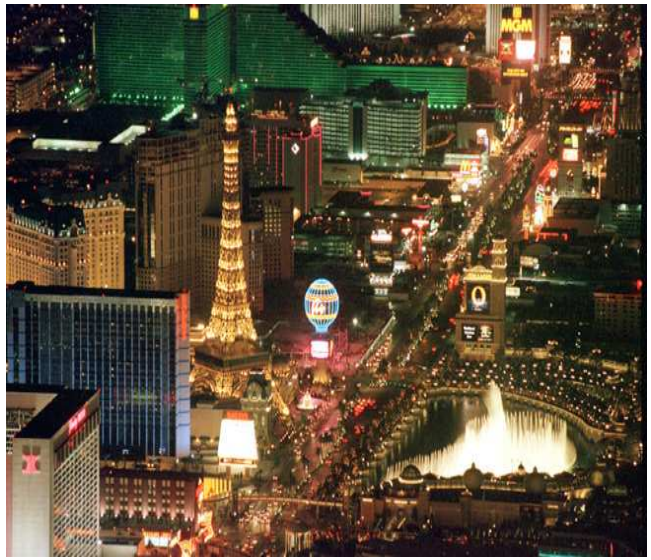
Risk Assessment of EDCs and Pharmaceuticals in US Drinking Waters



Southern Nevada Water Authority

Shane Snyder, Ph.D.

Applied R&D Center – SNWA

Dept. of Chemistry - UNLV

UNLV
UNIVERSITY OF NEVADA LAS VEGAS

Director

Ron Zegers

Manager

Dave Rexing

R&D Project Manager

Shane Snyder, Ph.D.

Administrative Support

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Jereena Bosket

Research Chemists

Doug Mawhinney, Ph.D.

Oscar Quinones

Rebecca Trenholm

Brett Vanderford

Janie Zeigler

Post-Doctoral Researchers

Mark Benotti, Ph.D. (SUNY)
Fernando Rosario, Ph.D. (UCLA)
Ben Stanford, Ph.D. (UNC)
ONE current opening!

Water Quality Analysts

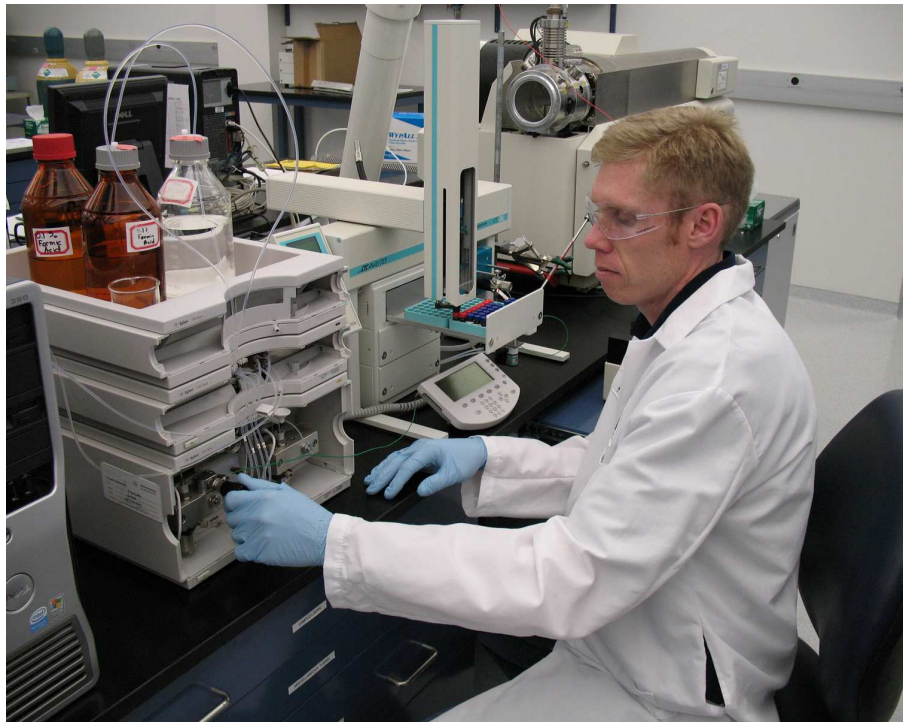
Shannon Ferguson
Spencer Porter

Process Enhancement

Julia Lew
Eric Wert, P.E.

Research Interns

Tony Baik (U. of Buffalo)
Elaine Go (UNLV)
Christy Meza (UNLV)
Sarper Sarp (GIST)
Mei Xin, Ph.D. (UNR)
TWO current openings!

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MGM

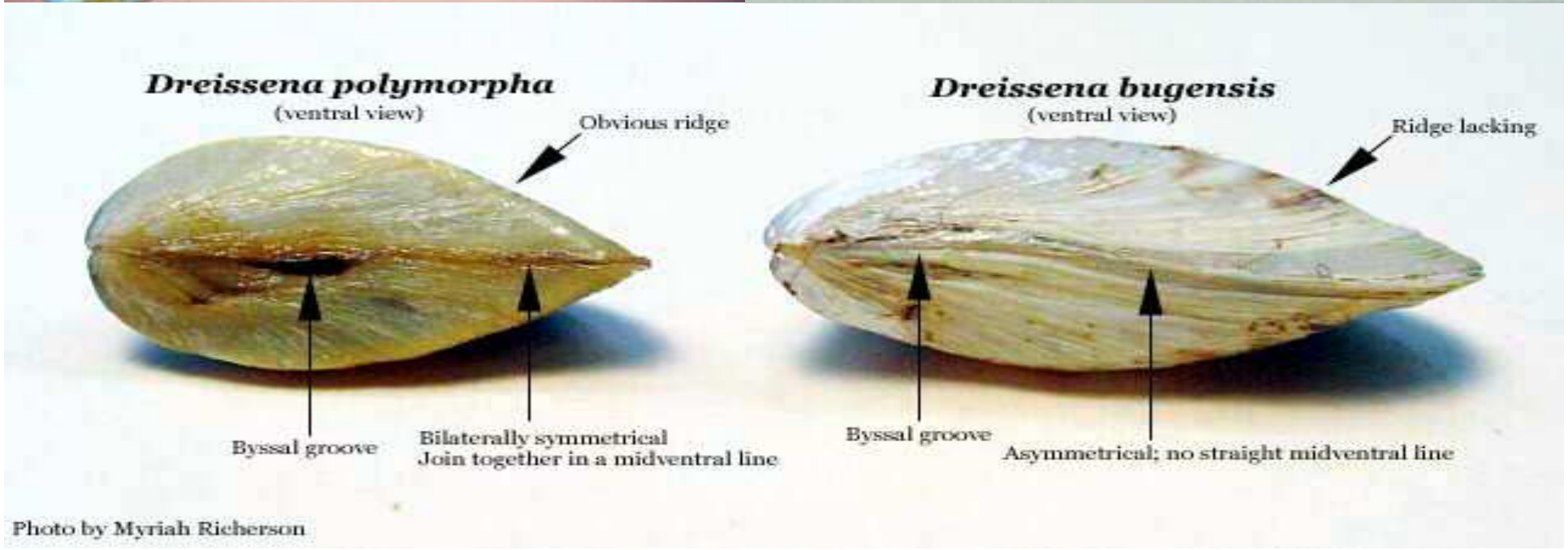

Photo by Myriah Richerson

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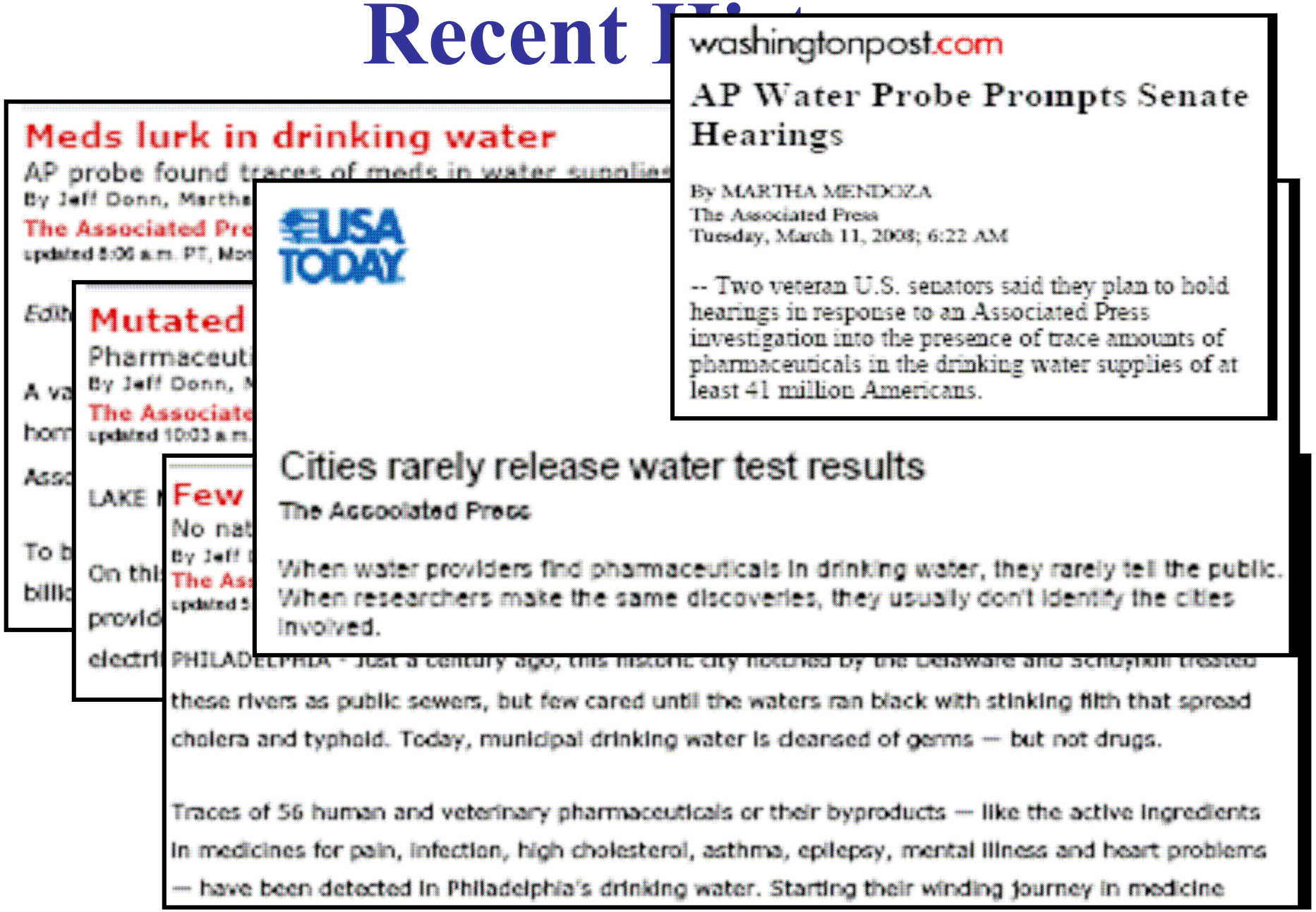

Meds lurk in drinking water

AP probe found traces of meds in water supplies

By Jeff Donn, Martha

The Associated Pre

updated 5:06 a.m. PT, Mo

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By Jeff Donn, M

The Associate

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By Jeff

The As

updated 5

PHILADELPHIA - Just a century ago, this historic city notched by the Delaware and Schuylkill treated these rivers as public sewers, but few cared until the waters ran black with stinking filth that spread cholera and typhoid. Today, municipal drinking water is cleansed of germs — but not drugs.

