Pharmaceuticals and Endocrine Disruptors: Implications for Water Sustainability

Southern Nevada Water Authority

Shane Snyder, Ph.D.

Applied R&D Center

Southern Nevada Water Authority

WATER RESEARCH FOUNDATION

ADVANCING THE SCIENCE OF WATER

The New York Times
nytimes.com

August 10, 2008

A Tall, Cool Drink of ... Sewage?

By ELIZABETH ROYTE

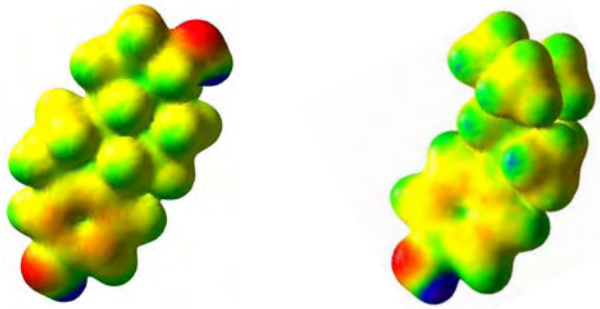
All water on earth is recycled: the same drops that misted Devonian ferns and dripped from the fur of woolly mammoths are watering us today. From evaporation to condensation and

Sex Hormonal Action and Chemical Constitution

F. W. Schueler

University of Chicago

The following communication presents a new hypothesis regarding the essential chemical and structural features sufficient for male and female sex hormonal activity as evidenced by comb growth in the



BIODEGRADATION OF STEROID HORMONES

Elisabeth Stumm-Zollinger and Gordon M. Fair

Hormones in Wastewaters

Steroid hormones generally find their way into wastewaters and with them into natural surface and under-

in notable degree. Nevertheless, it is our responsibility to learn in what amounts steroid hormones may occur in our drinking waters under the most unfavorable conditions, some of which already have been cited. To this pur-

CHAPTER 30

GC/MS ANALYSIS OF ORGANIC COMPOUNDS IN DOMESTIC WASTEWATERS

A. W. Garrison, J. D. Pope and F. R. Allen

U.S. Environmental Protection Agency
Southeast Environmental Research Laboratory
Athens, Georgia

INTRODUCTION

In 1971 this laboratory began a program to identify extractable, volatile organic compounds in domestic wastewaters. Objectives were to develop analytical techniques for such analyses, to identify compounds being discharged into surface waters after secondary or advanced treatment, and to provide specific compound data that will help to determine waste treatment effectiveness. Knowledge of the specific compounds discharged is needed to study health effects of pollutants, to help determine the sources of compounds found in drinking water surveys,[1] and to establish effluent guidelines. Finally, some parts of the world are

Table 30.1, Continued

	Concentration in Wastewater, μg/l (+ = Present, not quantified)							
	Raw Wastewater		Activated Sludge Effluent		Physical-Chemical Effluent		Lime-Clarified Raw Sewage	
Compound by Class	8/72	12/73	8/72	12/73	8/72	12/73	Before Chlorination	After Chlorination
1,1,2,2-Tetrachloroethane	+							+
1,1,1,2-Tetrachloroethane								+
Steroids								
Cholesterol		+		+				
Coprostanol		+		+				
Drugs and Drug Metabolites								
Caffeine	+	+		+			+	
2-(4-Chlorophenoxy)-2-methylpropionic acid[a] [Clofibrate metabolite]		0.8	1.0	2.0		0.1	+	+
Nicotine		+		+			+	
Salicylic acid[a]	+	+						

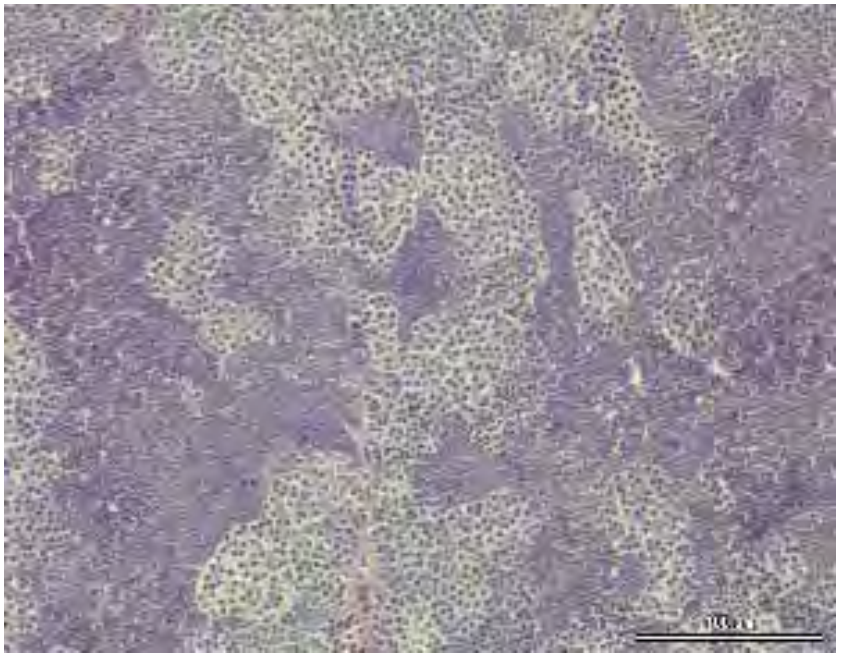
Garrison, Pope, and Allen - 1975

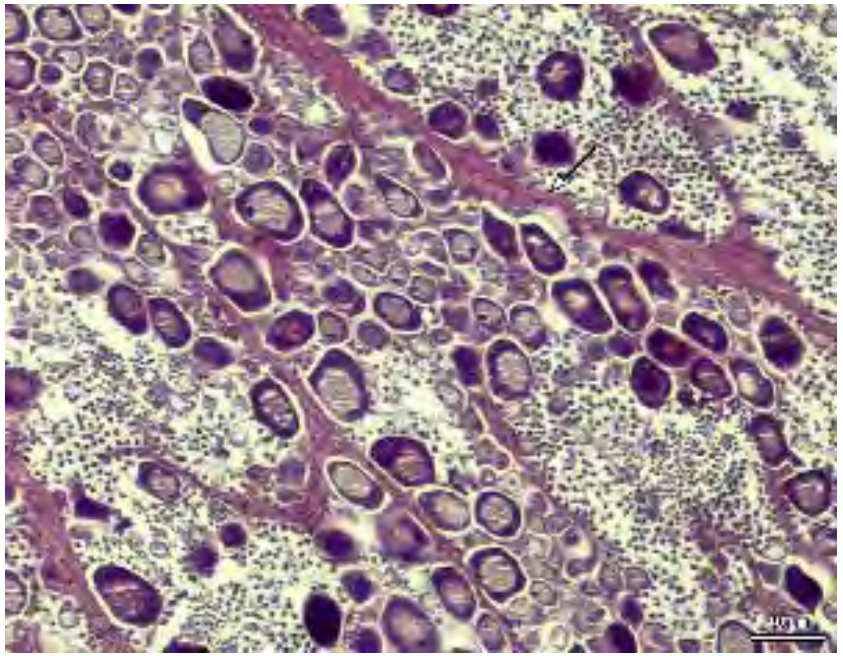
Chemistry and Ecology, 1994, Vol. 8, pp. 275–285

ESTROGENIC EFFECTS OF EFFLUENTS FROM SEWAGE TREATMENT WORKS

C.E. PURDOM,[1] P.A. HARDIMAN,[1] V.J. BYE,[1] N.C. ENO[1],
C.R. TYLER[2] and J.P. SUMPTER[2]

[1]*Ministry of Agriculture, Fisheries and Food, Fisheries Laboratory, Lowestoft NR33 0HT;* [2]*Department of Biology and Biochemistry, Brunel University, Uxbridge UB8 3PH*





U.S. Department of the Interior—U.S. Geological Survey

SYNTHETIC ORGANIC COMPOUNDS AND CARP ENDOCRINOLOGY AND HISTOLOGY IN LAS VEGAS WASH AND LAS VEGAS AND CALLVILLE BAYS OF LAKE MEAD, NEVADA, 1992 AND 1995

Water-Resources Investigations Report 96-4266

Nevada Basin and Range Study Unit
National Water-Quality Assessment Program

By Hugh E. Bevans[1], Steven L. Goodbred[2], John F. Miesner[3], Sharon A. Watkins[1], Timothy S. Gross[4], Nancy D. Denslow[4], *and* Trenton Schoeb[4]

ABSTRACT

The Nevada Basin and Range study unit of the National Water-Quality Assessment Program, U.S. Geological Survey, in cooperation with the National Park Service, National Biological Service, and U.S. Fish and Wildlife Service, investigated the occurrence of organochlorines and semivolatile industrial compounds in the water column, bottom sediment, and carp (*Cyprinus carpio*) tissue at five sites in Las Vegas Wash and Lake Mead. Endocrine systems of carp were assessed by analyzing concentrations of female and male sex-steroid hormones, 17β-estradiol and 11-ketotestosterone, and vitellogenin (an estrogen-controlled egg protein) in blood-plasma samples. The histology of carp gonads, hepatopancreas, kidney, gill, and lower intestine were analyzed for effects that can result from endocrine disruption or exposure to toxicants.

Organochlorines (pesticides and industrial compounds) and semivolatile industrial compounds were detected in semipermeable membrane devices and bottom-sediment samples; only organochlorines were detected in carp-tissue samples. Concentrations of organochlorines were higher in Las Vegas Wash and Bay than in Callville Bay (the reference site) for the three media that were sampled. Results of a carp-tissue bioassay indicated the presence of dioxins or furans with low toxic-equivalent factors relative to 2,3,7,8-tetrachlorodibenzo-*p*-dioxin in Las Vegas Wash and Las Vegas and Callville Bays. Patterns of necrosis observed in hepatopancreas and kidney samples from carp are consistent with long-term subchronic exposure to toxicants. Polycyclic aromatic hydrocarbons, phthalates, and phenols also were detected at higher concentrations in bottom-sediment samples from Las Vegas Bay than in a comparable sample from Callville Bay. Polycyclic aromatic hydrocarbons were detected in samples from semipermeable membrane devices from all sites.

Endocrine disruption in carp from Las Vegas Wash and Bay, as compared to Callville Bay, is evidenced by high concentrations of 11-ketotestosterone levels in blood-plasma samples of female carp in Las Vegas Wash, low concentrations in male carp from Las Vegas Bay, and low 17β-estradiol concentrations in male carp from Las Vegas Bay. The most compelling evidence of endocrine disruption is the presence of vitellogenin in blood-plasma samples of male carp from Las Vegas Wash and Bay and elevated concentrations in female carp from Las Vegas Bay.

Many of the organochlorines and semivolatile industrial compounds detected in semipermeable membrane devices, bottom sediment, and carp tissue from Las Vegas Wash and Bay have been linked to endocrine disruption in fish by previous investigations of other areas. The endocrine disruption observed in carp from Las Vegas Wash and Bay could be due to the presence of these compounds.

Aerial view of lower Las Vegas Wash and Las Vegas Bay of Lake Mead. View to the northwest, Oct. 12, 1995. Photograph by A.S. VanDenburgh.

ENVIRONMENTAL NEWS

Human estrogens linked to endocrine disruption

For the first time in North America, high levels of natural and synthetic hormones in municipal wastewater treatment plant effluent have been linked with endocrine disruption in fish. The study by researchers at Michigan State University's Department of Zoology indicates that human hormones, not industrial chemicals, in the effluent caused male fish to produce vitellogenin, a well-accepted indicator of endocrine disruption.

"This is a significant, if not a surprising, result," commented Gary Ankley, an EPA toxicologist who studies endocrine disrupters. The results were similar to findings published last year by U.K. researchers that identified hormones secreted in women's urine as the cause of vitellogenesis in caged fish exposed to sewage effluent in U.K. waters.

High levels of a female protein in male fish found in Lake Mead, Nev., led to a search for the cause in the effluent-dominated waters of the Las Vegas Wash. (Courtesy Shane Snyder, Michigan State University)

the compounds that were likely to act like estrogens in the fish. They also used an innovative method that involves solid-phase extraction and in vitro cellular bioassays to detect endocrine-modulating compounds in complex aqueous mixtures. Of the

the highest level of estrogenic activity in effluent downstream from a small plant (55,000 gal/day) with relatively few treatment processes.

Results from a companion Michigan State study, in which caged fish were exposed to Michigan wastewater effluent, suggest

Resourc

PUBLISHED BY ASAE – THE SOCIETY FOR ENGINEERING IN AGRICULTURAL, FOOD, AND BIOLOGICAL S

MAY 1999

- *Bad Medicine*
- *Grease Relief*
- *Giving Barn Waste the Treat*
- *Biotrickling Filter*
- *1999 ASAE/CSAE-SCGR Annu International Meeting*

Bad Medicine

Pharmaceuticals taken by humans and animals can end up in waterways

Shane Snyder and Erin Snyder

Pharmaceuticals have improved human health and lengthened the human life span.

But new research is showing that although most medicine taken into the body is absorbed, some of the non-degraded or biologically activated drugs may be excreted as waste. These human-passed drugs ultimately end up in wastewater treatment plants (WWTPs) where they are processed and often released into waterways.

The degree to which these drugs are eliminated by WWTPs depends on the treatment method. Some percentage of the pharmaceuticals passes through WWTPs unaffected and is discharged into lakes or rivers.

Concerns about pharmaceuticals entering natural U.S. waters have surfaced in the past. In 1970, Henry H. Tabak of the U.S. Environmental Protection Agency (EPA) investigated synthetic ovulation-inhibiting hormones in wastewater. He found significant levels of natural and synthetic hormones in WWTP effluent.

"Although a prediction of possible future danger from the accumulation of synthetic steroid compounds in treated wastewater is not possible at present," Tabak said in 1970, "it is certain that if treatment processes are not modified in the future to encourage high conversion rates of these compounds into safe end products, one might predict their accumulation in water courses."

Pinpointing the problem

European scientists recently detected clofibric acid, a drug used to lower blood cholesterol, in high concentrations in lakes and rivers in their countries. As early as 1976, clofibric acid and salicylic acid were discovered in wastewater effluents in the United States.

Pharmaceuticals discharged into U.S. natural waters are at low levels, generally a few parts per trillion (ppt) or less. The U.S. Food and Drug Administration (FDA) suggests that a drug or bioactivated metabolite enter the aquatic environment at levels no greater than 1 part per billion (ppb).

Michigan State University researchers used this equipment to take samples of waste water effluents.

Reports of pharmaceuticals in natural U.S. waters are rare. There have been no reports of pharmaceuticals in drinking water.

But antibiotic-resistant bacteria strains have been detected in Michigan's Detroit River by R.C. Campeau of the University of Detroit Mercy. He believes the bacteria pose "a potential health risk." Similar strains have been reported in Asia and Europe. The problem is magnified by large concentrations of antibiotics used in raising livestock.

