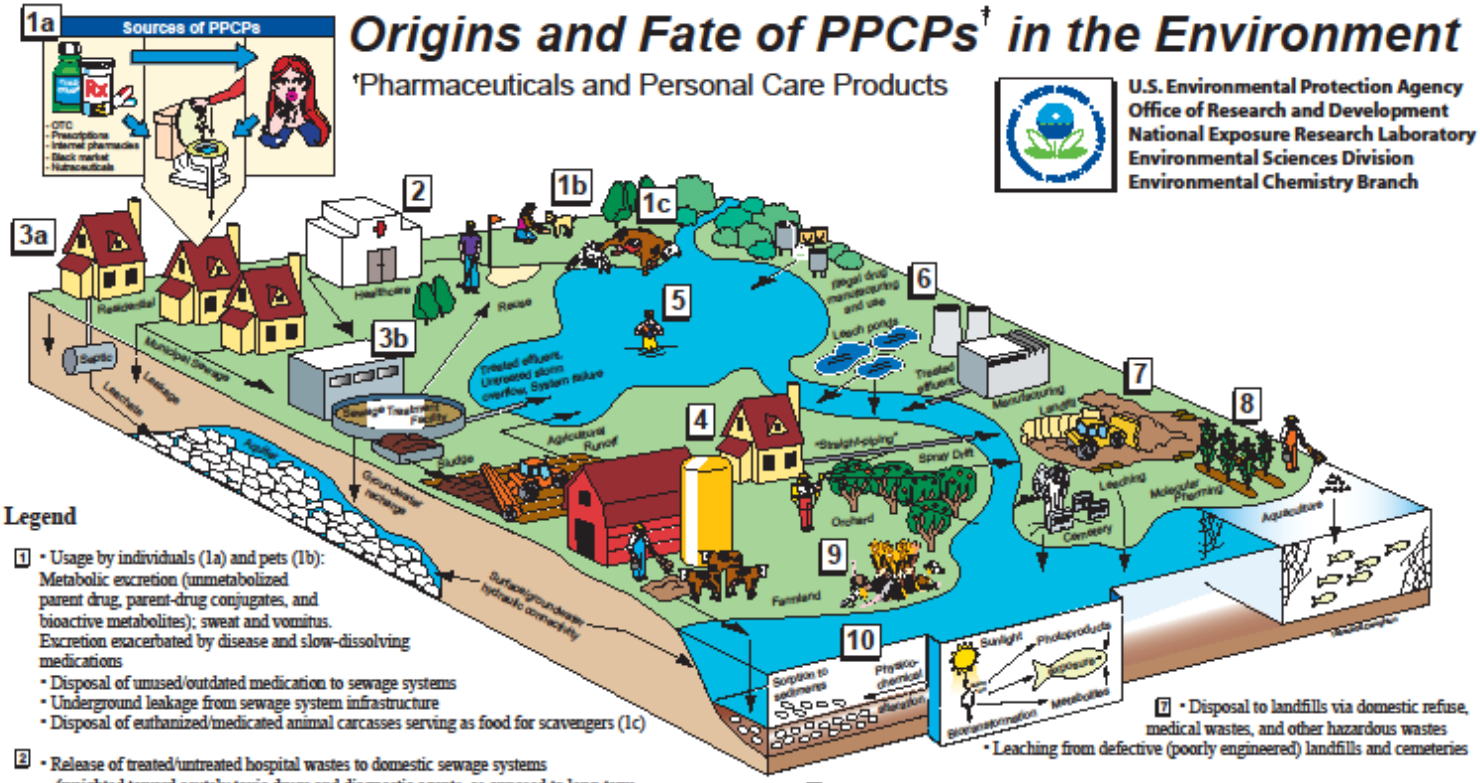
What Do The WHO Experts Think
(The June 2009 Singapore Meeting)

Human Health risk (contd.):

- Current evidence does not support a general requirement for additional or specialized drinking water treatment to reduce levels of pharmaceuticals from water sources
- Enhanced preventive measures including education for prescribers and the public can reduce disposal and discharges to the environment and reduce human exposure from drinking water

QUESTIONS?

Pathway - USEPA



Legend

1 • Usage by individuals (1a) and pets (1b): 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/outdated medication to sewage systems
- Underground leakage from sewage system infrastructure
- Disposal of euthanized/medicated animal carcasses serving as food for scavengers (1c)

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 (3a)
- Treated effluent from domestic sewage treatment plants discharged to surface waters, re-injected into aquifers (recharge), recycled/reused (irrigation or domestic uses) (3b)
- Overflow of untreated sewage from storm events and system failures directly to surface waters (3b)

4 • Transfer of sewage solids ("biosolids") 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 and illicit drug usage

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

8 • Release to open waters from aquaculture (medicated feed and resulting excreta)
- Future potential for release from molecular pharming (production of therapeutics in crops)

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; caffeine, stimulant → *coqui* frog control

10 Ultimate environmental transport/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)
- some uptake by plants
- respirable particulates containing sorbed drugs (e.g., medicated-feed dusts)

Christian O. Daughton, U.S. EPA-Las Vegas

March 2006
(original February 2001)

http://epa.gov/nerlesd1/chemistry/pharma/images/drawing.pdf
from: http://epa.gov/nerlesd1/chemistry/pharma/