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

USA TODAY

Cities rarely release water test results

The Associated Press

When water providers find pharmaceuticals in drinking water, they rarely tell the public. When researchers make the same discoveries, they usually don't identify the cities involved.

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.

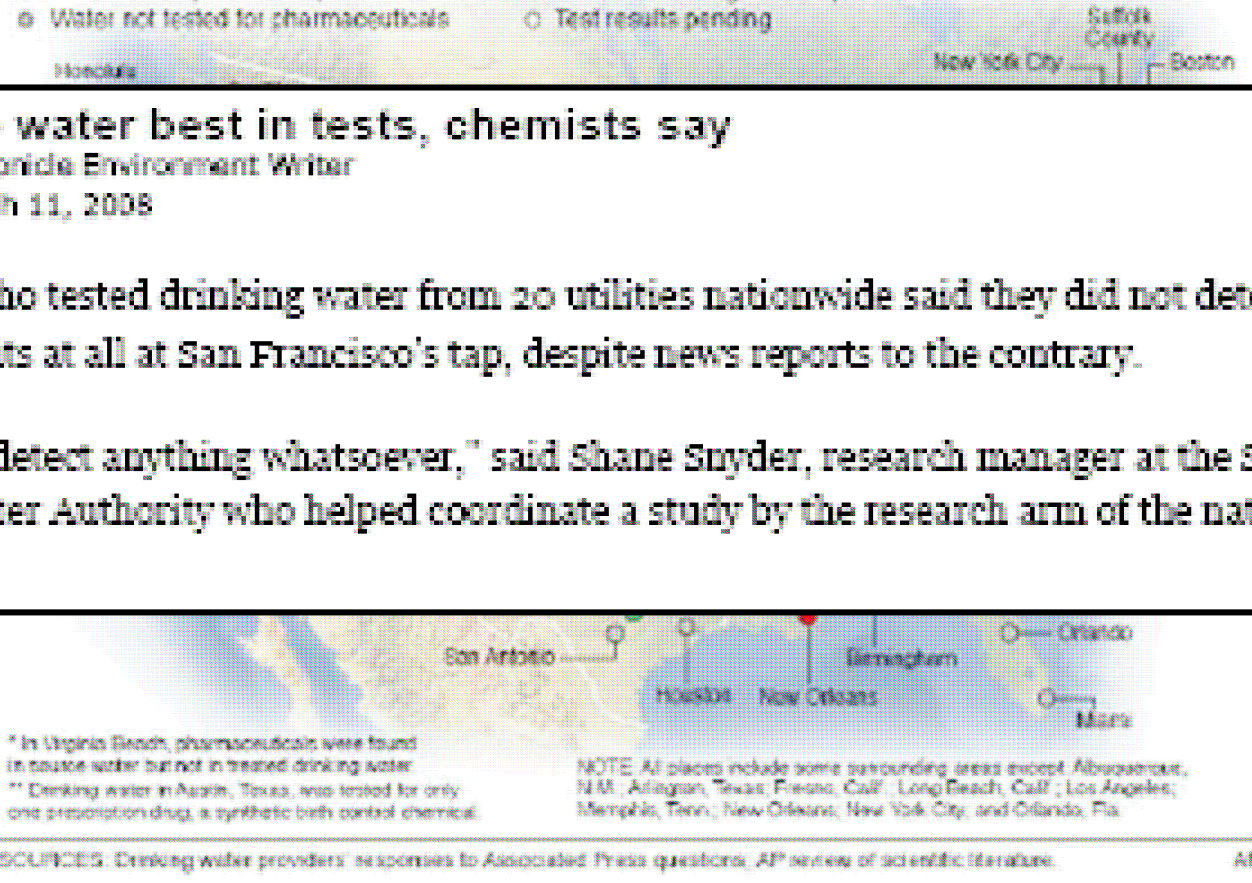
Recent History

Major water sources positive for pharmaceuticals

At least one pharmaceutical was detected in tests of finished drinking water supplies for 24 metropolitan areas, according to an Associated Press survey of 62 major water providers. Only 28 tested finished drinking water. Test results vary widely. Some water systems said tests had been negative, but the AP found independent research showing otherwise.

Pharmaceuticals in drinking water

- Water tested positive for pharmaceuticals
- Water tested negative for pharmaceuticals
- Water not tested for pharmaceuticals
- Test results pending



* In Virginia Beach, pharmaceuticals were found in source water but not in treated drinking water.
** Drinking water in Austin, Texas, was tested for only one prescription drug, a synthetic birth control chemical.

NOTE: All places include some surrounding areas except Albuquerque, N.M.; Arlington, Texas; Fresno, Calif.; Long Beach, Calif.; Los Angeles; Memphis, Tenn.; New Orleans; New York City; and Orlando, Fla.

SOURCES: Drinking water providers' responses to Associated Press questions; AP review of scientific literature. AP

S.F.'s tap water best in tests, chemists say

Jane Kay, Chronicle Environment Writer
Tuesday, March 11, 2008

Chemists who tested drinking water from 20 utilities nationwide said they did not detect any contaminants at all at San Francisco's tap, despite news reports to the contrary.

"We didn't detect anything whatsoever," said Shane Snyder, research manager at the Southern Nevada Water Authority who helped coordinate a study by the research arm of the nation's water utilities.

Awwa Research Foundation
Advancing the Science of Water®

Removal of EDCs and Pharmaceuticals in Drinking and Reuse Treatment Processes

Removal of EDCs and Pharmaceuticals in Drinking and Reuse Treatment Processes

Prepared by:
Shane A. Snyder, **Eric C. Wert**, and **Hongxia (Dawn) Lei**
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Subject Area:
High-Quality Water

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American Water Works Association
IWA Publishing

Table 13.2
Summary of EDCs/PPCPs in Finished Drinking Waters (n=20)

	Finished Drinking Water					
	Hits	% Freq	Min	Max	Median	Ave
DEET	18	90	2.1	30	5.1	8.2
Atrazine	15	75	1.4	430	29	74
Meprobamate	15	75	1.6	13	3.8	6.1
Dilantin	14	70	1.1	6.7	2.3	2.7
Ibuprofen	13	65	1	32	3.8	7.9
Iopromide	13	65	1.1	31	6.5	8.5
Caffeine	12	60	2.6	83	23	25
Carbamazepine	11	55	1.1	5.7	2.8	2.8
TCEP	7	35	3	19	5.5	10.1
Gemfibrozil	5	25	1.3	6.5	4.2	3.9
Metalochlor	4	20	14	160	86	86
Estrone	2	10	1.1	2.3	1.7	1.7
Progesterone	2	10	1.1	1.1	1.1	1.1
Erythromycin	1	5	1.3	1.3	1.3	1.3
Musk Ketone	1	5	17	17	17	17
Naproxen	1	5	8	8	8	8.0
Oxybenzone	1	5	1.1	1.1	1.1	1.1
Sulfamethoxazole	1	5	20	20	20	20
Triclosan	1	5	43	43	43	43
Trimethoprim	1	5	1.3	1.3	1.3	1.3

Note: min, median, and ave based only on detectable concentrations


STOP—THEY FOUND TRACE AMOUNTS OF AN ANTI-ANXIETY DRUG IN OUR DRINKING WATER!
OK—SO IF I DRINK ENOUGH WATER I WON'T WORRY ABOUT WHAT'S IN IT....?
Jim Day '08
LAS VEGAS REVIEW-JOURNAL

“Ancient” History

Developments in Industrial Microbiology - 1970

Steroid Hormones as Water Pollutants

I. Metabolism of Natural and Synthetic Ovulation-Inhibiting Hormones by Microorganisms of Activated Sludge and Primary Settled Sewage

HENRY H. TABAK AND ROBERT L. BUNCH

U. S. Department of the Interior, Federal Water Pollution Control Administration, Advanced Waste Treatment Research Laboratory, Cincinnati, Ohio

Our knowledge of the fate of steroids normally present in domestic wastewater is rather meager. A better understanding of steroid biodegradation was sought. The data obtained showed that the susceptibility of the natural and synthetic ovulation-inhibiting steroids varied as to the rate of oxidation by the microorganisms of activated sludge. The synthetic estrogen and progestin components of oral contraceptives exhibited greater overall resistance to microbial degradation than the natural hormones.

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 concerned about the possible need to renovate domestic wastewater for human consumption,[2,3] and the identification of hazardous compounds

Table 30.1, Continued

Compound by Class	Concentration in Wastewater, μg/l (+ = Present, not quantified)							
	Raw Wastewater		Activated Sludge Effluent		Physical-Chemical Effluent		Lime-Clarified Raw Sewage	
	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)							+	
Nicotine		0.8		1.0		2.0		0.1
Salicylic acid[a]	+	+				+	+	+

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

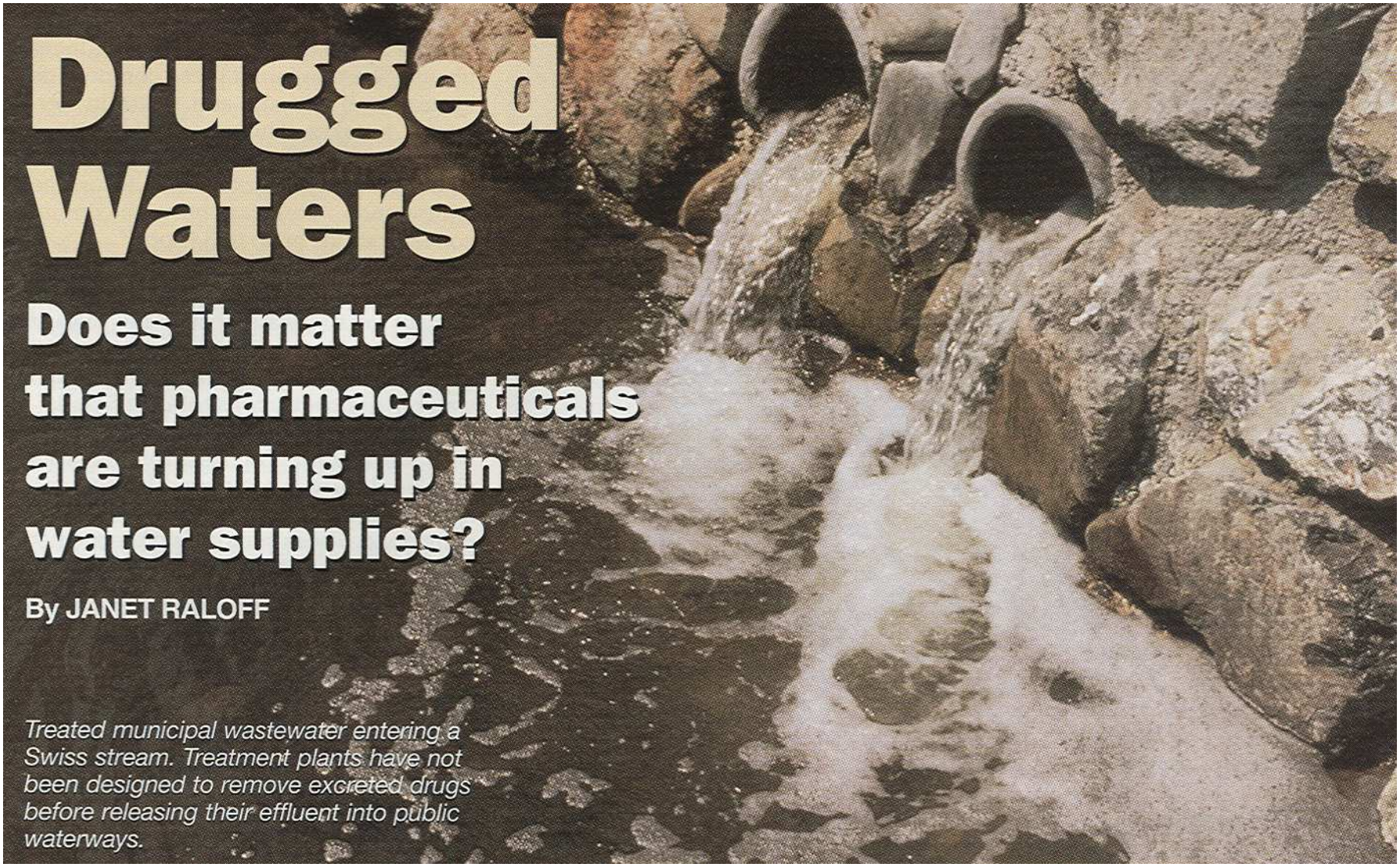
the highest level of estrogenic activity in effluent downstream from a small plant (55,000 gal/day) with relatively few treatment processes.