Endocrine disruption in the aquatic environment has brought the issue of pharmaceuticals in wastewater effluents to the forefront. Much of the current interest in endocrine disrupting chemicals in wastewater was generated by a finding in the United Kingdom that fish living in water influenced by wastewater effluents showed reproductive abnormalities. These abnormalities were seen infrequently in fish not exposed to wastewater.

In 1996, Hugh Bevans of the U.S. Geological Survey (USGS) in Carson City, Nevada, reported that feral carp captured in a bay of Nevada's Lake Mead, which received large amounts of treated wastewater, showed reproductive abnormalities. No cause has been established for these effects.

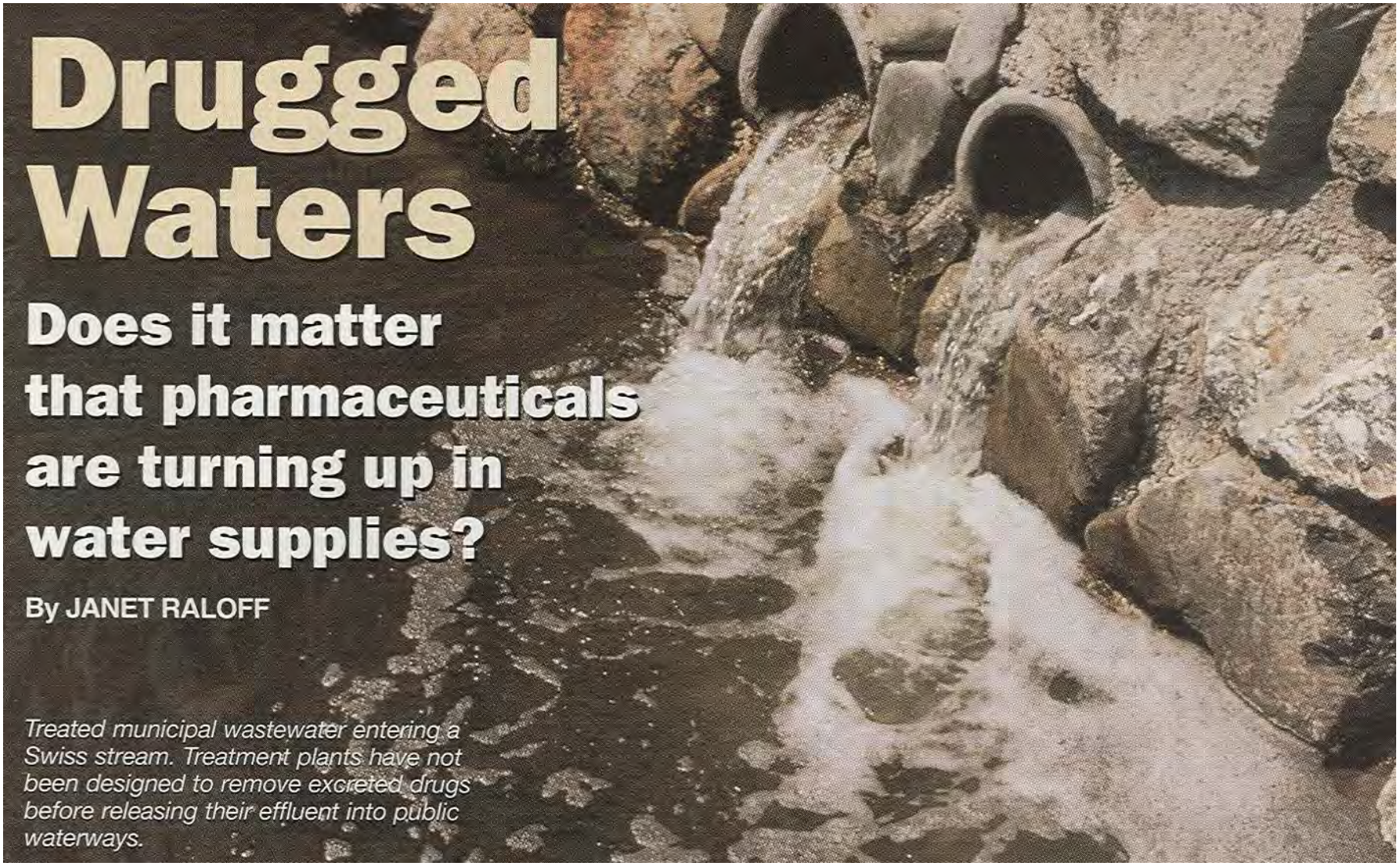
In spring 1997, the National Park Service and the Southern Nevada Water Authority (SNWA) contacted the Aquatic Toxicology Laboratory (ATL) at Michigan State University (MSU) regarding the USGS report of endocrine disruption in feral carp. At the time, MSU researchers were developing the Toxicity Identification and Evaluation (TIE) method to screen for estrogenic and anti-estrogenic compounds in effluents and rivers in Michigan.

The method involved extracting 5.3 qt. (5 L) of water *in situ* using solid-phase extraction (SPE) disks. The chemicals trapped on the disks were eluted in the laboratory and the resulting extract was fractionated and tested using analytical techniques.

Drugged Waters

Does it matter that pharmaceuticals are turning up in water supplies?

By JANET RALOFF



Treated municipal wastewater entering a Swiss stream. Treatment plants have not been designed to remove excreted drugs before releasing their effluent into public waterways.

LAS VEGAS SUN

MONDAY, OCTOBER 16, 2000

Traces of drugs found in LV Wash

Effects on area's water supply unknown

By Mary Manning
LAS VEGAS SUN

Pill-popping, sun screen-smearing people living in and visiting Southern Nevada are leaving traces of drugs, detergents and DDT in the Las Vegas Wash.

The good news is that the contaminant levels discovered in the wash and the Las Vegas Bay are so low they might not disrupt human health. But scientists are still concerned over what they don't know about the new discovery — how it might affect the environment and water supplies.

The Las Vegas Wash runs into Lake Mead, where Southern Nevada draws most of its drinking water.

Scientists had found pesticides and detergents in the wash before, but this is the first time the presence of prescription and nonprescription drugs — as well as one pesticide previously only suspected, lindane — has been confirmed.

The Southern Nevada Water Authority first guessed drugs may be finding their way into the Las Vegas Valley's wastewater after German and British studies found evidence of prescription and over-the-counter drugs in the water supplies of their countries.

But now research by University of Michigan toxicologist Shane Snyder, hired by the water authority to test

See Drugs, 4A

CONTAMINANTS

Toxicology studies of the Las Vegas Wash and the Las Vegas Bay have revealed traces of:

- Pesticides such as DDT and lindane
- Boat fuel compounds
- Oral contraceptives
- Seizure drugs such as Dilantin
- Pain medication such as hydrocodone and codeine
- Valium
- Robitussin
- Blood thinner such as Trental

October 20, 2006

LAS VEGAS SUN

Chemicals cause changes in fish and raise concerns for humans

By Launce Rake <lrake@lasvegassun.com>

Las Vegas Sun

There's something wrong with the fish.

It's been confounding scientists for years: Male fish are developing female sexual characteristics in Lake Mead and other freshwater sources around the country.

On Thursday, the U.S. Geological Survey released a four-page summary of more than a decade of studies linking wastewater chemicals to those changes.

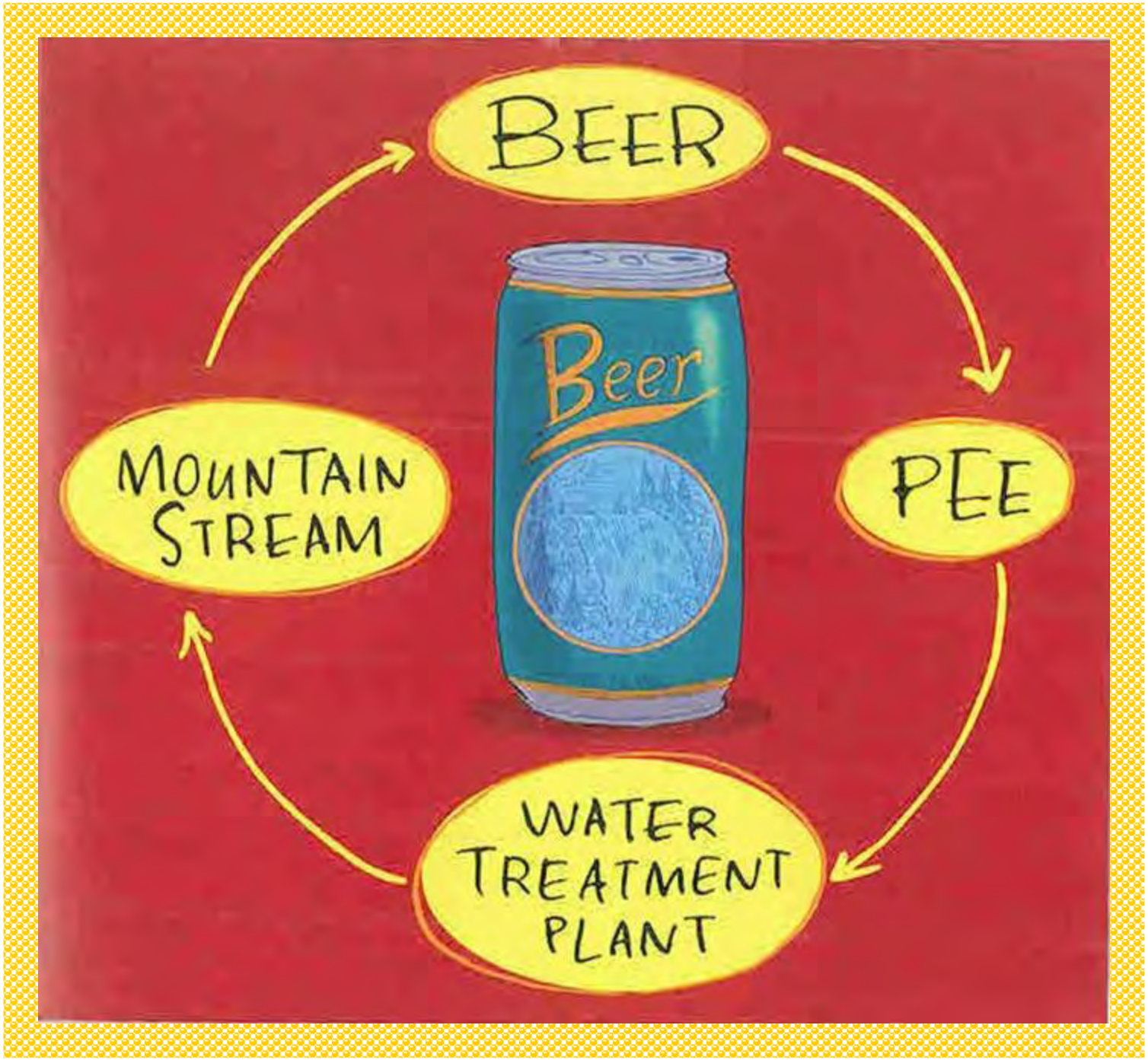
Facing the Yuck Factor

FEATURE ARTICLE - September 17, 2007 *by Peter Friederici*

Facing the yuck factor. PAUL LACHINE

How has the West embraced water recycling? Very (gulp) cautiously

Source: http://www.hcn.org/issues/354/17227


BEER
Beer
PEE
WATER TREATMENT PLANT
MOUNTAIN STREAM

"We know the value of water when the well runs dry."

Benjamin Franklin

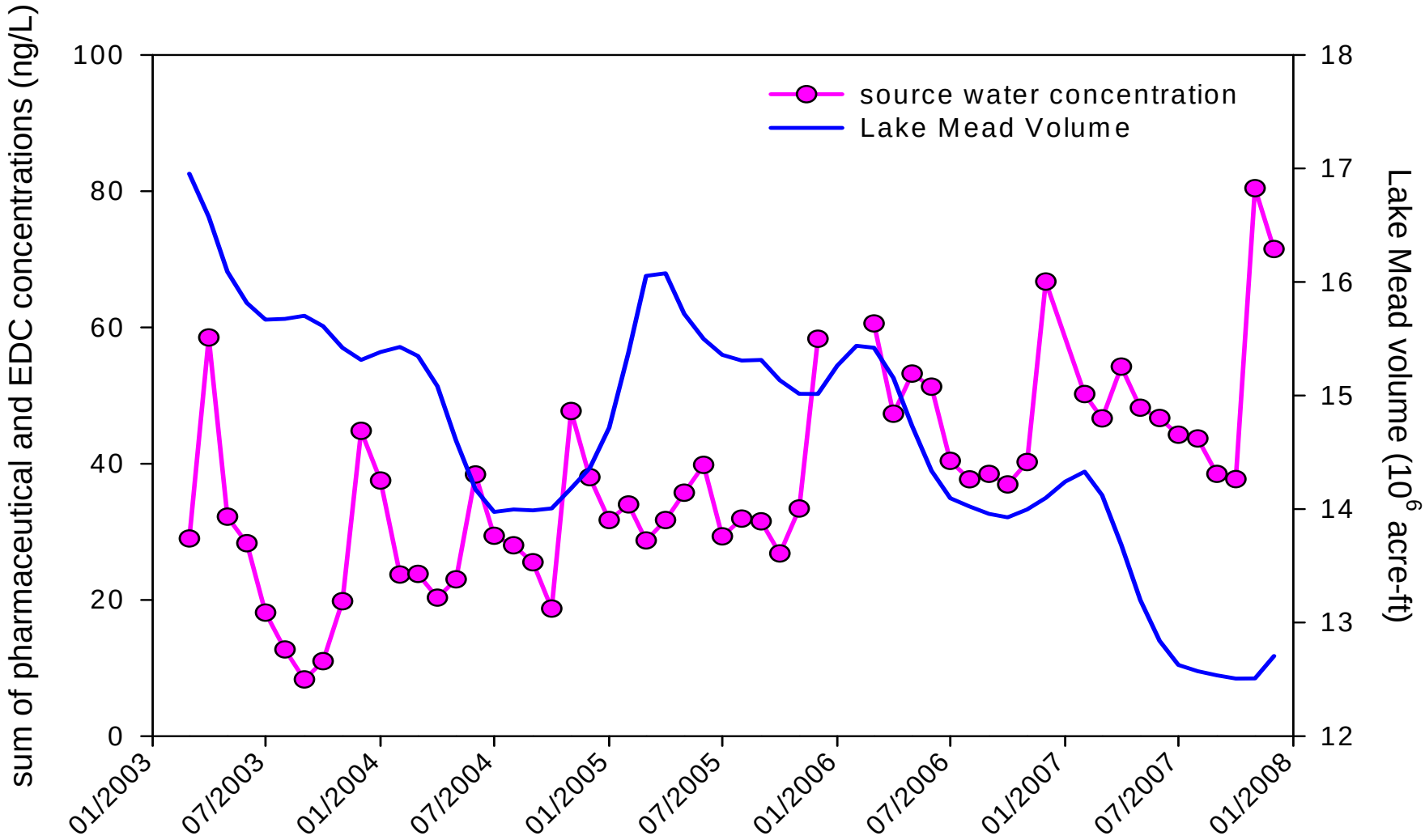
Poor Richard's Almanac - 1732

Fishing Dock at Lake Mead

Wivenhoe Dam – Australia

Drought

Effect on Pharmaceutical and EDC Concentrations



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Removal of EDCs and Pharmaceuticals in Drinking and Reuse Treatment Processes