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

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.

AwwaRF & WateReuse Foundations
Tailored Collaboration:

"*Toxicological Relevance of EDCs and Pharmaceuticals in Water*"

Projects 3085/04-003

- Dr. Djanette Khiari – AwwaRF

- Mr. Joshua Dickinson - WRF

Awwa Research Foundation

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WATEREUSE FOUNDATION

Study Objective

To provide water utilities, regulators, the scientific community, and the public with information regarding the occurrence and health relevance of EDCs and pharmaceuticals in drinking water.

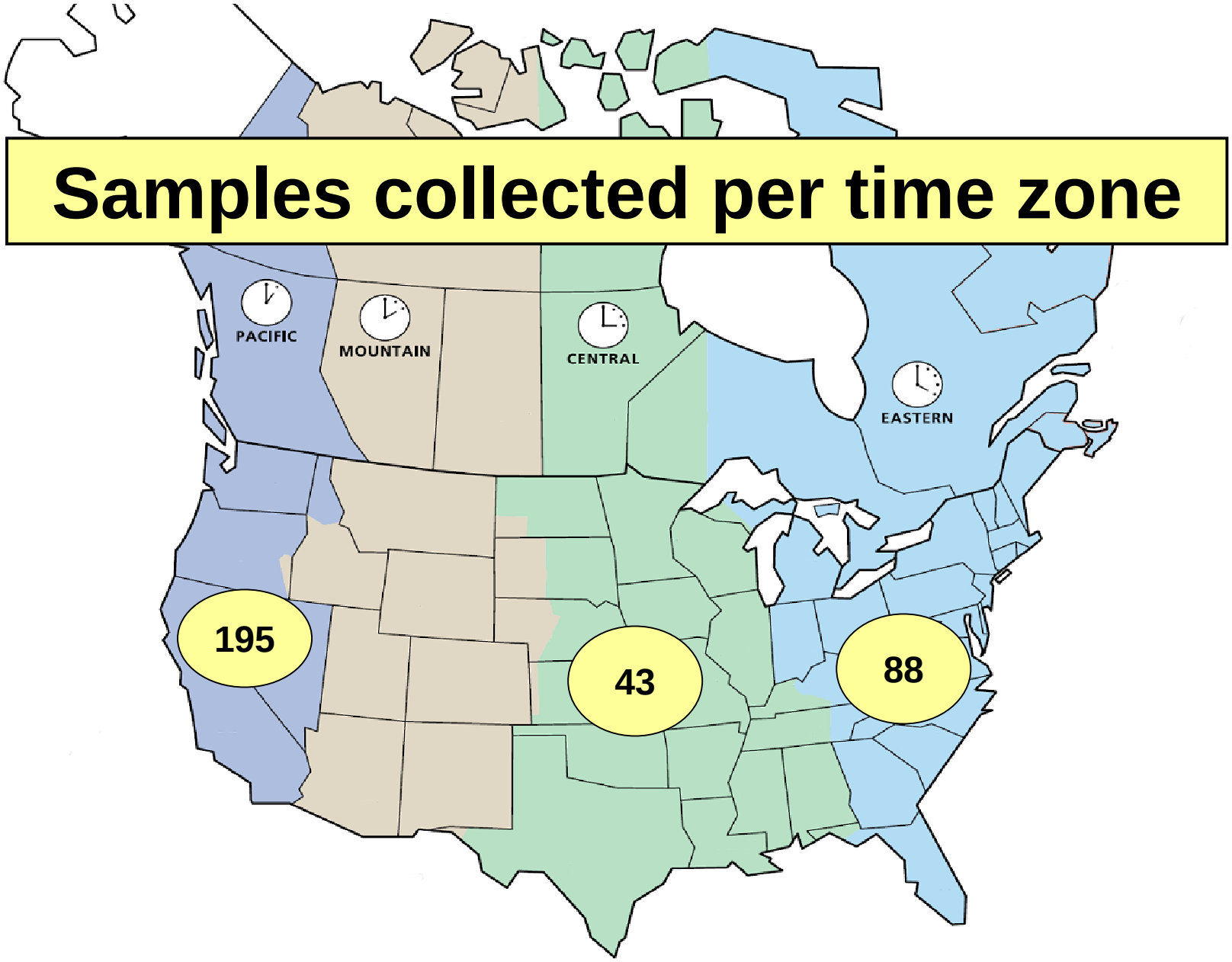
These data provide guidance for allocating resources responsibly. Meaningful treatment goals and analytical reporting limits must be based on human health protection.

Core Team

Principal Investigators:	Dr. Shane Snyder Dr. Richard Pleus Ms. Gretchen Bruce Dr. Erin Snyder Dr. Jocelyn Hemming
Public Information:	Mr. JC Davis Mr. Roger Buehrer
Administration:	Mr. David Rexing
AwwaRF Project Manager:	Dr. Djanette Khiari
PAC:	Dr. Pankaj Parekh Dr, Charles Staples Mr. Steve Macaulay Mr. Mike Wehner