Subject Area:
High-Quality Water

Removal of EDCs and Pharmaceuticals in Drinking and Reuse Treatment Processes

Prepared by:
Shane A. Snyder, **Eric C. Wert**, and **Hongxia (Dawn) Lei**
Water Quality Research and Development Division
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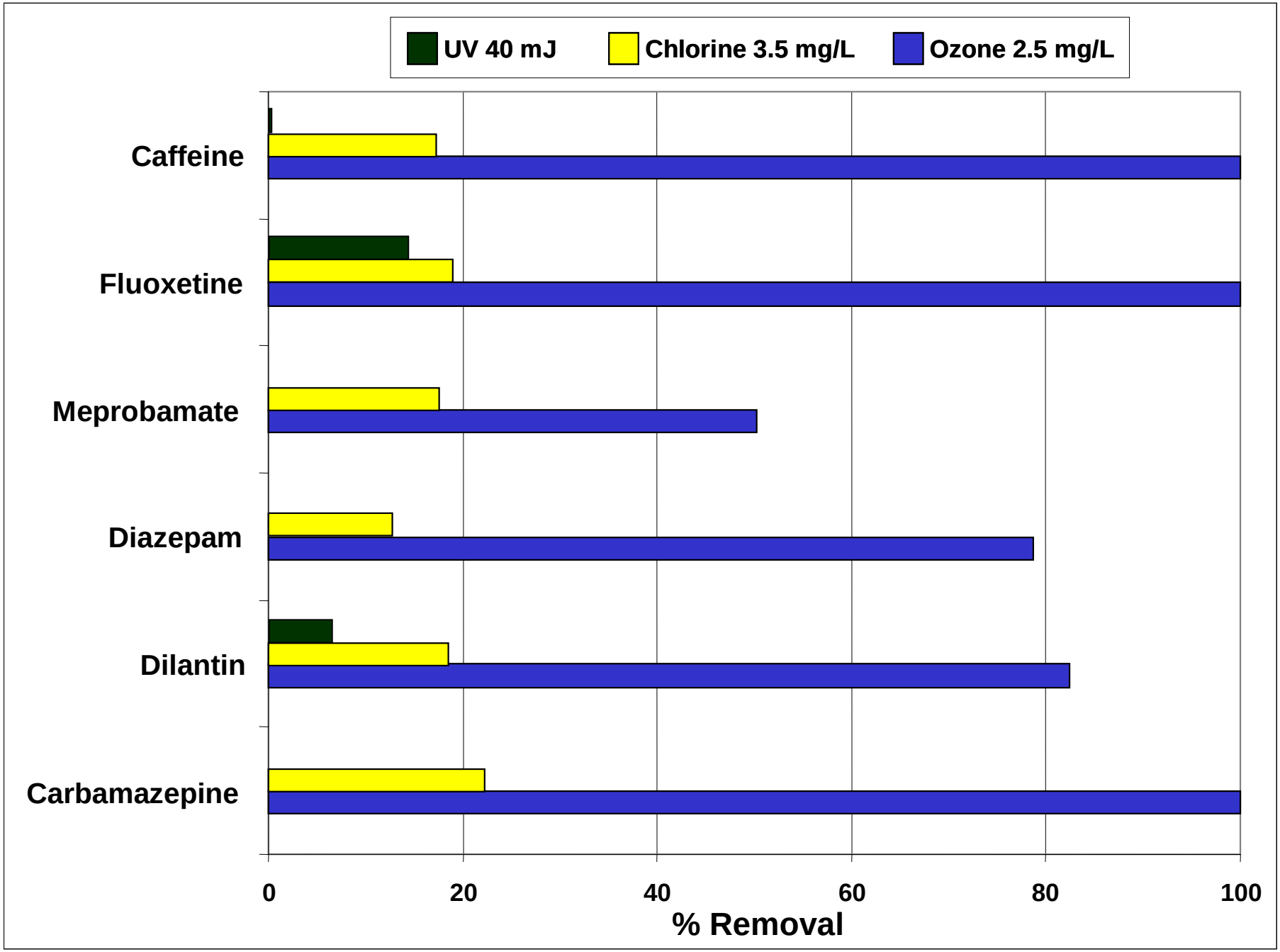
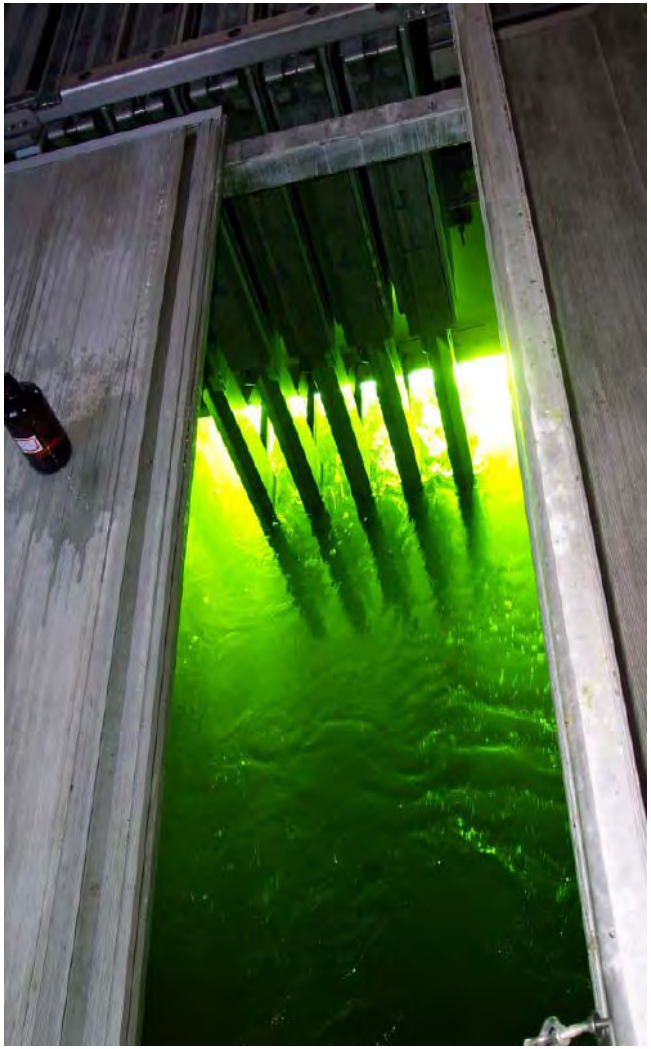

UV 40 mJ
Chlorine 3.5 mg/L
Ozone 2.5 mg/L
Caffeine
Fluoxetine
Meprobamate
Diazepam
Dilantin
Carbamazepine
0
20
40
60
80
100
% Removal

<30% Removal	30-70% Removal	>70% Removal
Testosterone	Sulfamethoxazole	
Progesterone	Triclosan	
Androstenedione	Diclofenac	
Estriol	Acetaminophen	
Ethynylestradiol		
Estrone		
Estradiol		
Erythromycin		
Trimethoprim		
Naproxen		
Hydrocodone		
Ibuprofen		
Caffeine		
Fluoxetine		
Meprobamate		
Diazepam		
Dilantin		
Carbamazepine		
DEET		
Atrazine		
Galaxolide		
TCEP		
Iopromide		
Pentoxifylline		
Metolachlor		
Gemfibrozil		
Musk Ketone		



UV

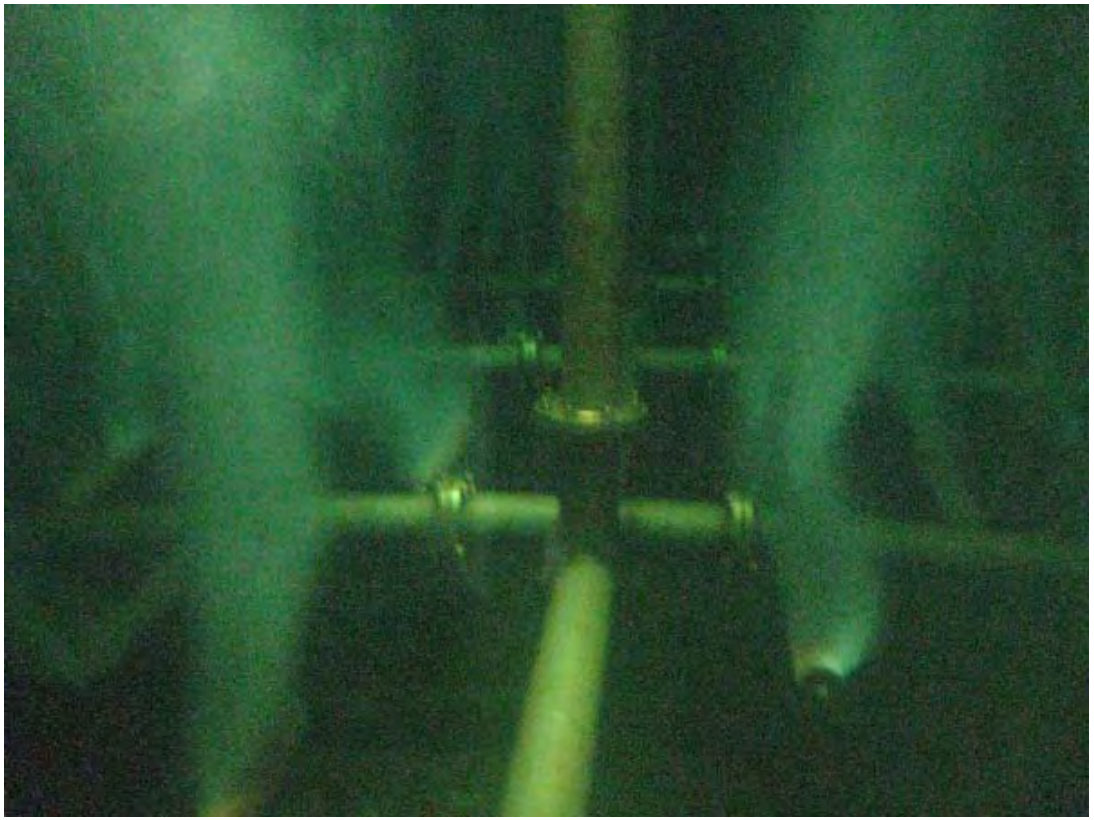
40mJ/cm^2

Chlorine 3.5 mg/L (pH 7 24hr)

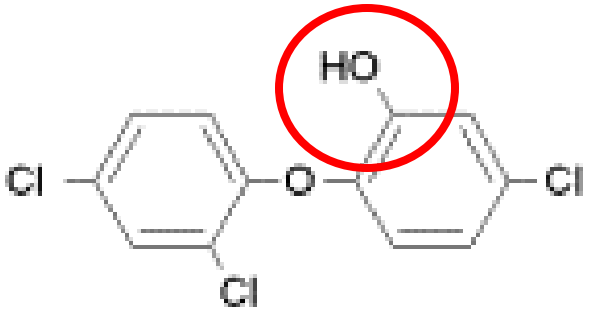
<30% Removal	30-70% Removal	>70% Removal
Testosterone	Ibuprofen	Estriol
Progesterone	Metolachlor	Ethynylestradiol
Androstenedione	Gemfibrozil	Estrone
Caffeine		Estradiol
Fluoxetine		Erythromycin
Meprobamate		Sulfamethoxazole
Diazepam		Triclosan
Dilantin		Trimethoprim
Carbamazepine		Naproxen
DEET		Diclofenac
Atrazine		Hydrocodone
Galaxolide		Acetaminophen
TCEP		Musk Ketone
Iopromide		
Pentoxifylline		

<30% Removal	30-70% Removal	>70% Removal
Musk Ketone	Meprobamate	Testosterone
TCEP	Atrazine	Progesterone
	Iopromide	Androstenedione
		Estriol
		Ethynylestradiol
		Estrone
		Estradiol
		Erythromycin-H2O
		Sulfamethoxazole
		Triclosan
		Trimethoprim
		Naproxen
		Diclofenac
		Ibuprofen
		Hydrocodone
		Acetaminophen
		Carbamazepine
		Dilantin
		Diazepam
		Caffeine
		Fluoxetine
		DEET
		Metolachlor
		Galaxolide
		Pentoxifylline
		Gemfibrozil

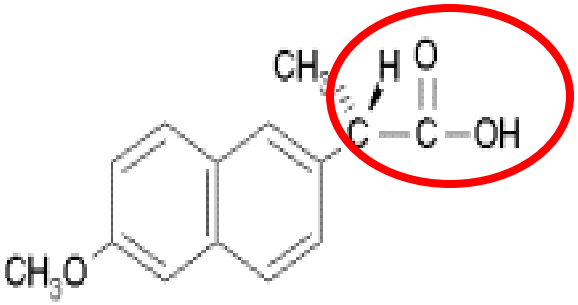
Ozone 2.5 mg/L or UV-H_2O_2 ≈ 700 mJ + 5 mg/L



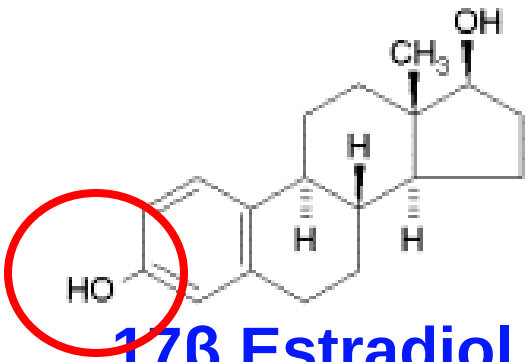
Easy to Oxidize



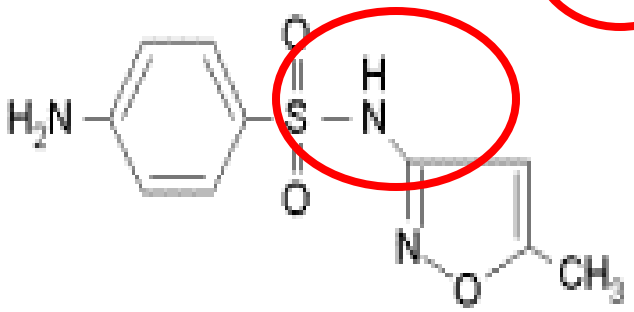
Triclosan



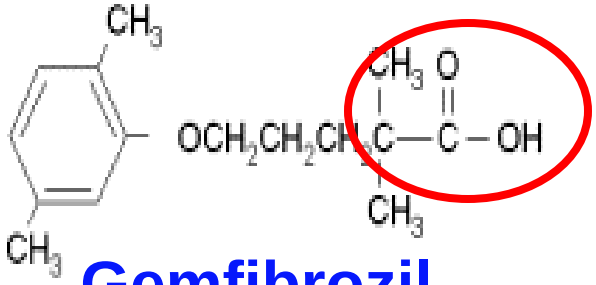
Naproxen



17β Estradiol

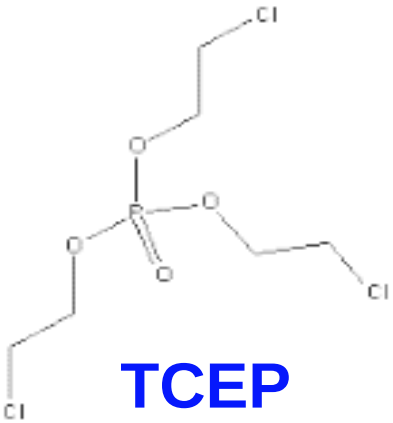


Sulfamethoxazole

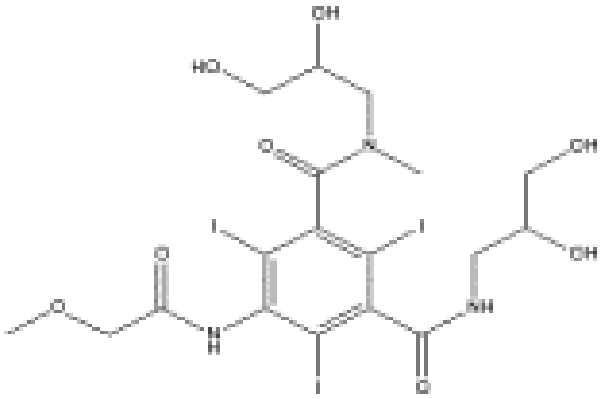


Gemfibrozil

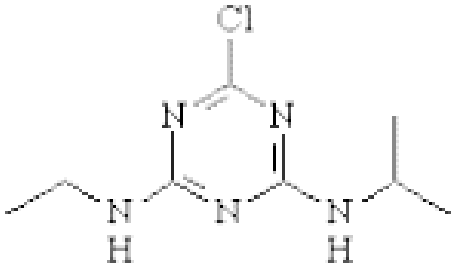
Difficult to Oxidize



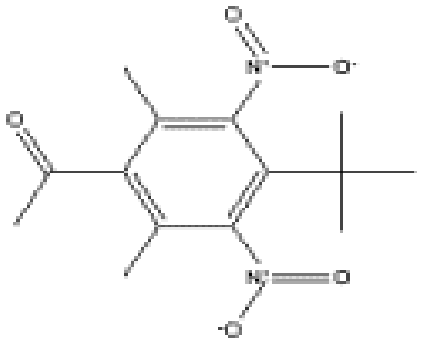
TCEP



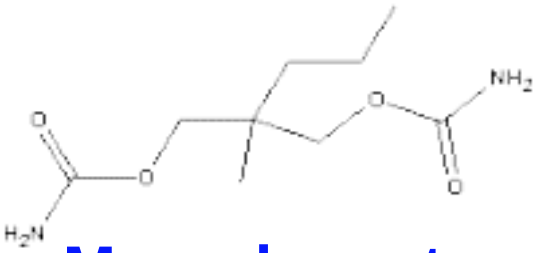
Iopromide



Atrazine



Musk Ketone



Meprobamate

WATER RESEARCH 41 (2007) 3271–3280

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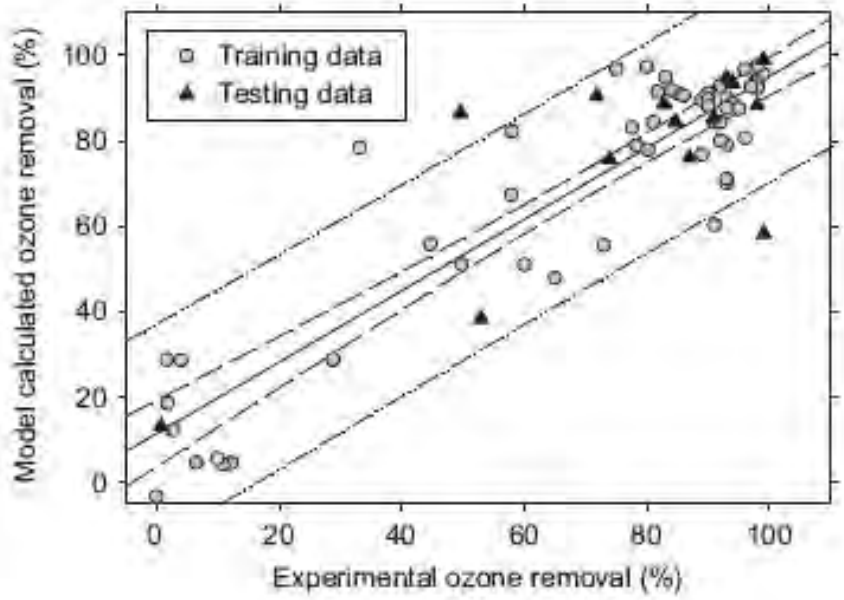
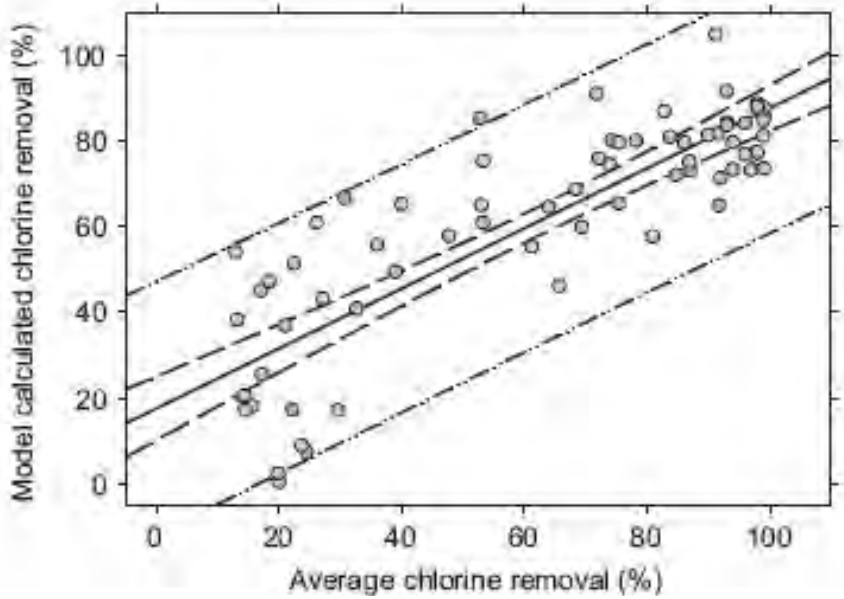
3D QSPR models for the removal of trace organic contaminants by ozone and free chlorine

*Hongxia Lei**, *Shane A. Snyder*

Southern Nevada Water Authority, 1350 Richard Bunker Avenue, Henderson, NV 89015, USA

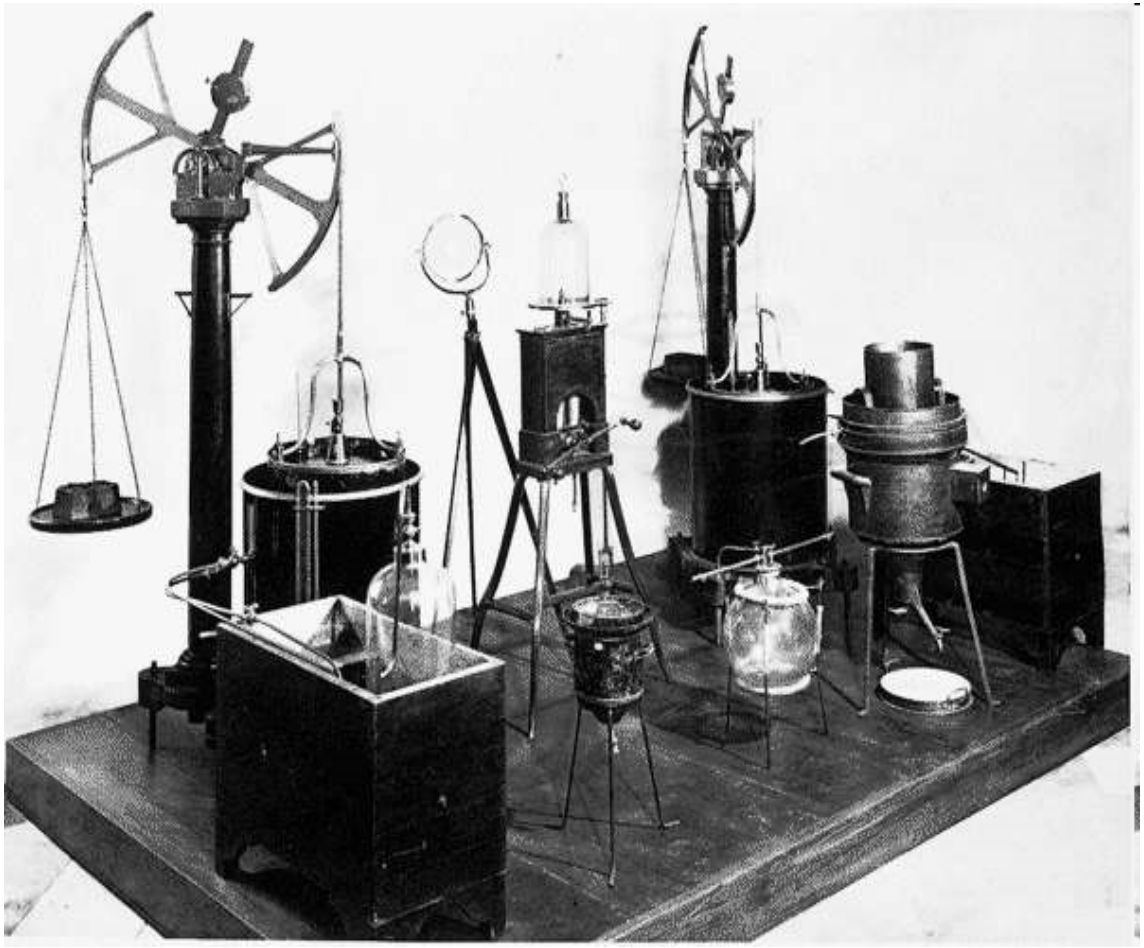




Antoine-Laurent de Lavoisier (26 August 1743 – 8 May 1794)

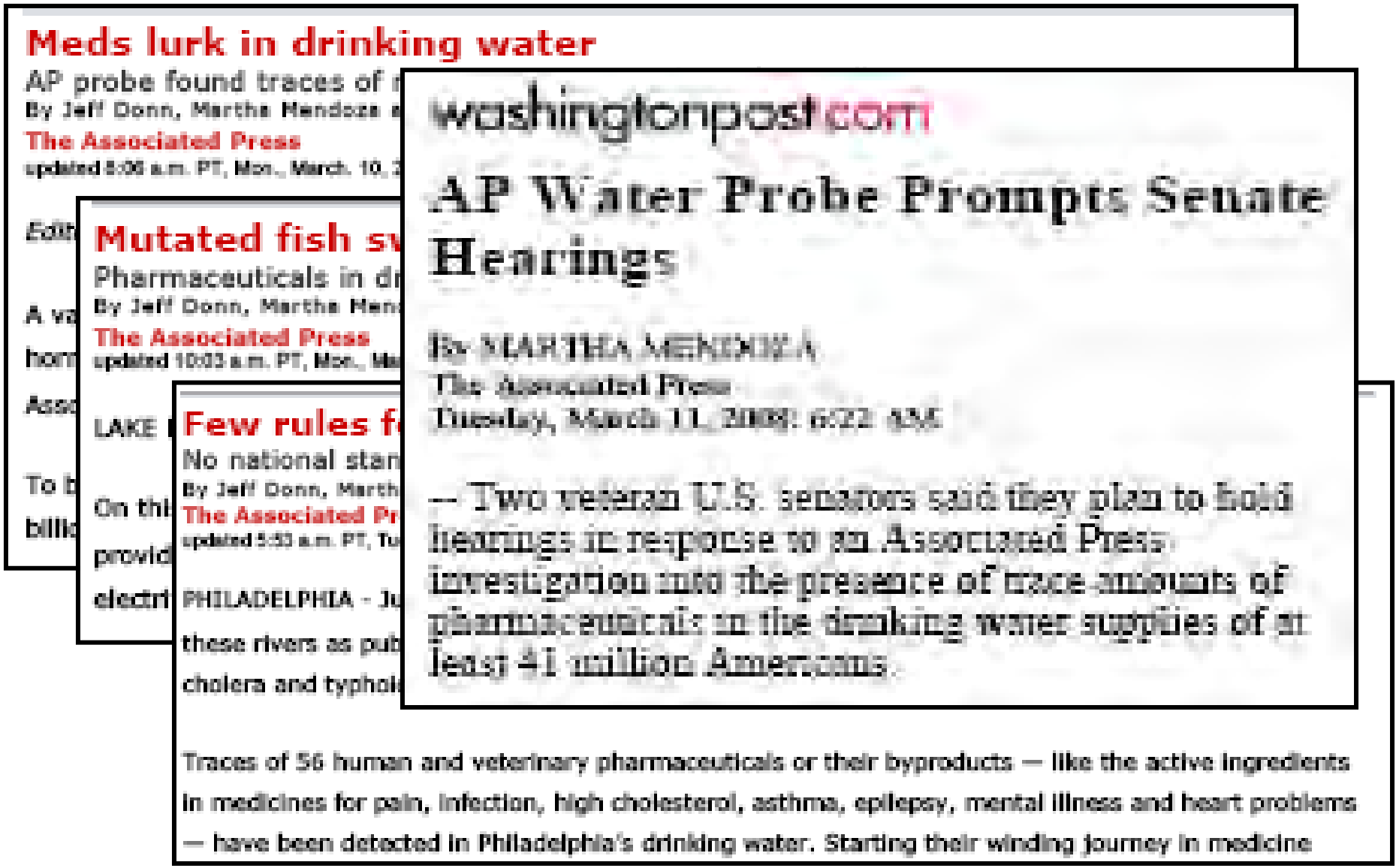
- Called the father of modern chemistry
- Conservation of mass:

  "although matter can change its state in a chemical reaction, the quantity of matter is the same at the end as at the beginning of every chemical change"



http://en.wikipedia.org/wiki/Antoine_Lavoisier

Recent History



Meds lurk in drinking water

AP probe found traces of

By Jeff Donn, Martha Mendoza

The Associated Press

updated 8:06 a.m. PT, Mon., March 10,

Mutated fish sv

Pharmaceuticals in dr

By Jeff Donn, Martha Men

The Associated Press

updated 10:03 a.m. PT, Mon., Ma

LAKE

Few rules fe

No national stan

By Jeff Donn, Martha

The Associated Pr

updated 5:53 a.m. PT, Tu

PHILADELPHIA - Ju

these rivers as pub

cholera and typhoi

washingtonpost.com

AP Water Probe Prompts Senate Hearings

By MARTHA MENDOZA

The Associated Press

Tuesday, March 11, 2008; 6:22 AM

— Two veteran U.S. senators said they plan to hold hearings in response to an Associated Press investigation into the presence of trace amounts of pharmaceuticals in the drinking water supplies of at least 41 million Americans.