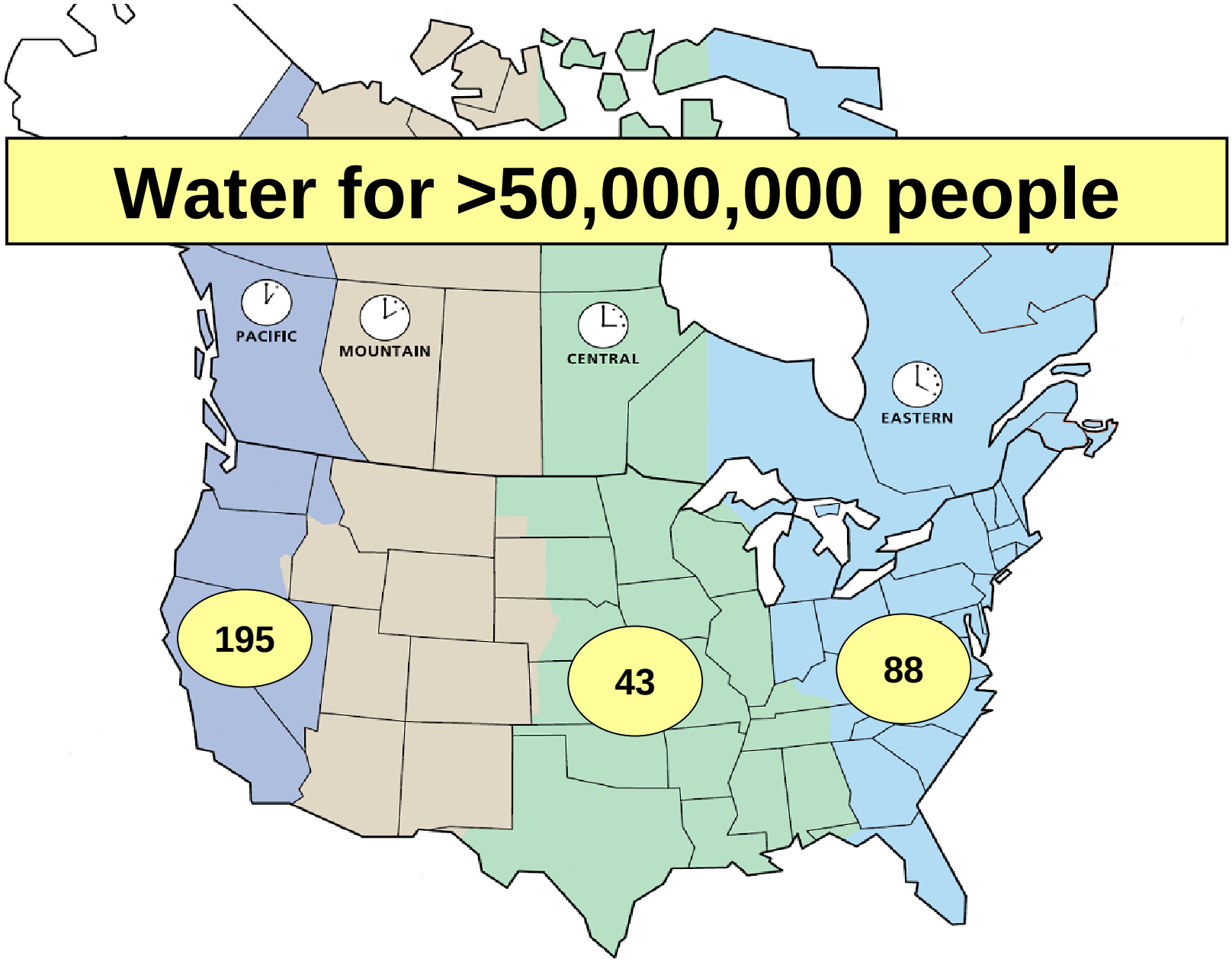
Site Selection

Samples collected per time zone



17 Participating Utilities

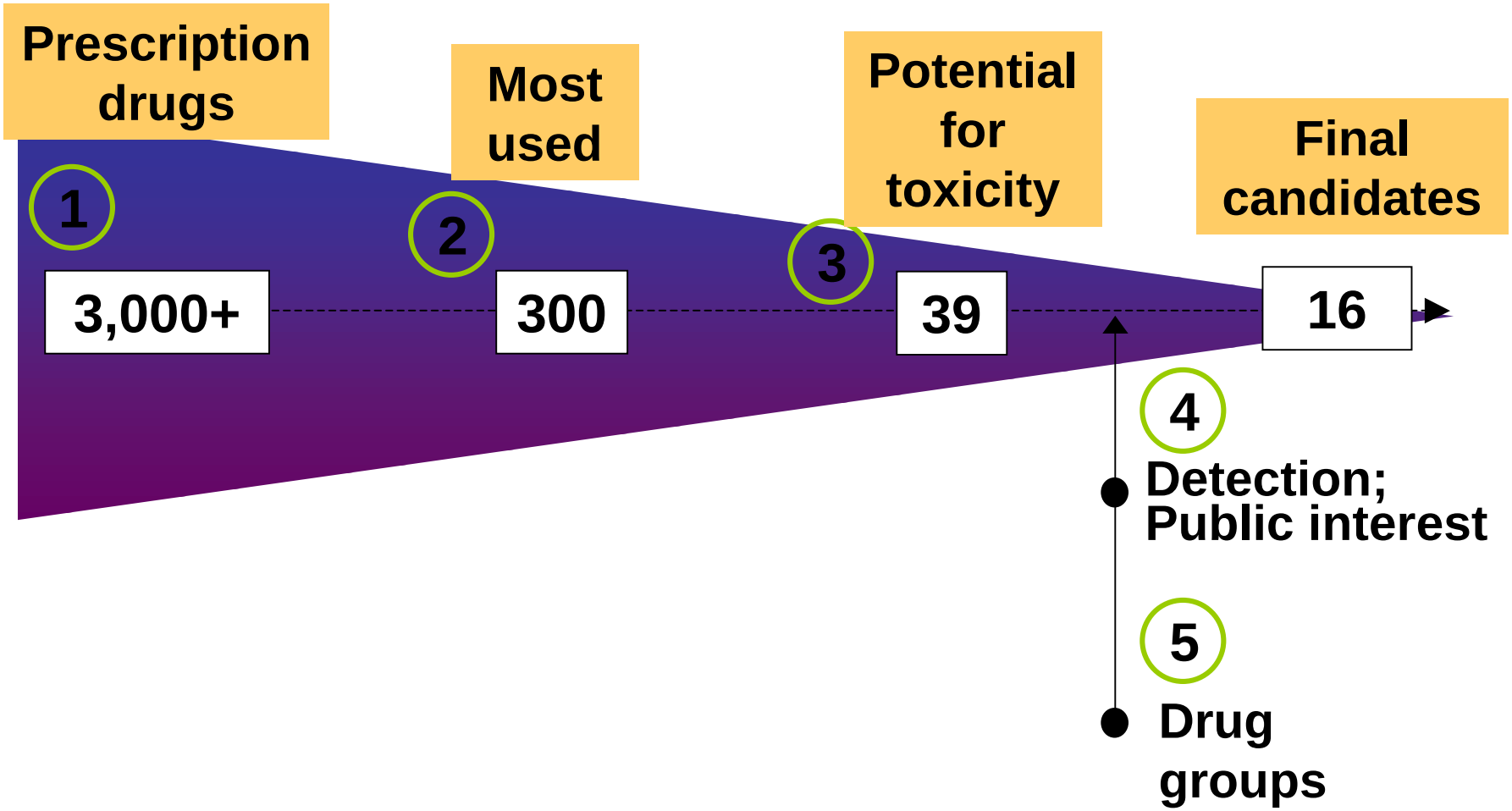
Water for >50,000,000 people



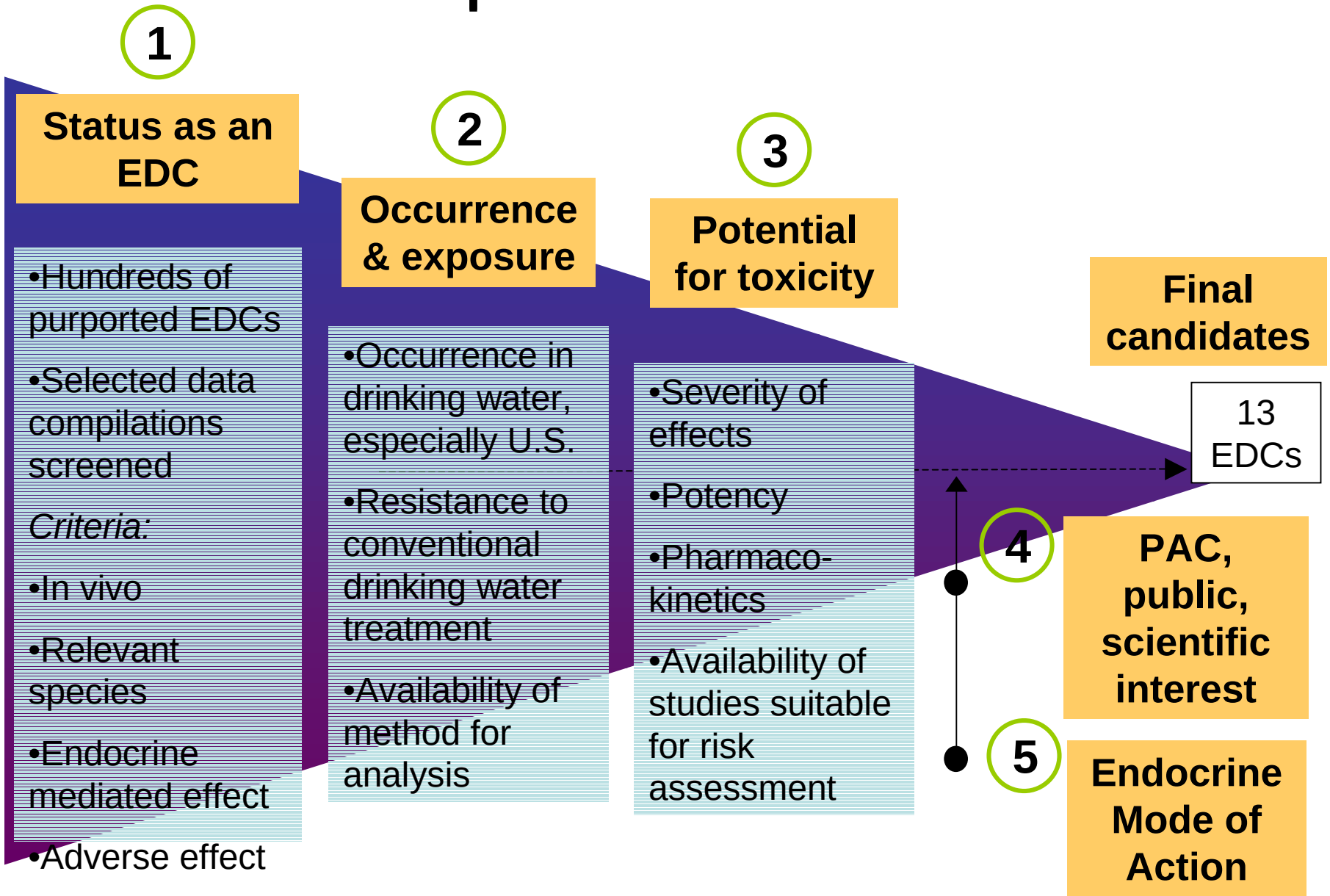
17 Participating Utilities

Compound Selection

Pharmaceuticals



Suspected EDCs

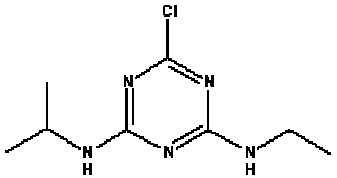


Pharmaceuticals (n=20)

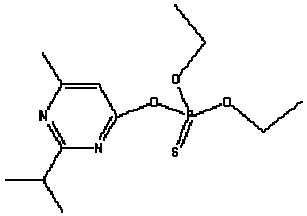
Pharmaceuticals	Synonym(s)	Use	MRL (ng/L)
Atenolol	Tenormin	Beta-blocker	0.25
Atorvastatin	Lipitor	Antilipidemic	0.25
o-Hydroxy atorvastatin		Atorvastatin metabolite	0.50
p-Hydroxy atorvastatin		Atorvastatin metabolite	0.50
Carbamazepine	Tegretol	Anticonvulsant	0.50
Diazepam	Valium	Tranquilizer	0.25
Diclofenac	Voltaren	NSAID	0.25
Enalapril	Renitec, Vasotec	ACE Inhibitor	0.25
Fluoxetine	Prozac	Antidepressant	0.50
Norfluoxetine		Fluoxetine metabolite	0.50
Gemfibrozil	Lopid	Antilipidemic	0.25
Meprobamate	Miltown	Anti-anxiety	0.25
Naproxen	Aleve	NSAID	0.50
Phenytoin	Dilantin	Antiepileptic	1.0
Risperidone	Risperidal	Antipsychotic	1.0
Simvastatin	Zocor	Antilipidemic	0.25
Simvastatin hydroxy acid		Simvastatin metabolite	0.25
Sulfamethoxazole	Bactrim	Antibiotic	0.25
Triclosan		Antimicrobial	1.0
Trimethoprim		Antibiotic	0.25

Potential EDCs (n=26)

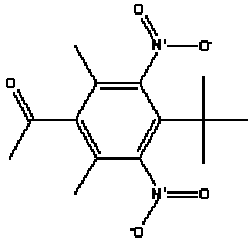
Potential EDCs	MRL (ng/L)	Potential EDCs	MRL (ng/L)
Atrazine	0.25	Galaxolide	25
Benzophenone	25	Linuron	0.50
BHA	25	Methoxychlor	10
BHT	25	Metolachlor	10
α-BHC	10	Musk Ketone	25
β-BHC	10	Nonylphenol	100
γ-BHC (Lindane)	10	Octachlorstyrene	10
δ-BHC	10	Octylphenol	25
Bisphenol A	5.0	TCEP	50
Butylbenzylphthalate	50	TCPP	50
DEET	25	Tonalide	25
Diazinon	10	Traseolide	25
Bis(2-ethylhexyl)phthalate	100	Vinclozolin	10



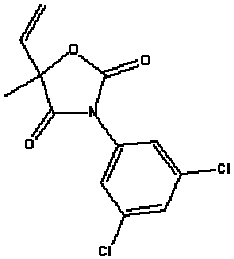
Atrazine



Diazinon

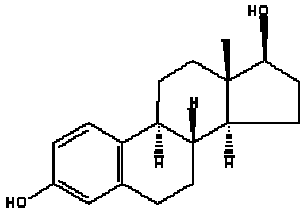


Musk Ketone



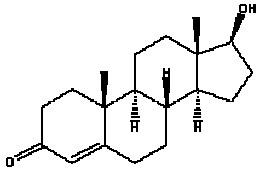
Vinclozolin

Steroids and Phytoestrogens (n=16)

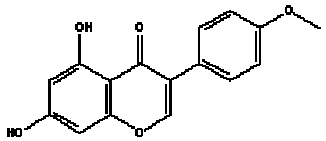


Estradiol

Steroids	Synonym	Source	MRL (ng/L)
Estradiol	E2	Human estrogen	0.50
Estrone	E1	Human estrogen	0.20
Ethynylestradiol	EE2	Synthetic birth control	1.0
Progesterone		Human estrogen	0.50
Testosterone	T	Human androgen	0.50

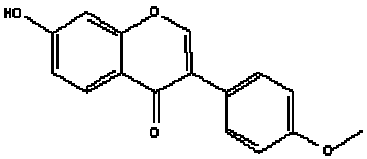


Testosterone

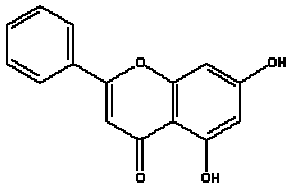


Biochanin A

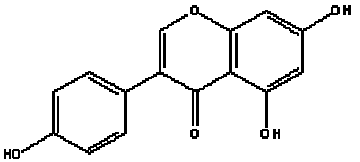
Phytoestrogens	Source(s)	MRL (ng/L)
Apigenin	Leafy plants	1.0
Biochanin A	Legumes and red clover	1.0
Chrysin	Passiflora caerula (passion flower)	1.0
Coumestrol	Alfalfa	1.0
Daidzein	Legumes and red clover	1.0
Equol	Daidzein metabolite	10
Formononetin	Clover	1.0
Genistein	Legumes and red clover	1.0
Glycitein	Legumes	1.0
Matairesinol	Oilseeds (such as sesame)	5.0
Naringenin	Citrus fruits and tomatoes	1.0



Formononetin



Chrysin



Genistein

Analytical Methods

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.