Traces of 56 human and veterinary pharmaceuticals or their byproducts — like the active ingredients in medicines for pain, infection, high cholesterol, asthma, epilepsy, mental illness and heart problems — have been detected in Philadelphia's drinking water. Starting their winding journey in medicine

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United States Senate

COMMITTEE ON ENVIRONMENT AND PUBLIC WORKS

WASHINGTON, DC 20510-6175

April 8, 2008

Shane Snyder, Ph.D.
R&D Project Manager
Applied Research and Development Center
Southern Nevada Water Authority
1350 Richard Bunker Ave.
Henderson, Nevada 89015

Dear Dr. Snyder:

On behalf of the Senate Committee on Environment and Public Works, we invite you to testify before the Subcommittee on Transportation Safety, Infrastructure Security, and Water Quality at a hearing entitled, "Pharmaceuticals in the Nation's Water: Assessing Potential Risks and Actions to Address the Issue" on Tuesday, April 15, 2008, beginning at 3:00 p.m. in Room 406 of the Dirksen Senate Office Building.

In order to maximize the opportunity to discuss this matter with you, we ask that your oral testimony be limited

Awwa Research Foundation
Advancing the Science of Water®

State of Knowledge of Endocrine Disruptors and Pharmaceuticals in Drinking Water

Subject Area:
High-Quality Water

State of Knowledge of Endocrine Disruptors and Pharmaceuticals in Drinking Water

Prepared by:
Shane A. Snyder and **Brett J. Vanderford**
Southern Nevada Water Authority
Henderson, NV 89015

Jörg Drewes and **Eric Dickenson**
Colorado School of Mines, Environmental Science and Engineering Division
Golden, CO 80401

and

Erin M. Snyder[*†], **Gretchen M. Bruce**[*], and **Richard C. Pleus**[*]
[*] Intertox, Inc., Seattle, WA 98121
[†] Black & Veatch Corp., Kansas City, MO 64114

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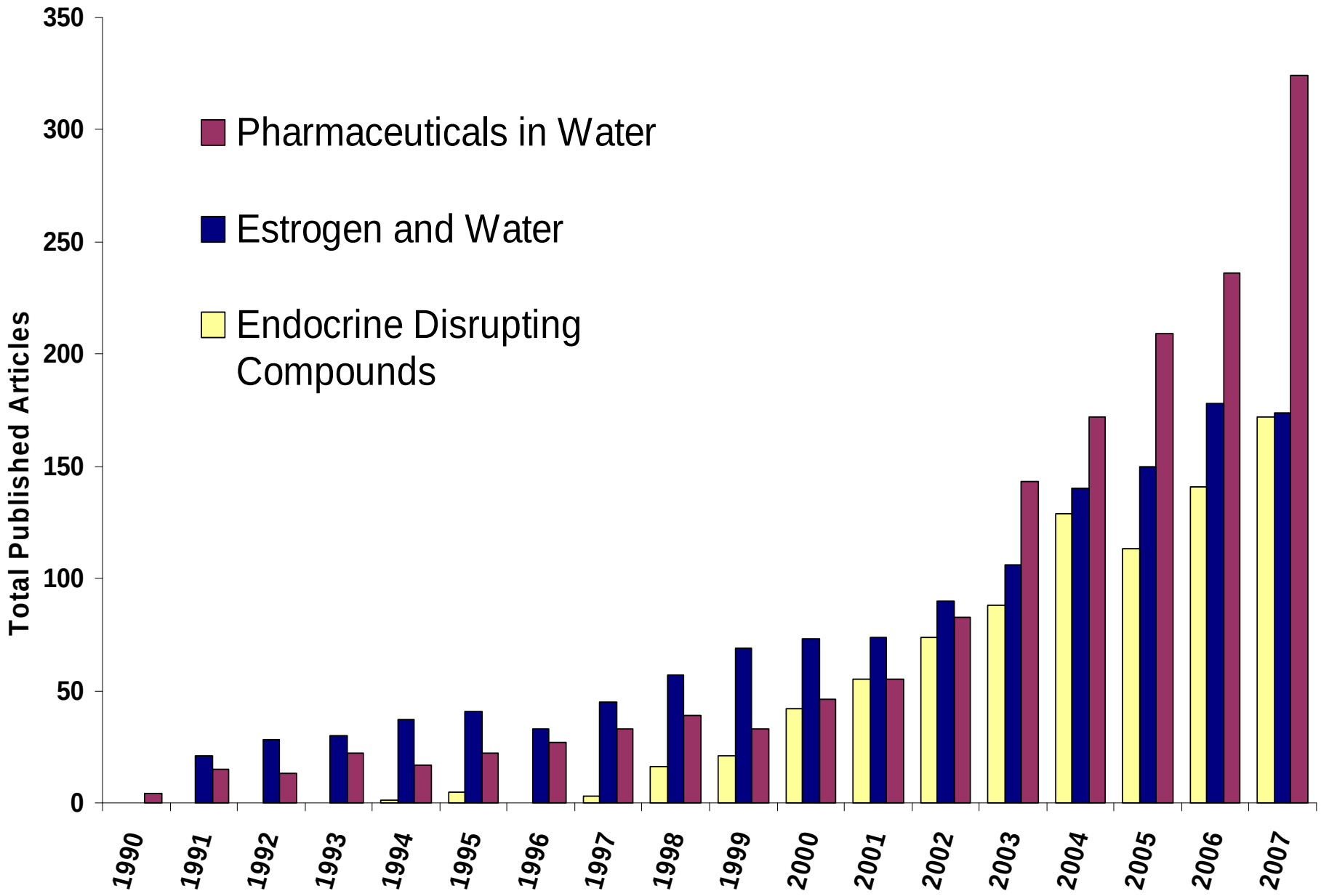
Total Published Articles
350
300
250
200
150
100
50
0
Pharmaceuticals in Water
Estrogen and Water
Endocrine Disrupting Compounds
1990
1991
1992
1993
1994
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2006
2007

Record high drug levels entering India stream

Wastewater at nation's plants 150 times the highest found in U.S.

The Associated Press

updated 4:56 p.m. PT, Sun., Jan. 25, 2009

Polar drug residues in sewage and natural waters in the state of Rio de Janeiro, Brazil

Detection of pharmaceutical contaminations of river, pond, and tap water from Cologne (Germany) and surroundings

OCCURRENCE OF PHENAZONE ANALGESICS AND CAFFEINE IN CROATIAN MUNICIPAL WASTEWATERS

Occurrence and removal of pharmaceuticals and endocrine disruptors in South Korean surface, drinking, and waste waters

USGS
science for a changing world

- **Prevent sample contamination:**
  - On the day of sampling activities, avoid contact with or consumption of the products listed below. Where contact with or consumption of these products is unavoidable, the collection of field blanks is strongly recommended.
    - Prescription drugs, medications, and hormonal substances
    - Soaps and detergents, including antibacterial cleansers
    - DEET (active ingredient in most insect repellents)
    - Fragrances (cologne, aftershave, perfume)
    - Sunscreen
    - Animal or human urine or excrement
    - Caffeine (coffee, tea, colas)
  - Avoid breathing directly over open samples/equipment.
  - Avoid direct contact between yourself (including clothing) and the sample, sampling device, and processing equipment. Clothing is a source of detergents, fragrances, and fire retardants.

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California Urban Water Agencies

Tailored Collaboration

Toxicological Relevance of EDCs and Pharmaceuticals in Drinking Water

Subject Area:
Environmental Leadership

Toxicological Relevance of EDCs and Pharmaceuticals in Drinking Water

Prepared by:
Shane A. Snyder and **Rebecca A. Trenholm**
Southern Nevada Water Authority
Applied Research and Development Center, Henderson, NV 89015

Erin M. Snyder, **Gretchen M. Bruce**, and **Richard C. Pleus**
Intertox, Inc., Seattle, WA 98121

and

Jocelyn D.C. Hemming
Wisconsin State Laboratory of Hygiene
2601 Agriculture Drive, Madison, WI 53718

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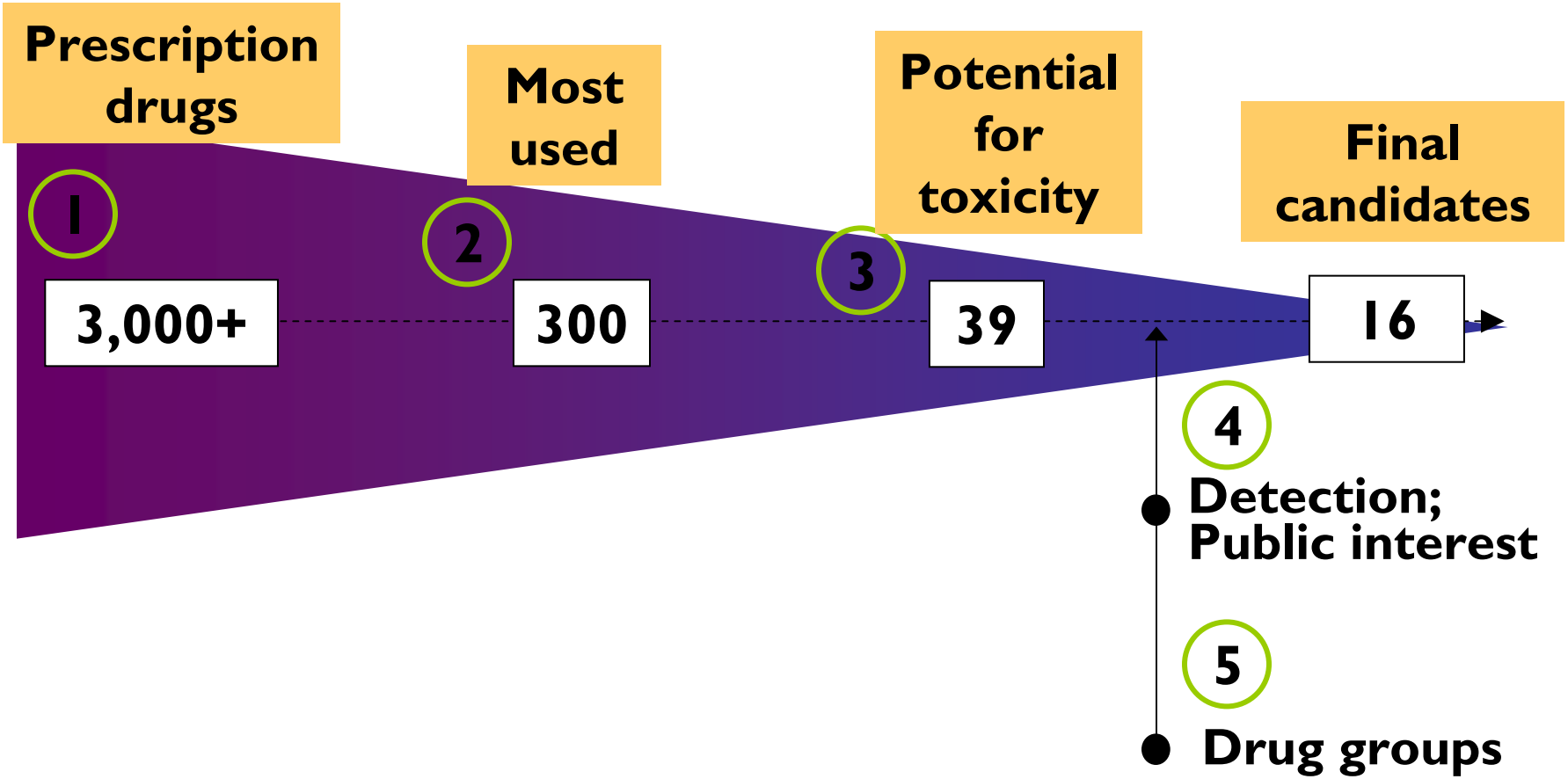
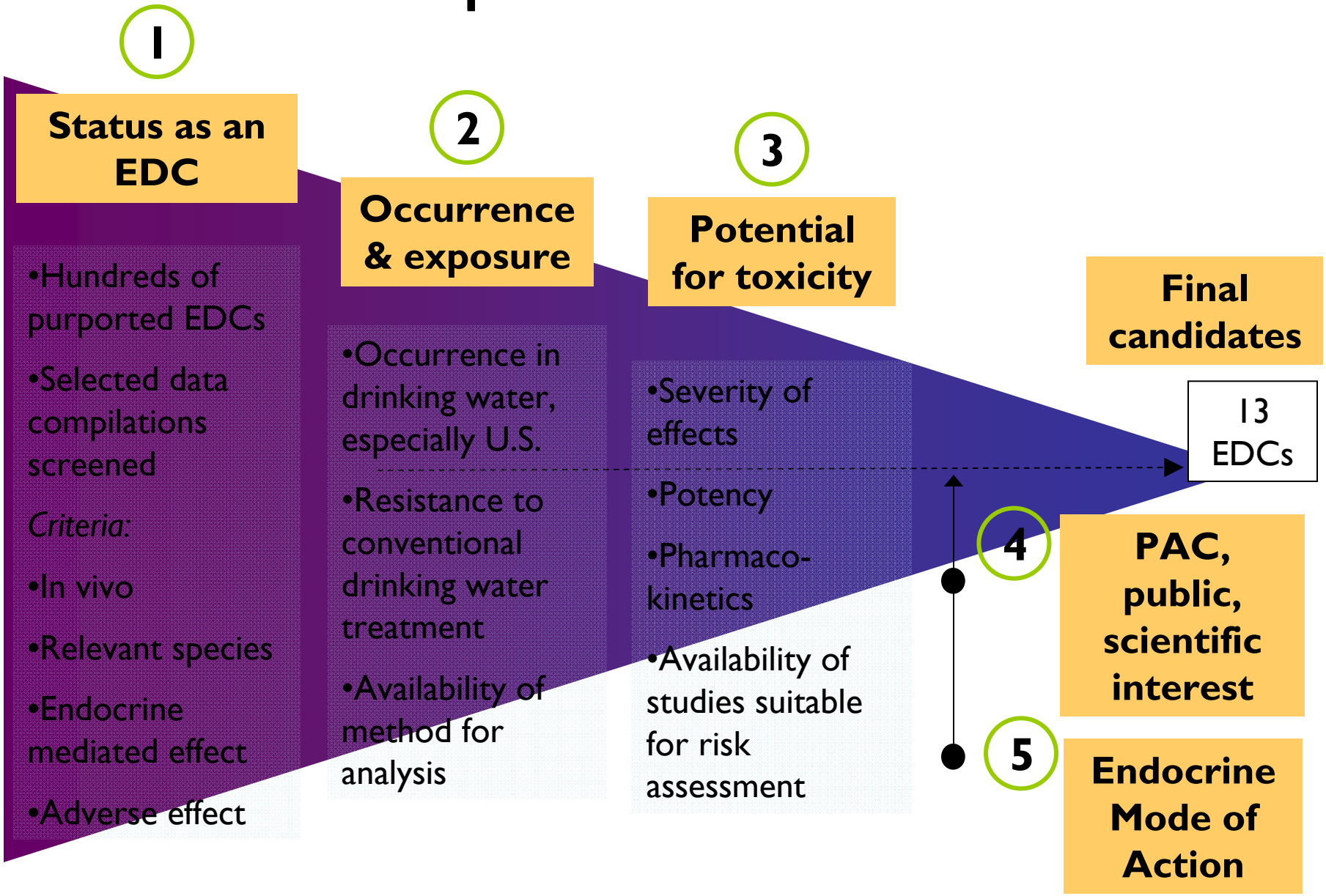
Pharmaceuticals