ELSEVIER

Chemosphere 65 (2006) 1990–1998

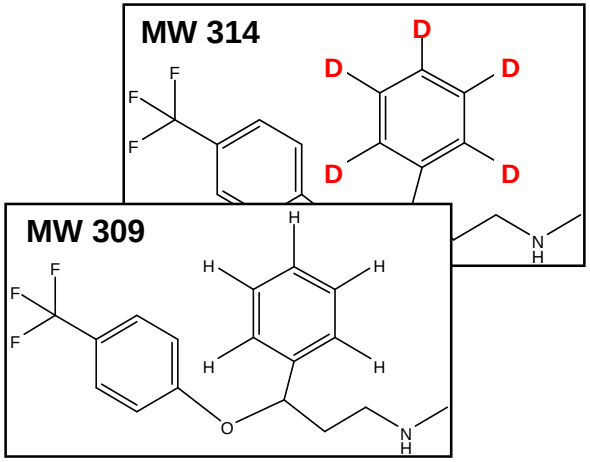
CHEMOSPHERE

www.elsevier.com/locate/chemosphere

Broad range analysis of endocrine disruptors and pharmaceuticals using gas chromatography and liquid chromatography tandem mass spectrometry

Rebecca A. Trenholm *, Brett J. Vanderford, Janie C. Holady, David J. Rexing, Shane A. Snyder

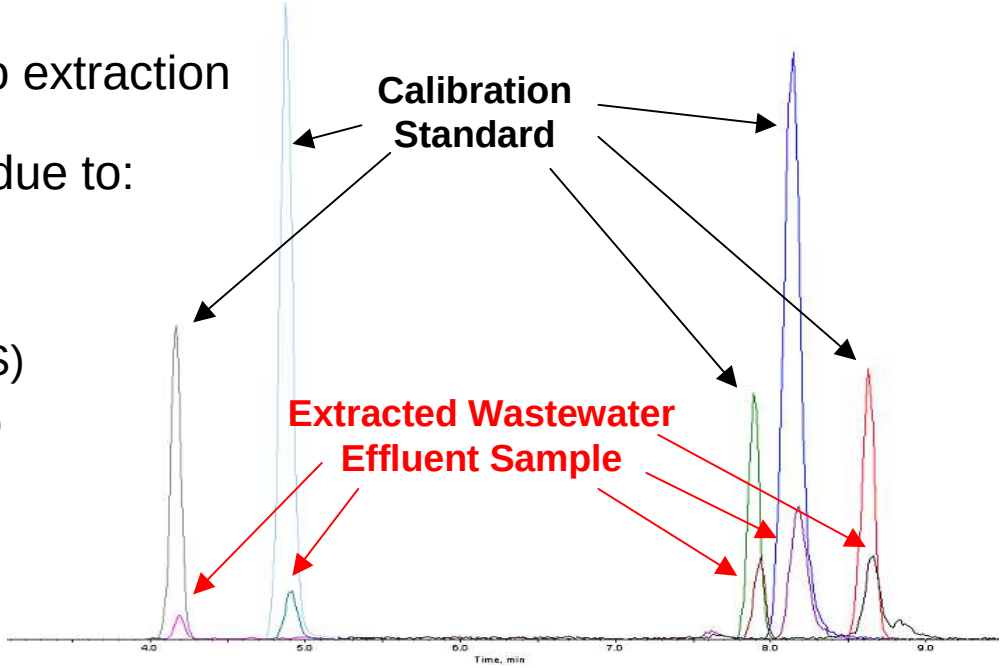
Isotope Dilution

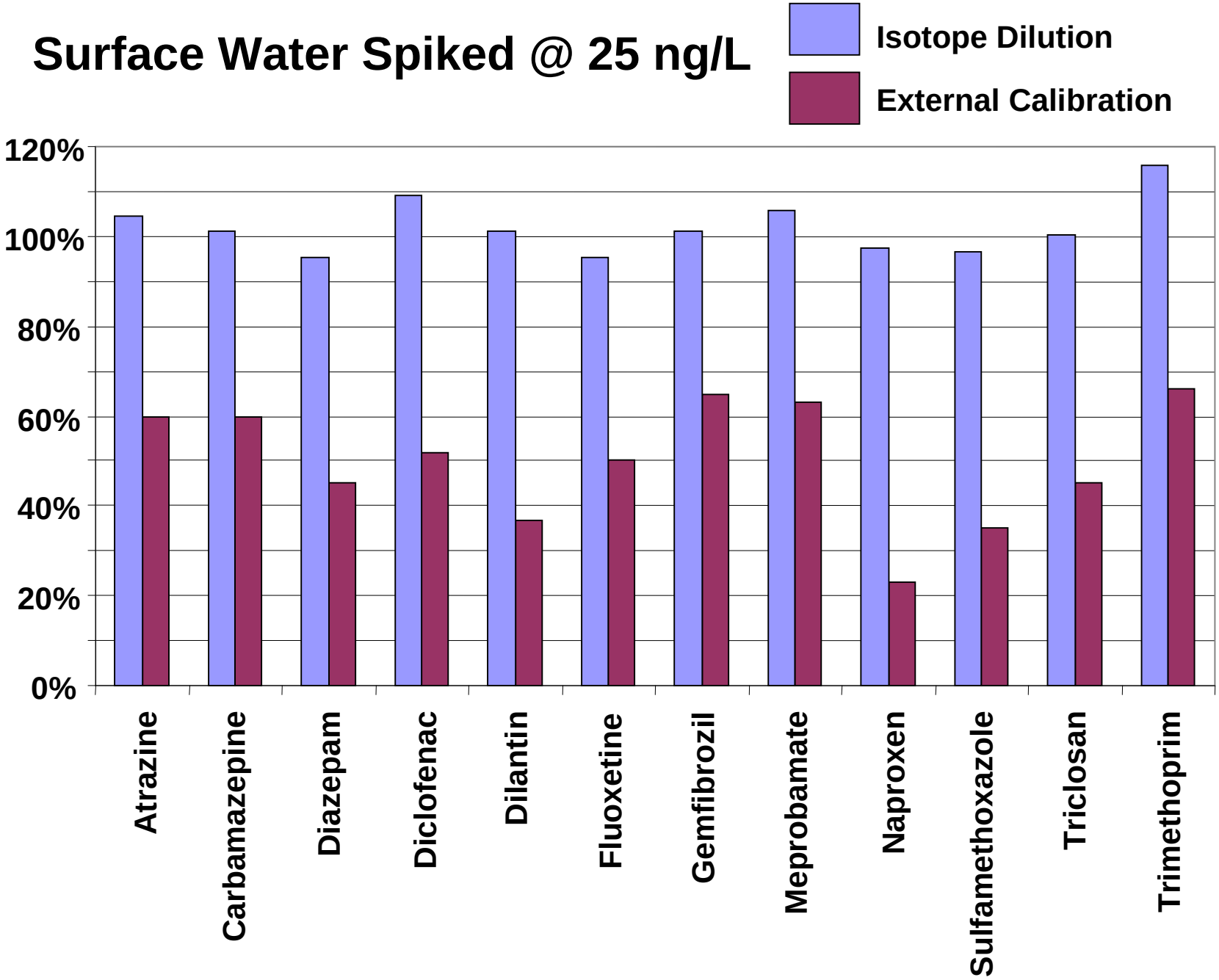


Fluoxetine (-d_5)

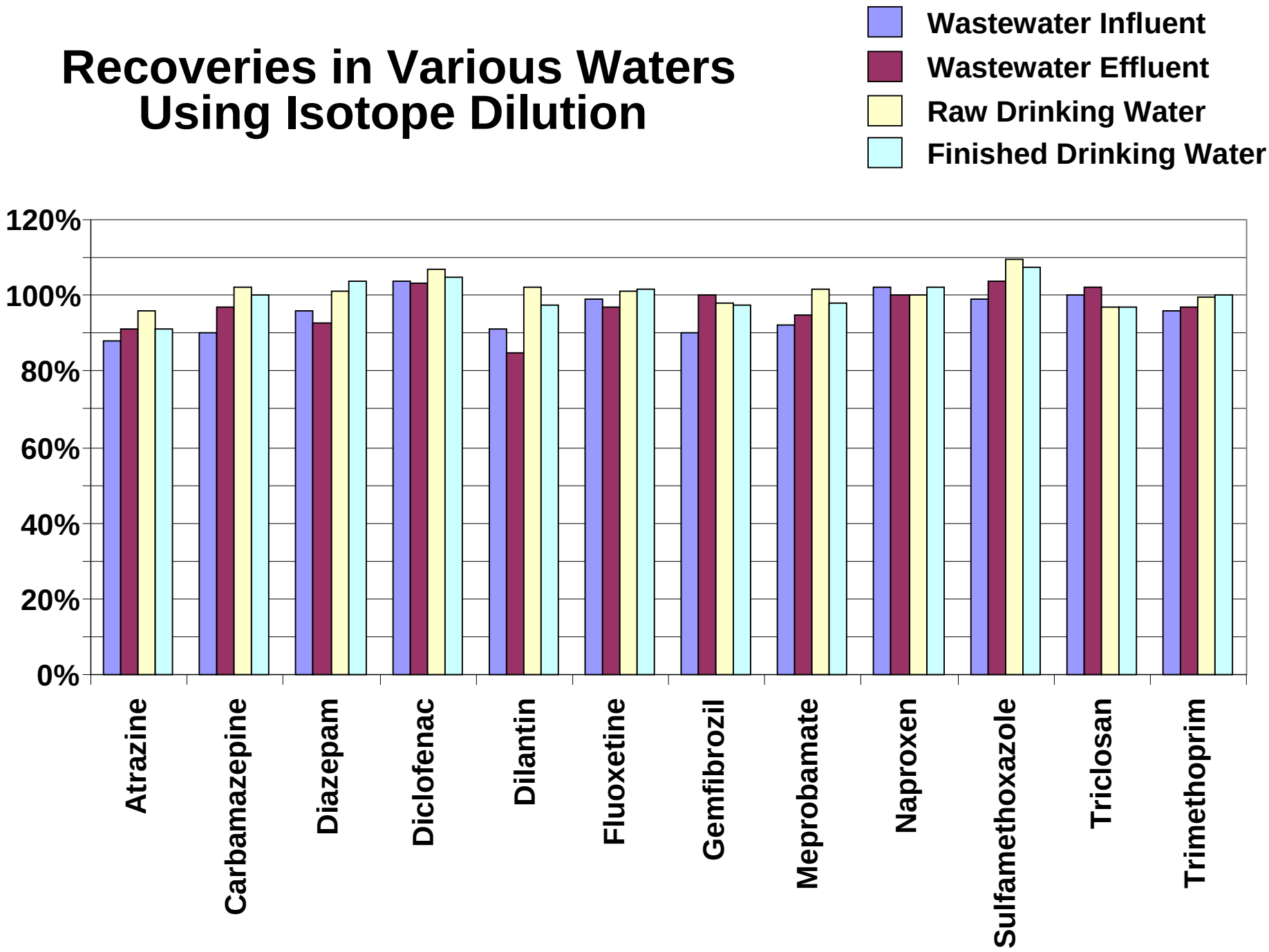
- Atoms are replaced with stable, heavier isotopes
  $^{12}C \rightarrow {}^{13}C$, $^{14}N \rightarrow {}^{15}N$, $^{1}H \rightarrow {}^{2}H$ (deuterium)
- Little interference, not abundant in nature
- Isotopes virtually identical in all chemical characteristics to native compound → act as a "perfect" internal standard
- Change in MW → Can be differentiated in MS detectors