Suspected EDCs



Environ. Sci. Technol. **2006**, *40*, 7312–7320

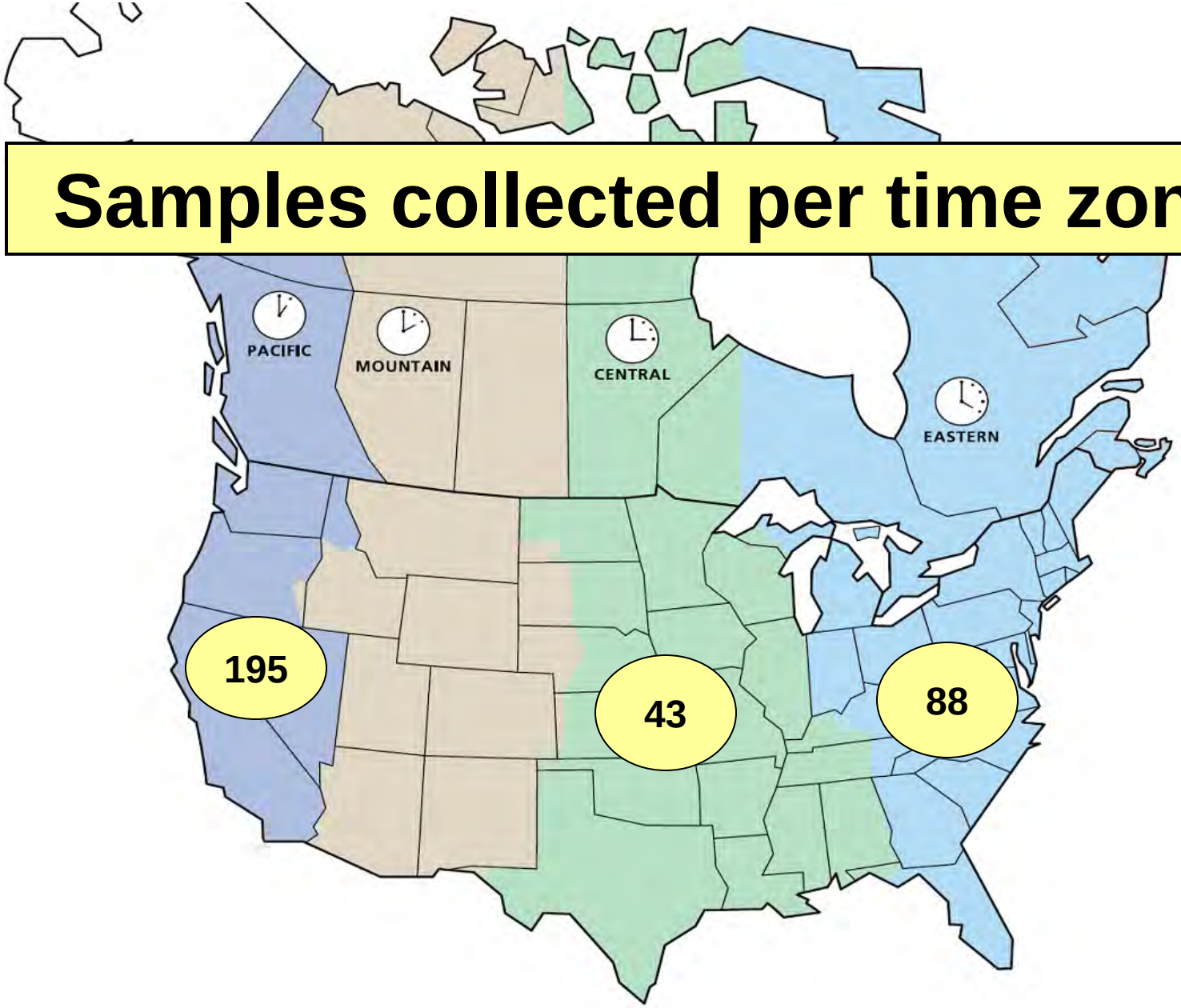
Analysis of Pharmaceuticals in Water by Isotope Dilution Liquid Chromatography/Tandem Mass Spectrometry†

BRETT J. VANDERFORD* AND SHANE A. SNYDER

Southern Nevada Water Authority, 1350 Richard Bunker Avenue, Henderson, Nevada 89015

pensate for matrix effects by using different calibration techniques, including standard addition (*13*, *17*, *22*), surrogate monitoring (*15*, *20*), and various forms of internal calibration (*14*–*16*, *19*, *23*). Still more have been developed to minimize matrix effects using different extraction, cleanup and elution techniques, including size-exclusion chromatography (*18*, *24*), solid-phase extraction (*22*), LC chromatographic procedures (*14*, *22*), ultra performance liquid chromatography (*25*), hollow fiber liquid-phase microextraction (*26*), flow-splitting and reduced eluent flow rates (*24*, *27*). However, most become problematic when applied to the simultaneous analysis of a broad range of compounds that encompass many different classes and structures in matrices having varying degrees of suppression and enhancement.

Samples collected per time zone



17 Participating Utilities

Environ. Sci. Technol. **2009**, *43*, 597–603

Pharmaceuticals and Endocrine Disrupting Compounds in U.S. Drinking Water

MARK J. BENOTTI,
REBECCA A. TRENHOLM,
BRETT J. VANDERFORD,
JANIE C. HOLADY,
BENJAMIN D. STANFORD, AND
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Received July 3, 2008. Revised manuscript received October 3, 2008. Accepted October 13, 2008.

some researchers have postulated that the long-term risk to humans from any single pharmaceutical at sub-μg/L levels is negligible (*8*), it is not clear what toxicological implications chronic exposure to suites of trace contaminants may pose (*9, 10*). The degree to which this issue has drawn interest across disciplines is illustrated by the voices of concern stemming from medical professionals, environmental scientists, drinking water municipalities, government agencies, and the general media (*9, 11*–*13*). However, if risk assessors and epidemiologists are to link any potential health outcomes with pharmaceutical and EDC exposure, a better understanding of their occurrence in drinking water is critical.

There is relatively sparse information regarding pharmaceutical and EDC occurrence in drinking water. Researchers in Germany measured ng/L concentrations of clofibric acid in Berlin tap water (*14*), a case which remains a strong illustration of the sometimes close wastewater to drinking water coupling of unintended water reuse. The elimination of pharmaceuticals at German DWTPs was attributed to ozone oxidation or adsorption to granular activated carbon (*15*): finished drinking water concentrations

Target Compounds

Pharmaceuticals (20)

Atenolol
Atorvastatin
o-Hydroxy atorvastatin
p-Hydroxy atorvastatin
Carbamazepine
Diazepam
Diclofenac
Dilantin
Enalapril
Fluoxetine
Norfluoxetine
Gemfibrozil
Meprobamate
Naproxen
Risperidone
Simvastatin
Simvastatin hydroxy acid
Sulfamethoxazole
Triclosan
Trimethoprim

Potential EDCs (26)

Atrazine
Benzophenone
BHA
BHT
α-BHC
β-BHC
γ-BHC
δ-BHC
Bisphenol A
Butylbenzyl phthalate
DEET
Diazinon
Dioctyl phthalate
Galaxolide
Linuron
Methoxychlor
Metolachlor
Musk ketone
Nonylphenol
Octachlorostyrene
Octylphenol
TCEP
TCPP
Tonalide
Traseolide
Vinclozolin

Steroid Hormones (5)

Estradiol
Estrone
Ethinylestradiol
Progesterone
Testosterone

Phytoestrogens (11)

Apigenin
Biochanin A
Chrysin
Coumestrol
Daidzein
Equol
Formononetin
Genistein
Glycitein
Matairesinol
Naringenin

Detected in Raw Water* (24/62)

Pharmaceuticals

Atenolol
Atorvastatin
o-Hydroxy atorvastatin
p-Hydroxy atorvastatin
Carbamazepine
Diazepam
Diclofenac
Dilantin
Enalapril
Fluoxetine
Norfluoxetine
Gemfibrozil
Meprobamate
Naproxen
Risperidone
Simvastatin
Simvastatin hydroxy acid
Sulfamethoxazole
Triclosan
Trimethoprim

Potential EDCs

Atrazine
Benzophenone
BHA
BHT
α-BHC
β-BHC
γ-BHC
δ-BHC
Bisphenol A
Butylbenzyl phthalate
DEET
Diazinon
Dioctyl phthalate
Galaxolide
Linuron
Methoxychlor
Metolachlor
Musk ketone
Nonylphenol
Octachlorostyrene
Octylphenol
TCEP
TCPP
Tonalide
Traseolide
Vinclozolin

Steroid Hormones

Estradiol
Estrone
Ethinylestradiol
Progesterone
Testosterone

Phytoestrogens

Apigenin
Biochanin A
Chrysin
Coumestrol
Daidzein
Equol
Formononetin
Genistein
Glycitein
Matairesinol
Naringenin

*** In at least 20% of samples**

Detected in Drinking Water* (11/62)

Pharmaceuticals

Atenolol
Atorvastatin
o-Hydroxy atorvastatin
p-Hydroxy atorvastatin
Carbamazepine
Diazepam
Diclofenac
Dilantin
Enalapril
Fluoxetine
Norfluoxetine
Gemfibrozil
Meprobamate
Naproxen
Risperidone
Simvastatin
Simvastatin hydroxy acid
Sulfamethoxazole
Triclosan
Trimethoprim

Potential EDCs

Atrazine
Benzophenone
BHA
BHT
α-BHC
β-BHC
γ-BHC
δ-BHC
Bisphenol A
Butylbenzyl phthalate
DEET
Diazinon
Dioctyl phthalate
Galaxolide
Linuron
Methoxychlor
Metolachlor
Musk ketone
Nonylphenol
Octachlorostyrene
Octylphenol
TCEP
TCPP
Tonalide
Traseolide
Vinclozolin

Steroid Hormones

Estradiol
Estrone
Ethinylestradiol
Progesterone
Testosterone

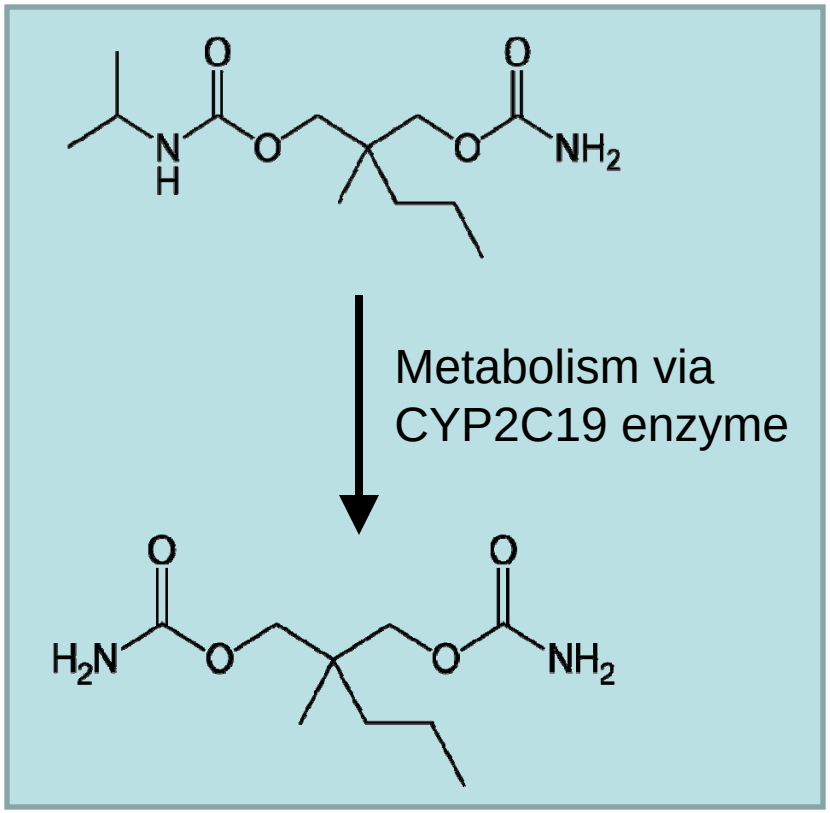
Phytoestrogens

Apigenin
Biochanin A
Chrysin
Coumestrol
Daidzein
Equol
Formononetin
Genistein
Glycitein
Matairesinol
Naringenin

*** In at least 20% of samples**

Carisoprodol – The Source of Meprobamate in the Environment?

Carisoprodol



Meprobamate

Olsen, H. et al. *Therapeutic Drug Monitoring* **1994**, 16, 337-340.

Mosby's Drug Consult lists carisoprodol as the 75th most prescribed drug in 2003.

Meprobamate was not listed in the top 200.