- Samples spiked with isotopes prior to extraction
- Correct for loss of native compound due to:
  - Matrix adsorption
  - Preparation/Extraction loss
  - Matrix suppression (LC-MS)
  - Change in sensitivity due to active sites (GC-MS)




Surface Water Spiked @ 25 ng/L
Isotope Dilution
External Calibration
120%
100%
80%
60%
40%
20%
0%
Atrazine
Carbamazepine
Diazepam
Diclofenac
Dilantin
Fluoxetine
Gemfibrozil
Meprobamate
Naproxen
Sulfamethoxazole
Triclosan
Trimethoprim

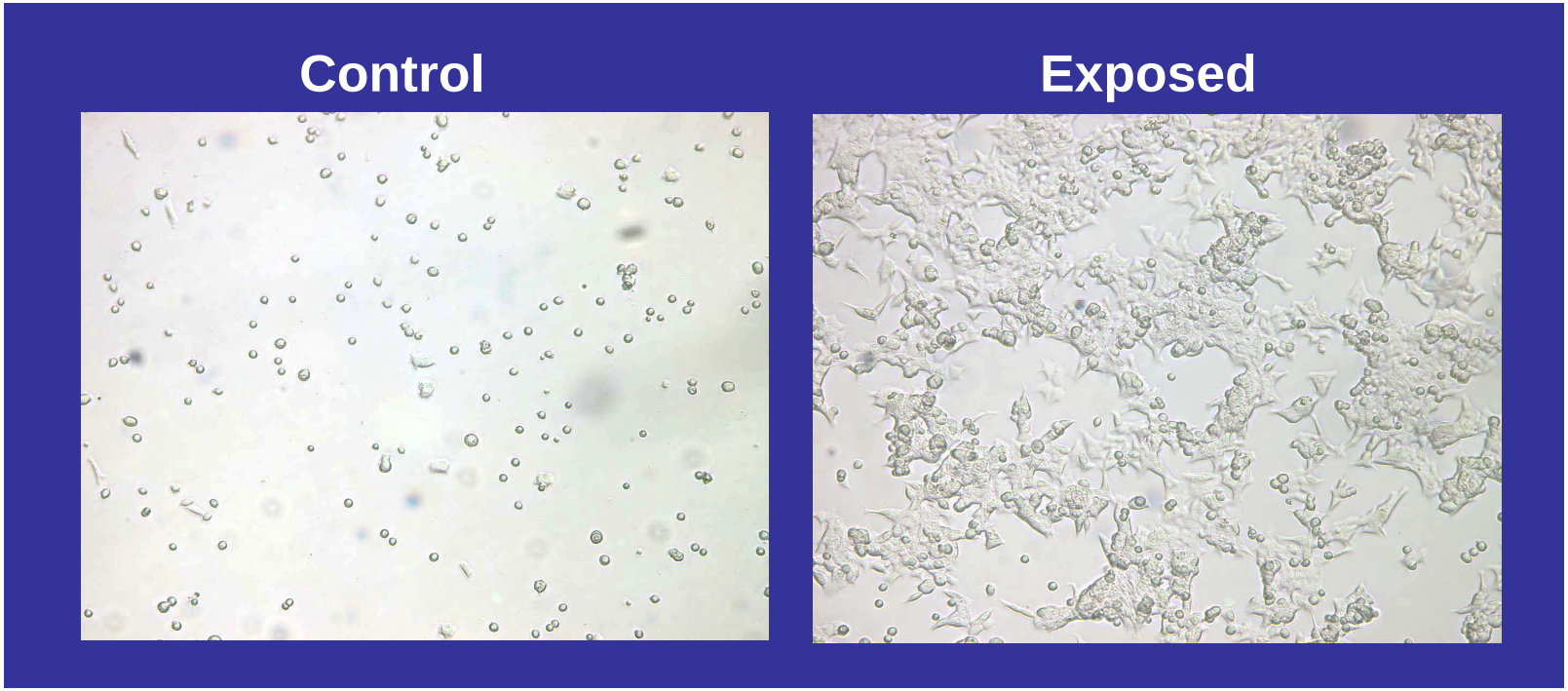
Recoveries in Various Waters Using Isotope Dilution



E-screen Assay

(Dr. Jocelyn Hemming – WSLH)

- Human breast cancer cells proliferate in response to estrogenic compounds
- Calibrated using estrogen (E2) and results reported as estradiol equivalents (EEq)



Results

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*

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**

Raw Intake for “Impacted” Drinking Water Facilities (n=19)			
Compound	Max (ng/L)	Median (ng/L)	Frequency (>50%)
Sulfamethoxazole	110	12	89
Meprobamate	73	8.2	84
Carbamazepine	51	4.1	79
Atrazine	870	32	79
Estrone	0.90	0.33	79
Dilantin	29	5.0	74
Atenolol	36	2.2	63
Trimethoprim	11	0.75	58
Gemfibrozil	24	2.2	58
Naproxen	32	0.93	58
Diethylhexyl phthalate	170	90	58
Nonylphenol	130	88	58
TCEP	530	120	53

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 Drinking Water*

Pharmaceuticals	Potential EDCs	Steroid Hormones	Phytoestrogens
Atenolol	**Atrazine**	Estradiol	Apigenin
Atorvastatin	Benzophenone	Estrone	Biochanin A
o-Hydroxy atorvastatin	BHA	Ethinylestradiol	Chrysin
p-Hydroxy atorvastatin	BHT	Progesterone	Coumestrol
Carbamazepine	α-BHC	Testosterone	Daidzein
Diazepam	β-BHC		Equol
Diclofenac	γ-BHC		Formononetin
Dilantin	δ-BHC		Genistein
Enalapril	Bisphenol A		Glycitein
Fluoxetine	Butylbenzyl phthalate		Matairesinol
Norfluoxetine	**DEET**		Naringenin
Gemfibrozil	Diazinon		
Meprobamate	Dioctyl phthalate		
Naproxen	Galaxolide		
Risperidone	Linuron		
Simvastatin	Methoxychlor		
Simvastatin hydroxy acid	**Metolachlor**		
Sulfamethoxazole	Musk ketone		
Triclosan	Nonylphenol		
Trimethoprim	Octachlorostyrene		
	Octylphenol		
	TCEP		
	TCPP		
	Tonalide		
	Traseolide		
	Vinclozolin		

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

Finished Water for Drinking Water Treatment Facility (n=18)			
Compound	**Max (ng/L)**	**Median (ng/L)**	**Frequency (%)**
Atrazine*	**870**	**49**	**83**
Meprobamate	**42**	**5.7**	**78**
Dilantin	**19**	**6.2**	**56**

***Atrazine is regulated under the Safe Drinking Water Act with an MCL of 3000 ng/L**

Food / Beverages

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

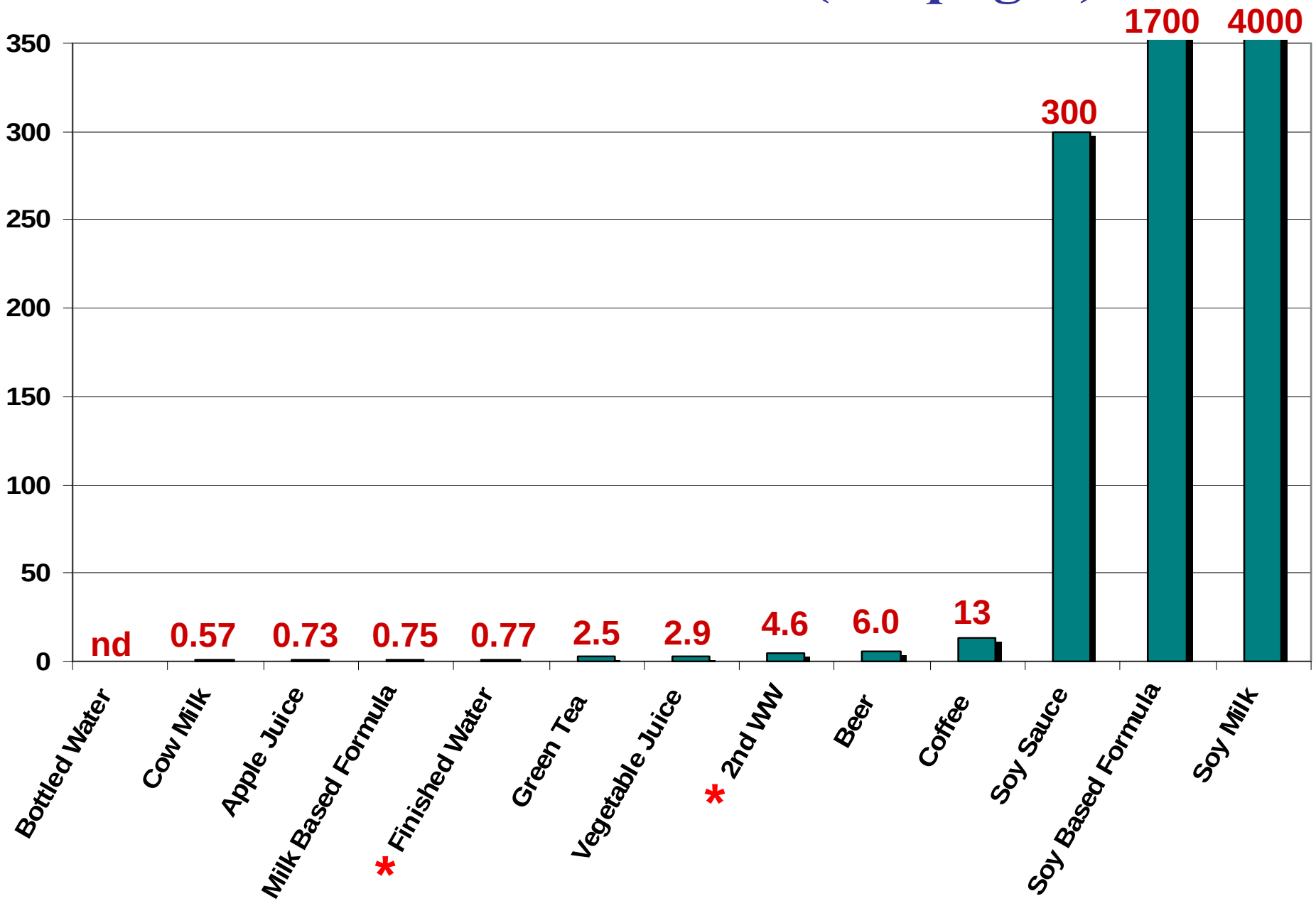
Chemical names:	ESTRA-1,3,5(10)-TRIENE-3,17beta-DIOL
Synonyms:	**ESTRADIOL**
Functional class:	VETERINARY DRUG (PRODUCTION AID)
Latest evaluation:	1999
ADI:	0-0.00005 mg/kg bw **= 50 ng/Kg = 3500 ng/70 Kg person**
Comments/MRLs:	MRLs: Muscle, liver, kidney and fat (cattle): NOT SPECIFIED
Report:	TRS 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

12 Nov 01

Sample Matrices

- Food/beverage items
  - Bottled water
  - Soy sauce
  - Beer
  - Tea
  - Coffee
  - Apple/vegetable juice
  - Milk (cow/soy based)
  - Baby formula (cow/soy based)

E-screen Results (EEq ng/L)



EEq Comparison
(Max Finished Water)

≈

1 cup coffee
(17 ng/L, 240 mL)

5.3 Liters Finished Drinking Water
(0.77 ng/L)

EEq Comparison

≈

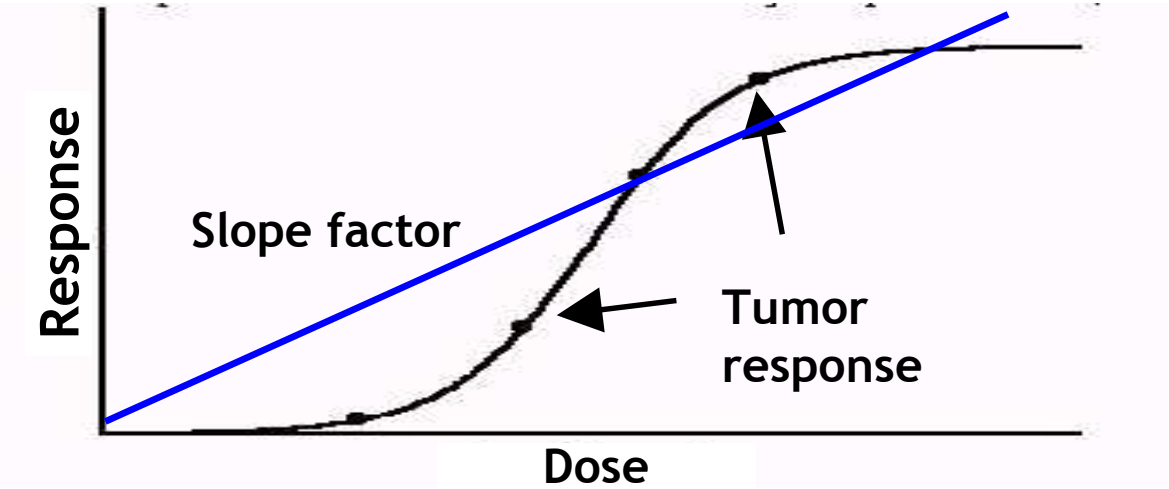
Soy Baby Formula
(1700 ng/L, 4 oz Bottle)

265 Liters of Finished Drinking Water
(0.77 ng/L)

Risk Assessment

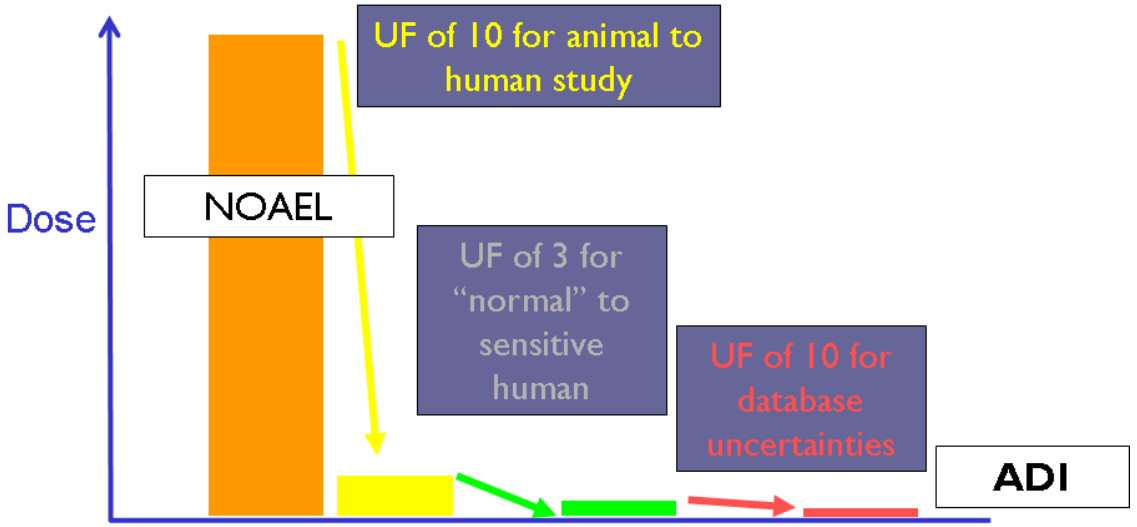
deriving ADIs / screening values

carcinogens



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

non cancer



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

EDCs
endocrine-mediated endpoints

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

Pharmaceuticals

Drug	Toxic Effect	ADI (µg/kg-d)	DWEL (µg/L)	Max Finished Water Conc. (µg/L)	Margin of Exposure (Finished Water)
Atenolol	Cancer, rat	2.0	70	**0.026**	**2,700**
Atorvastatin	Cancer, rat	0.54	19	<0.00025	>76,000
o-hydroxy atorvastatin		0.54	19	<0.00050	>38,000
o-hydroxy atorvastatin		0.54	19	<0.00050	>38,000
Carbamazepine	Cancer, rat	0.34	12	**0.018**	**670**
Diazepam	Developmental, rat	1.0	35	**0.00033**	**110,000**
Diclofenac	Developmental, mouse	67	2,300	<0.00025	>9,200,000
Enalapril	Developmental, human	0.23	8.1	<0.00025	>32,000
Fluoxetine	Developmental, human	1.0	35	**0.00082**	**43,000**
Norfluoxetine		1.0	35	<0.00050	>70,000
Gemfibrozil	Cancer, rat	1.3	45	**0.0021**	**21,000**
Meprobamate	Systemic, mouse	7.5	260	**0.043**	**6,000**
Naproxen	Reproductive/ Developmental, mouse	570	20,000	<0.00050	>40,000,000
Phenytoin	Cancer, mouse	0.19	6.8	**0.032**	**210**
Risperidone	Cancer, mouse & rat	0.014	0.49	**0.0020**	**240**
Simvastatin	Cancer, rat	0.54	19	<0.00025	>76,000
Simvastatin hydroxy acid		0.54	19	<0.00025	>76,000
Sulfamethoxazole	Developmental, rat	510	18,000	**0.0030**	**6,000,000**
Triclosan	Systemic, hamster	75	2,600	**0.0012**	**2,200,000**
Trimethoprim	Developmental, rat	190	6,700	<0.00025	>27,000,000

EDCs

Drug	Toxic Effect	ADI (µg/kg-d)	DWEL (µg/L)	Max Finished Water Conc. (µg/L)	Margin of Exposure (Finished Water)	Current Criterion (µg/kg-d)*
Atrazine	Neurologic/ behavioral, mouse	5.0	180	**1.0**	**180**	35 (EPA RfD, 2004) 3.0 (ATSDR MRL, 2003)†
Bisphenol A	Developmental (endocrine), mouse	0.0020	0.070	**0.025**	**2.8**	50 (EPA RfD, 1993)
Butylbenzyl phthalate	Developmental/ reproductive (endocrine), rat	100	3500	<0.050	>70,000	200 (EPA RfD, 1993)
DEHP	Developmental (endocrine), rat	12	430	<0.10	>4,300	20 (EPA RfD, 1998) 0.17 (EPA SF- cancer, equiv dose, 1993)
17ß-Estradiol	Endocrine-mediated effects, human	0.017	0.58	<0.00050	>1,200	0.0050 (Australia EPHC, 2007)‡ 0.050 (JEFCA WHO, 2000)**
Estrone	Endocrine-mediated effects, human	0.013	0.47	<0.00020	>2,400	0.0086 (Australia EPHC, 2007)‡
Ethinylestradiol	Endocrine-mediated effects, human	0.00010	0.0035	<0.0010	>3.5	0.00043 (Australia EPHC, 2007)‡
Lindane	Reproductive, rat	0.056	2.0	<0.010	>200	0.30 (EPA RfD, 1993) 0.00091 (CA OEHHA PHG- cancer, equiv dose, 2005)
Linuron	No new relevant studies	---	70	**0.0083**	**8,400**	2.0 (EPA RfD, 1993)
Methoxychlor	Developmental/ behavioral, mouse	0.020	0.70	<0.010	>70	0.85 (CA OEHHA PHG, 1999)† 5.0 (EPA RfD, 1993)
4-Nonylphenol	Renal toxicity, rat (3-gen reproductive study)	50	1800	**0.10**	**18,000**	None
4-tert-Octylphenol	Developmental, rat	13	440	<0.025	>17,000	None
Vinclozolin	No new relevant studies	---	880	<0.010	>88,000	25 (EPA RfD, 1992)

Amount of water to meet ADI / screening value
pharmaceuticals

	ADI-DWEL	Maximum Water Conc. Finished	Amount of water to meet ADI		
	µg/L	µg/L	8 oz Glasses/d	Gallons/d	55-Gallon drums/d
Atenolol	70	0.026	22,800	1,400	25
Carbamazepine	12	0.018	5,500	340	6.2
Diazepam	35	0.00033	890,000	55,000	1,000
Fluoxetine	35	0.00082	360,000	22,000	400
Gemfibrozil	45	0.0021	180,000	11,000	200
Meprobamate	260	0.043	51,000	3,200	58
Phenytoin	6.8	0.032	1,800	110	2.0
Risperidone	0.49	0.00034	12,000	770	14
Sulfamethoxazole	18,000	0.0030	51,000,000	3,200,000	58,000
Triclosan	2,600	0.0012	19,000,000	1,200,000	22,000

Amount of water to meet ADI /screening value
EDCs

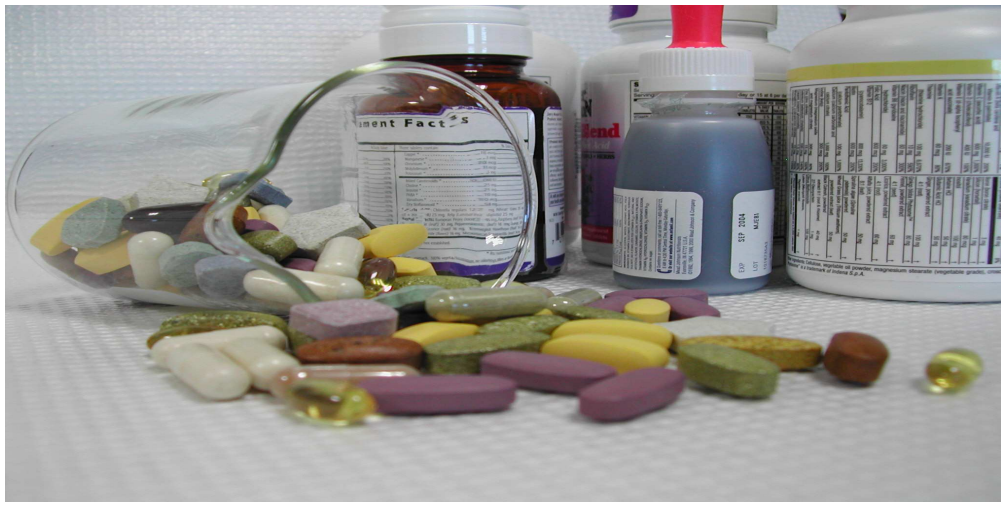
	ADI-DWEL	Maximum Water Conc.	Amount of water to meet ADI		
		Finished			
	µg/L	µg/L	8 oz Glasses/d	Gallons/d	55-Gallon drums/d
Atrazine	180	1.0	1,500	92	1.7
Bisphenol A	0.070	0.025	25	1.6	0.029
Linuron	70	0.0083	2,000	120	2.2
4-Nonylphenol	1800	0.10	148,000	9,200	170

BUT What about the MIXTURES?