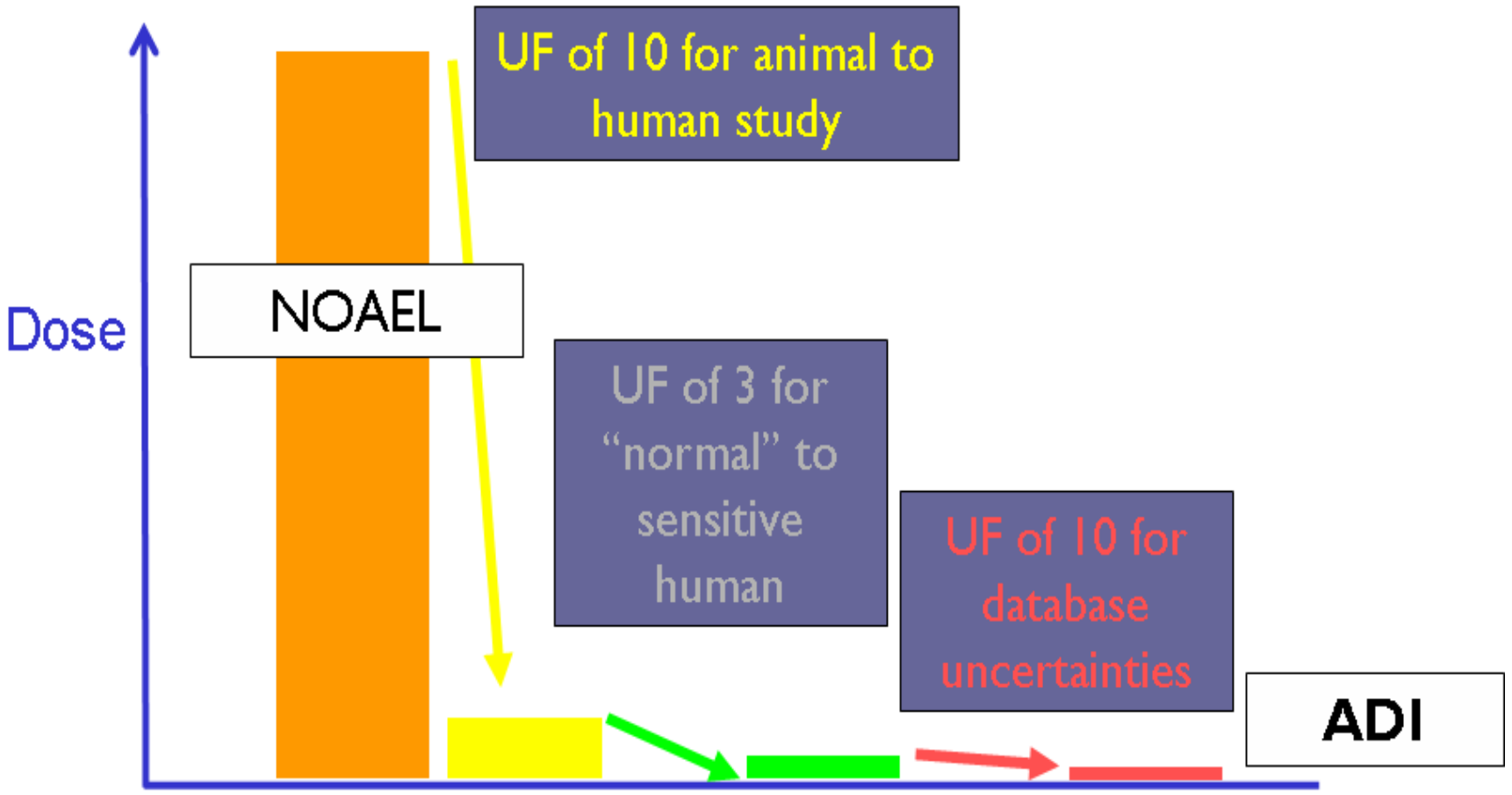
TABLE 4. Six Frequently Detected Indicator Compounds, Their Removal during Chlorine or Ozone Oxidation, And the Relative Number of Pharmaceuticals and EDCs Removed by Chlorine or Ozone[a]

	removal by	
	chlorine	ozone
group 1		
estrone	good	good
trimethoprim	good	good
group 2		
DEET	poor	good
atenolol[b]	poor	good
group 3		
atrazine	poor	poor
meprobamate	poor	poor
number of pharmaceuticals and EDCs >50% removed by each process[c]	16 of 36	25 of 29

“The critical question we must address is not ‘Do they exist?,’ but rather, ‘At what concentration are these compounds harmful to human health?’”

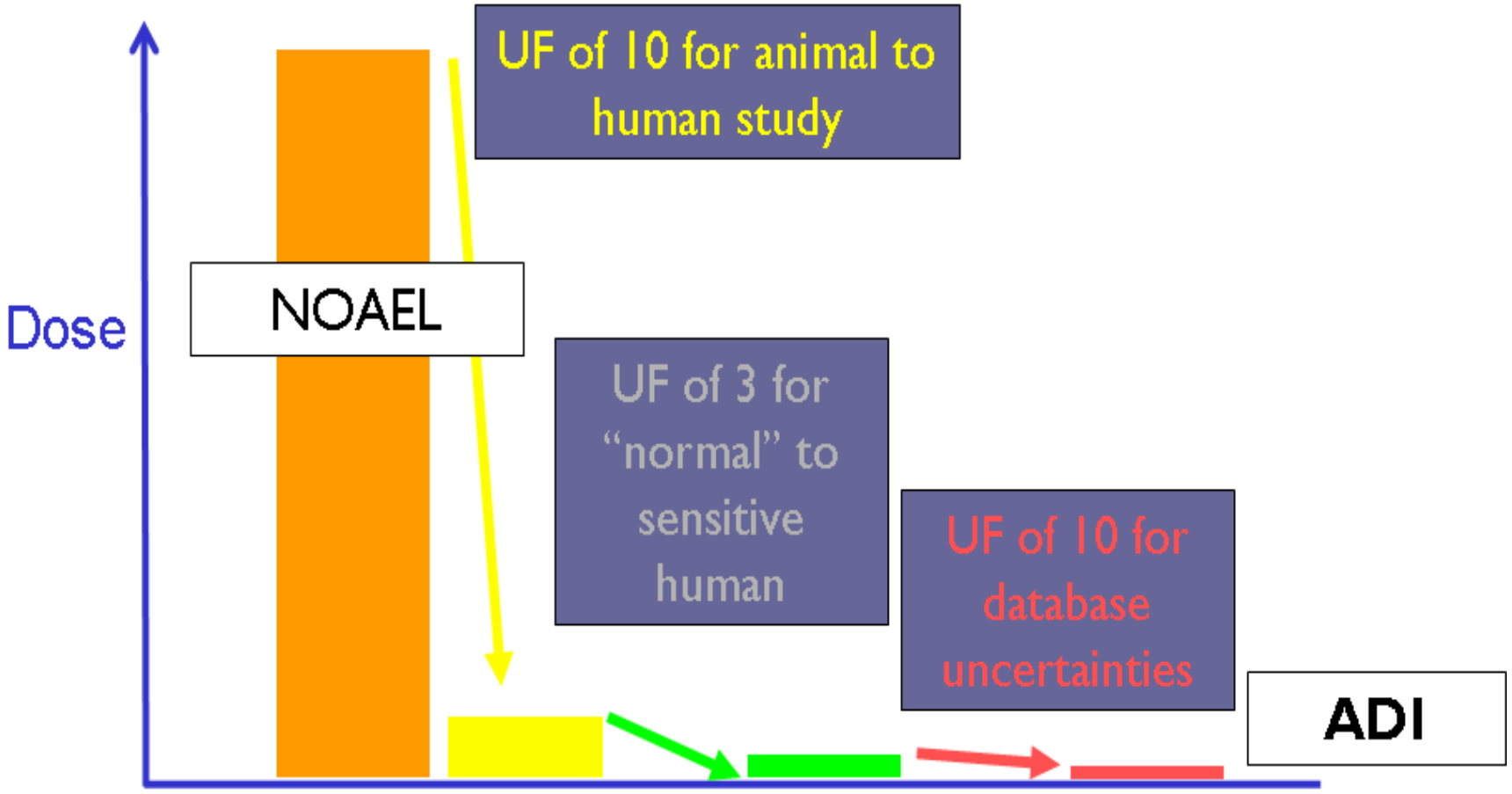
Acceptable Daily Intake (ADI)

$$\text{ADI} = \frac{\text{Highest NOAEL or lowest LOAEL}}{\text{Uncertainty factors}}$$



DWEL ≈ MCLG

Drinking Water Equivalent Level (DWEL) = $\frac{\text{ADI} * 70\ \text{kg}}{2\ \text{L}}$



Selected pharmaceuticals cancer and non cancer endpoints

	Drug	Effect dose (mg/kg-d)	Effect	UF
R	Atenolol	0.80 (LOAEL)	Developmental, human	300
R/M	Atorvastatin o-hydroxy atorvastatin o-hydroxy atorvastatin	20 (LOAEL)	Developmental, rat	3,000
R	Carbamazepine	3.0 (LOAEL)	Developmental, human	300
	Diazepam	1.0 (LOAEL)	Developmental, rat	1,000
	Diclofenac	20 (NOAEL)	Developmental, mouse	300
	Enalapril	0.070 (LOAEL)	Developmental, human	300
	Fluoxetine Norfluoxetine	0.30 (LOAEL)	Developmental, human	300
R	Gemfibrozil	92 (LOAEL)	Developmental, rat	3,000
	Meprobamate	75 (NOAEL)	Systemic, mouse	10,000
	Naproxen	170 (NOAEL)	Reproductive / Developmental, mouse	300
R/M	Phenytoin	17.5 (NOAEL)	Developmental, mouse	300
R/M	Risperidone	0.16 (LOAEL)	Reproductive, rat	3,000
R	Simvastatin Simvastatin hydroxy acid	0.2 (LOAEL)	Developmental, human	300
	Sulfamethoxazole	512 (NOAEL)	Developmental, rat	1,000
	Triclosan	75 (NOAEL)	Systemic, hamster	1,000
	Trimethoprim	192 (NOAEL)	Developmental, rat	1,000

Evidence of Cancer in Rat or Mouse

Pharmaceutical Evaluation

Drug	Class	ADI-DWEL (µg/L)	Max. conc. (µg/L)	Sites with Detection (n=18)	Liters per Day to Exceed DWEL
Risperidone	Antipsychotic	0.49	0.003	1	340
Phenytoin	Anticonvulsant	6.8	0.019	10	700
Carbamazepine	Anticonvulsant	12	0.018	8	1,300
Atenolol	Beta-blocker	70	0.018	8	7,800
Meprobamate	Antianxiety agent	260	0.042	14	13,000
Gemfibrozil	Antilipidemic	45	0.002	7	43,000
Fluoxetine	SSRI antidepressant	34	0.001	2	82,000
Norfluoxetine	Metabolite	34	0.001	1	88,000
Diazepam	Benzodiazepine tranquilizer	35	0.001	1	210,000
Sulfamethoxazole	Anti-infective	18,000	0.003	4	12,000,000

Endocrine Toxicology

EDC	Effect dose (mg/kg-d)	Effect	UF
Atrazine	5.0 (LOAEL)	Neurologic / behavioral, mouse	1,000
Bisphenol A	0.002 (LOAEL)	Developmental (endocrine), mouse	1,000
Butylbenzyl phthalate	100 (LOAEL)	Developmental/ reproductive (endocrine), rat	1,000
DEHP	1.215 (NOAEL)	Developmental (endocrine), rat	100
17ß-Estradiol	0.005 (NOAEL)	Endocrine-mediated effects, human	300
Estrone	0.004 (NOAEL)	Endocrine-mediated effects, human	300
Ethinylestradiol	0.0001 (LOAEL)	Endocrine-mediated effects, human	1,000
Lindane	0.056 (LOAEL)	Reproductive, rat	1,000
Linuron	No new relevant studies		
Methoxychlor	0.020 (LOAEL)	Developmental/ behavioral (endocrine), mouse	1,000
4-Nonylphenol	1.5 (NOAEL)	Renal toxicity, rat (3-gen reproductive study)	30
4-tert-Octylphenol	12.5 (LOAEL)*	Developmental, rat	1,000
Vinclozolin	No new relevant studies		

*LOAEL observed at lower dose (0.020 mg/kg-d), but not replicated in other studies

Potential EDC Evaluation

Drug	Class	ADI-DWEL (µg/L)	Max. conc. (µg/L)	Sites with Detection (n=18)	Liters per Day to Exceed DWEL
Atrazine	Herbicide	3	0.870	15	8
Linuron	Herbicide	70	0.006	2	23,000
p-Nonylphenol	Industrial chemical	1,800	0.100	2	35,000
Bisphenol A	Industrial chemical	1,800	0.025	1	140,000
Triclosan	Antibacterial	2,600	0.001	1	4,400,000
17b-Estradiol	Hormone	1.8	<0.0005	0	>7,000
Bis(2-ethylhexyl) phthalate	Industrial chemical	420	<0.100	0	>8,400
Butylbenzyl phthalate	Industrial chemical	3,500	<0.050	0	>140,000

World Health Organization
Drinking Water Quality Guidelines

8.2.9 Mixtures

Chemical contaminants of drinking-water supplies are present with numerous other inorganic and/or organic constituents. The guideline values are calculated separately for individual substances, without specific consideration of the potential for interaction of each substance with other compounds present. The large margin of uncertainty incorporated in the majority of the guideline values is considered to be sufficient to account for potential interactions. In addition, the majority of contaminants will not be continuously present at concentrations at or near their guideline value.