WHO – 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.



Conclusions

The public has difficulty with the concept of relative concentrations

- Instead, they apply the “present/absent” litmus test

- Adverse health effects are presumed if present

Micrograms per liter ?

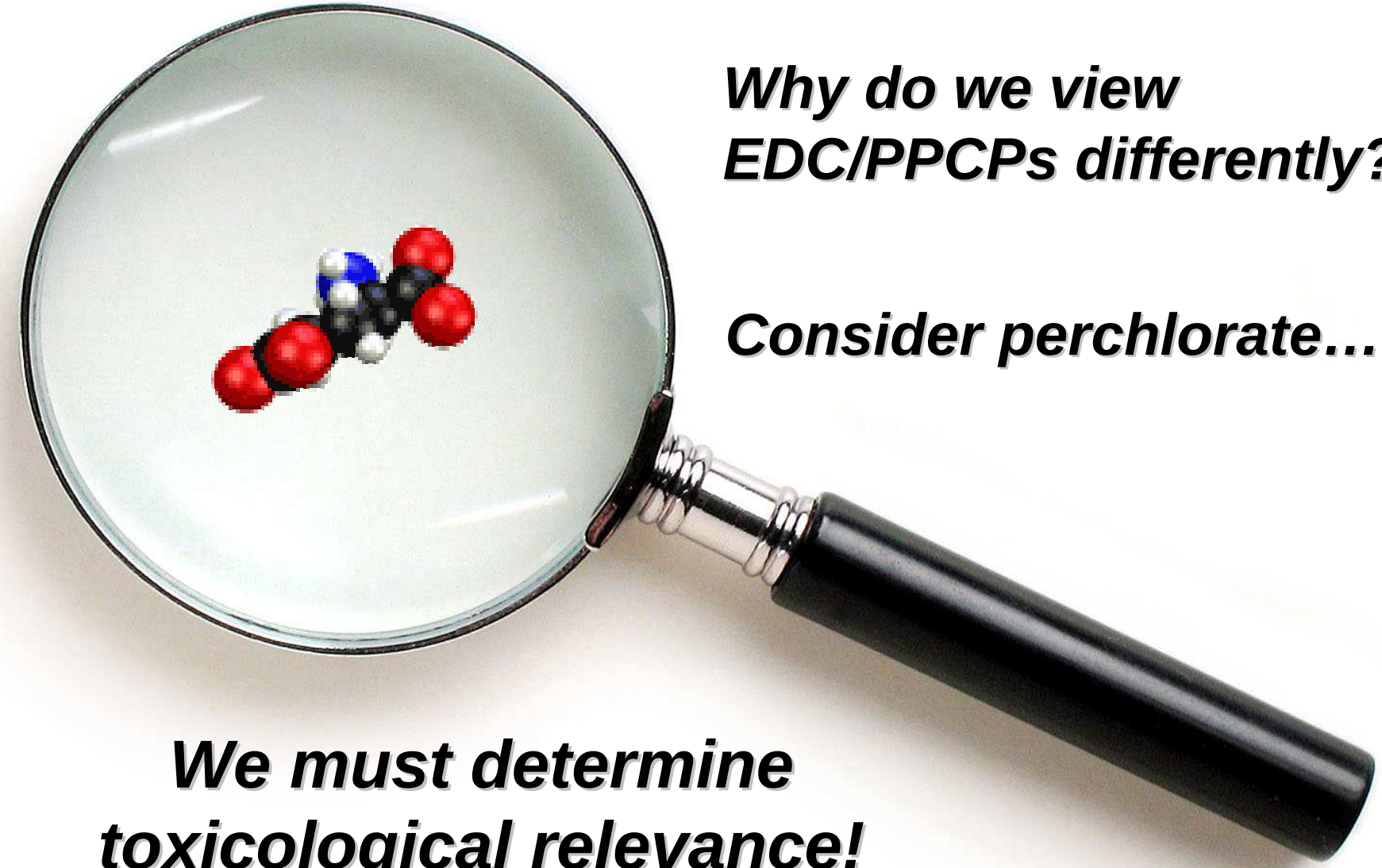
Nanograms per liter ?

Picograms per liter ?

Zeptograms per liter ?


ZERO

What will we find at pg/L, fg/L, åg/L?



Why do we view EDC/PPCPs differently?

Consider perchlorate…

We must determine toxicological relevance!

Chemical & Engineering News

Cover Story

February 25, 2008
Volume 86, Number 08
pp. 13-17

Side Effects

Pharmaceuticals have been finding their way into our environment for a long time, but just what are they doing there?

Bethany Halford

NO ONE EVER planned for fish to take birth control pills. But they are. As treated wastewater flows into rivers and streams every day, fish all over the world get a tiny dose of 17α-ethinylestradiol, a synthetic steroidal estrogen that's used in birth control pills. They also get a little sip of the anticonvulsant carbamazepine, a nip of the antidepressant fluoxetine, and a taste of hundreds of other drugs that we take to make our lives better.

Every drug begins its life as a promise—a promise to fight disease or improve our quality of life. It wends its way through the discovery process and clinical trials until it ends up in our bodies, ready to do its job.

EPA

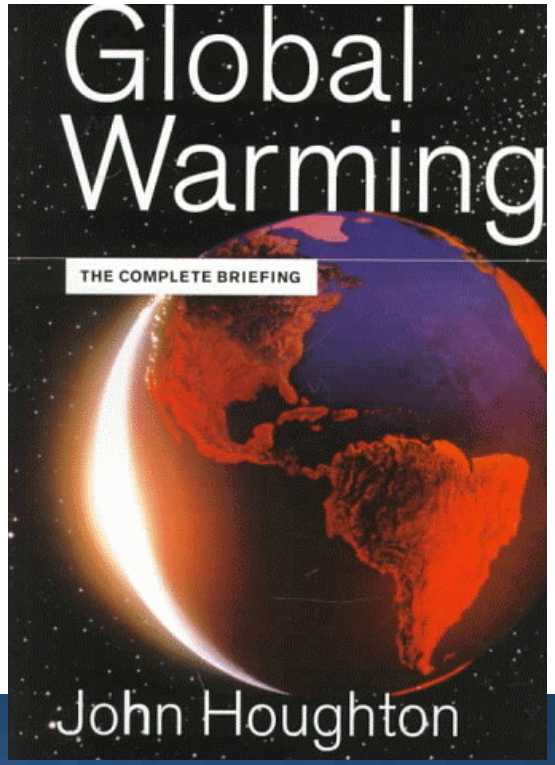
A Complex System Fish, plants, and other aquatic life are feeling the effects of pharmaceuticals in the environment.

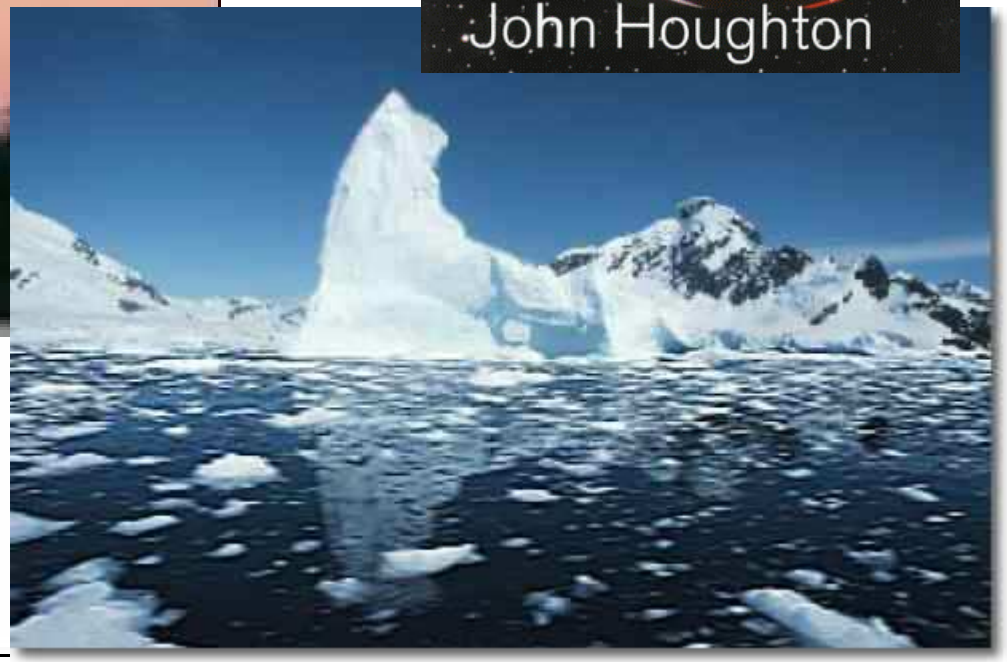

EAGLE

Wounded Waters

The Hidden Side of Power Plant Pollution

February 2004





Conclusions

- Trace amounts of steroids and pharmaceuticals have been reported in water for more than 30 years
- Robust analytical methods are capable of accurately detecting and quantifying chemicals in water at levels < 0.000000001 g/L
- Only 11 of 62 target compounds were detected in finished drinking water (>20% frequency)
  - Atrazine had highest frequency at 83%, but at less than 1/3rd the MCL
  - If MRLs were 10 ng/L, then 9 of 62 would have been detected
  - If MRLs were 100 ng/L, then 3 of 62 would have been detected
  - If MRLs were 1000 ng/L, then no compounds would have been detected
- Exposure to estrogenic chemicals in diet are far greater than in drinking water
- Toxicological relevance is critical in order to establish meaningful treatment and analytical goals

Conclusions

- Using EPA risk assessment paradigm, the DWELs for indicator pharmaceuticals and EDCs are FAR higher than occurrence
  - Conservative uncertainty factors used in each
  - Even if additional uncertain factors of 10-100x were applied for synergism/additivity, the DWELs would still be higher than occurrence
- The energy/water nexus is absolutely critical
  - We must avoid “moving” our pollution from water to air
  - Holistic risk evaluation is needed – “cradle to grave”
  - Energy efficient water treatment and health-based goals are key to sustainability
- Global partnerships are needed in order to disseminate findings, needs, and solutions

Shane Snyder

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