Summary of Evaluations Performed by the Joint FAO/WHO Expert Committee on Food Additives (JECFA 1956-2004) (First through sixty-third meetings)

Summary of Evaluations Performed by the Joint FAO/WHO Expert Committee on Food Additives

ESTRADIOL-17BETA	
Chemical names:	ESTRA-1,3,5(10)-TRIENE-3,17beta-DIOL
Synonyms:	**ESTRADIOL**
Functional class:	VETERINARY DRUG (PRODUCTION AID)
Latest evaluation:	1999
ADI:	0-0.00005 mg/kg bw **= 50 ng/Kg = 3500 ng/70 Kg person**
Comments/MRLs:	MRLs: Muscle, liver, kidney and fat (cattle): NOT SPECIFIED
Report:	TRS 893-JECFA 52/57
Residues:	FNP 41/12-JECFA 52/37
Tox monograph:	FAS 43-JECFA 52/43
Previous status:	1987, TRS 763-JECFA 32/17, FNP 41-JECFA 32/7, NOT PREPARED. ADI UNNECESSARY. ACCEPTABLE RESIDUE LEVEL: UNNECESSARY; HORMONE PRODUCED ENDOGENOUSLY AT VARIABLE LEVELS IN HUMAN BEINGS. RESIDUES FROM USE IN ACCORDANCE WITH GOOD ANIMAL HUSBANDRY PRACTICE UNLIKELY TO POSE A HAZARD TO HUMAN HEALTH. AC. MRL 1981, TRS 669-JECFA 25/15. UNLIKELY TO BE ANY CAUSE OF CONCERN WHEN PROPERLY USED

Estrogenicity Comparison

Teaspoon of Soy Sauce
(300 ng/L, 15 mL)

1 Liter Secondary Wastewater
(4.6 ng/L)

Newsweek

March 25th, 2009

Study: Range of pharmaceuticals in fish across US

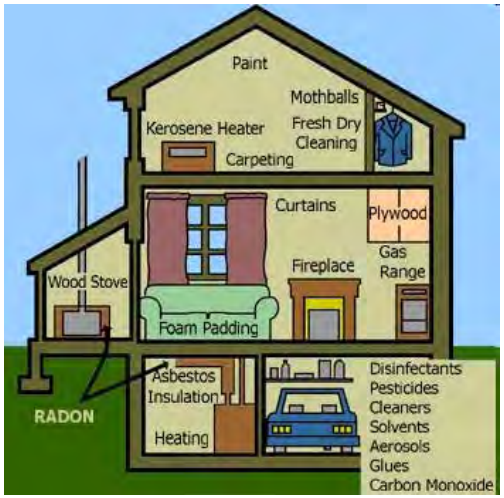
First national study finds range of pharmaceuticals in fish near US sewage treatment plants

MARTHA MENDOZA AP National Writer
AP

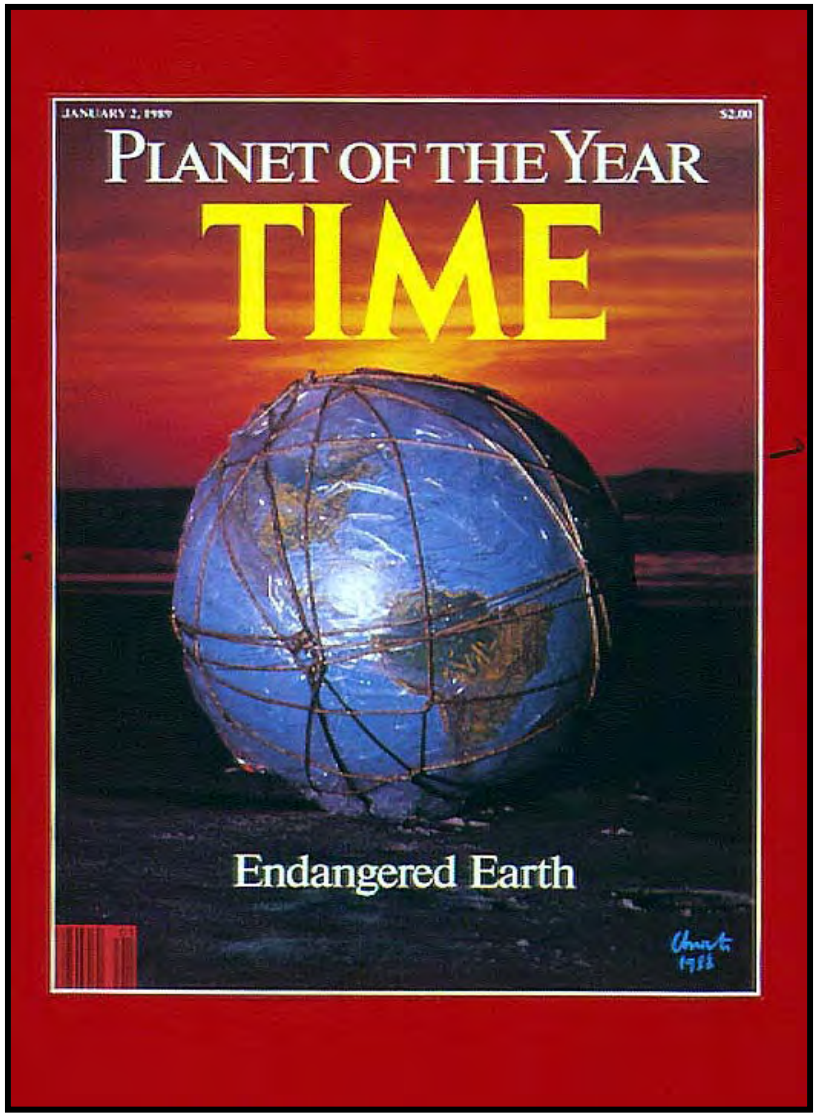
- 28.4 grams per serving
  - → 88 ng Carbamazepine
  - → 142 ng Norfluoxetine
  - → 540 ng Sertraline
  - → ~ 60,000 ng Galaxolide

- 142 grams per serving
  - → 440 ng Carbamazepine
  - → 710 ng Norfluoxetine
  - → 2,700 ng Sertraline
  - → ~300,000 ng Galaxolide

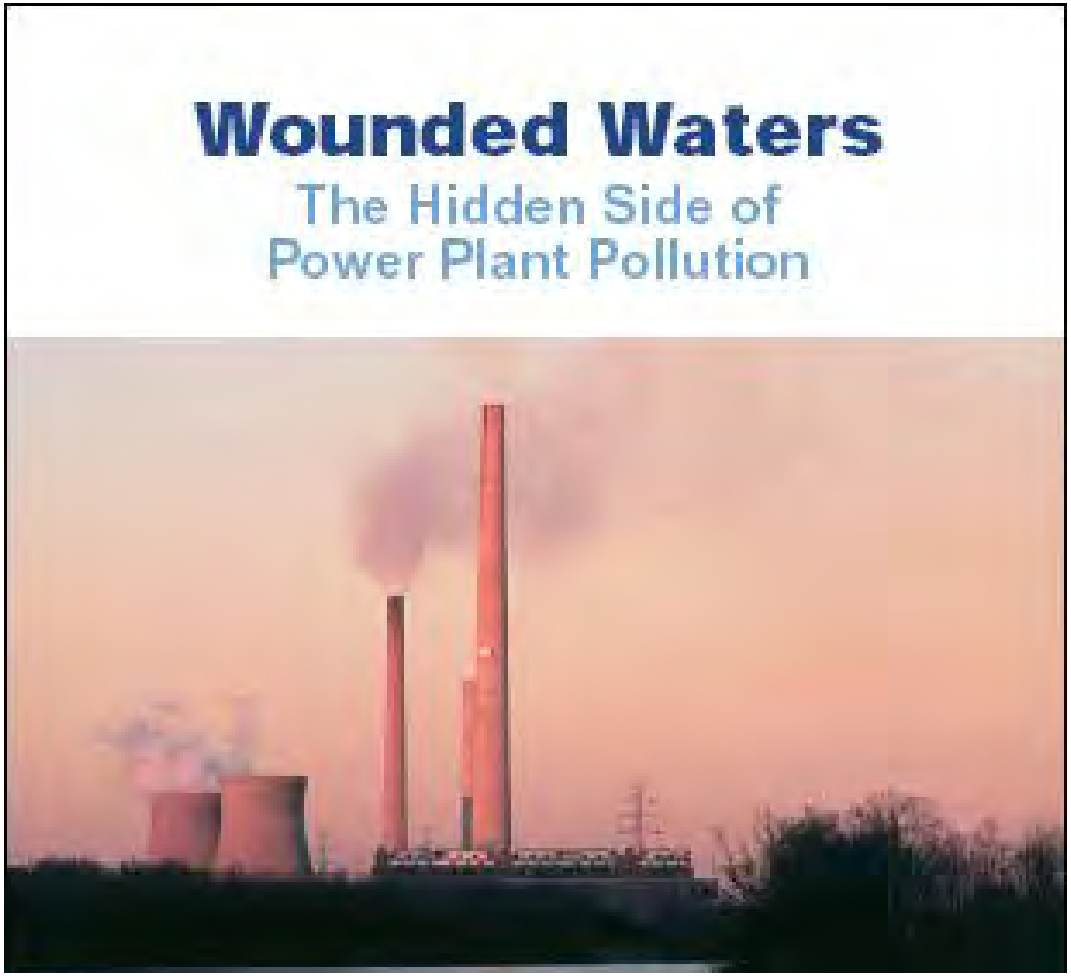
	WATER	
	Conc.	Exposure (2 L/day)
	(ng/L)	(µg)
BHT	49	**0.10**
TCPP (Fyrol PCF)	530	**1**
Galaxolide	280	**0.6**
Butylbenzyl phthalate	55	**0.1**
Nonylphenol	130	**0.3**

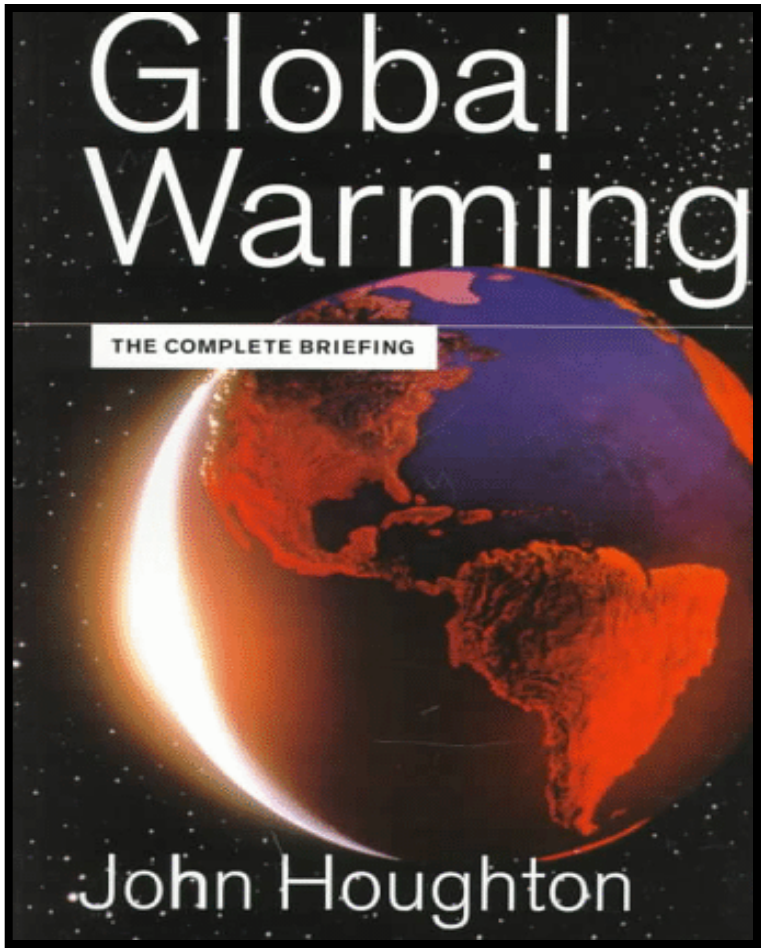


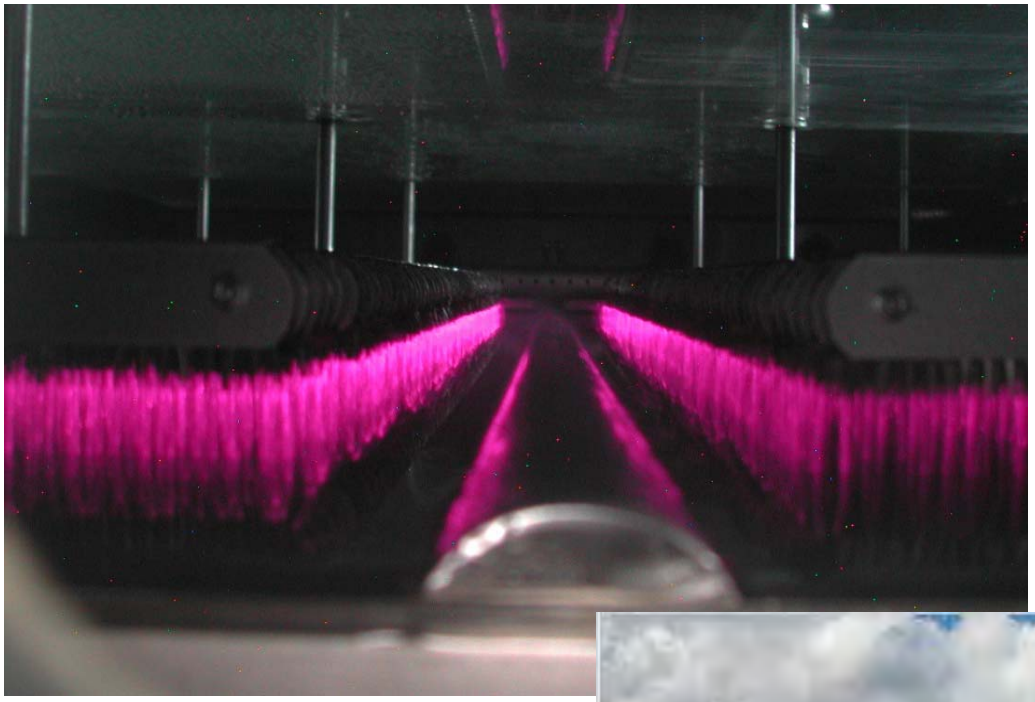
“It is imperative that the nation do a better job of protecting its waters, and especially sources of drinking water, from contamination.”



“In an age where we are concerned about greenhouse gas emissions and minimizing our nation’s energy demands, is it wise to dictate energy-intensive water treatment systems when there is no evidence of public health benefits?”







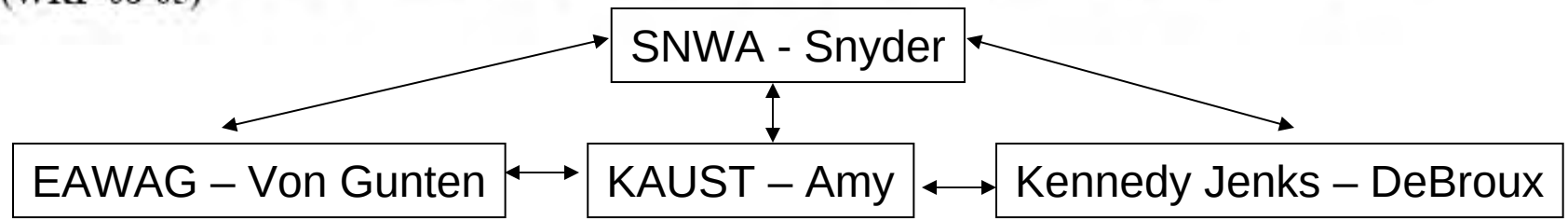
Summary

- All water has been, or will be, reused
  - Global sustainability depends on recycling water
  - Analytical instruments can detect nearly any substance in water
  - Population & urban density exacerbate water challenges
- Treatment can remove or transform contaminants
  - No system can provide complete removal (zero does not exist)
  - Most efficacious processes are energy intensive
  - Are we trading water quality for air quality?
- Meaningful water quality goals must be health-based
  - Monitoring alone will not establish safety
  - Detection does not = safe, just as non-detection does not = risk
  - Protection of public health must be based on sound science

APRIL 8, 2009

REQUEST FOR PROPOSALS

USE OF OZONE IN WATER RECLAMATION FOR CONTAMINANT OXIDATION (WRF-08-05)



Utilities/Agencies	Equipment	Engineering
Clark County	Air Products	Black & Veatch
Henderson	APT	CH2M Hill
Las Vegas	ABI	ECOLOGIC
Reno	Bruker	Hazen & Sawyer
Singapore	METAWATER	HDR
Zurich	General Electric	Kennedy Jenks
Japan	Hydranautics	
S. Korea	Ozonia	
Saudi Arabia	Trojan Tech.	
State Regulators	Wedeco	

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