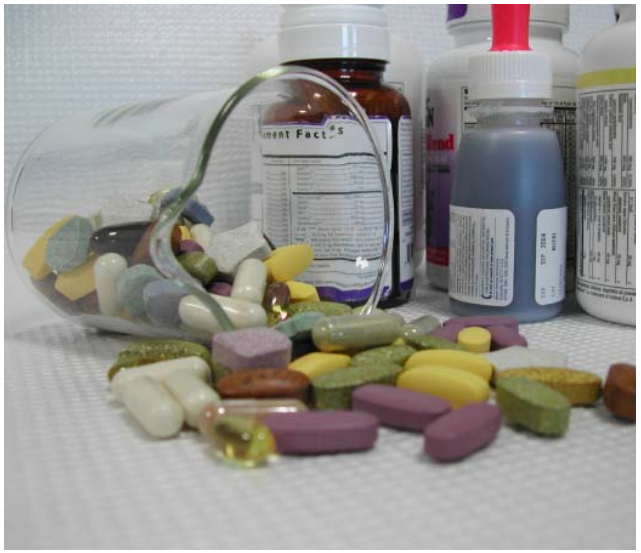
Toxicological Relevance of Pharmaceuticals and EDCs in Drinking Water



Southern Nevada Water Authority

Shane Snyder, Ph.D.

Applied R&D Center

Southern Nevada Water Authority

LAS VEGAS VALLEY WATER DISTRICT

PEOPLE LEADING THE WAY

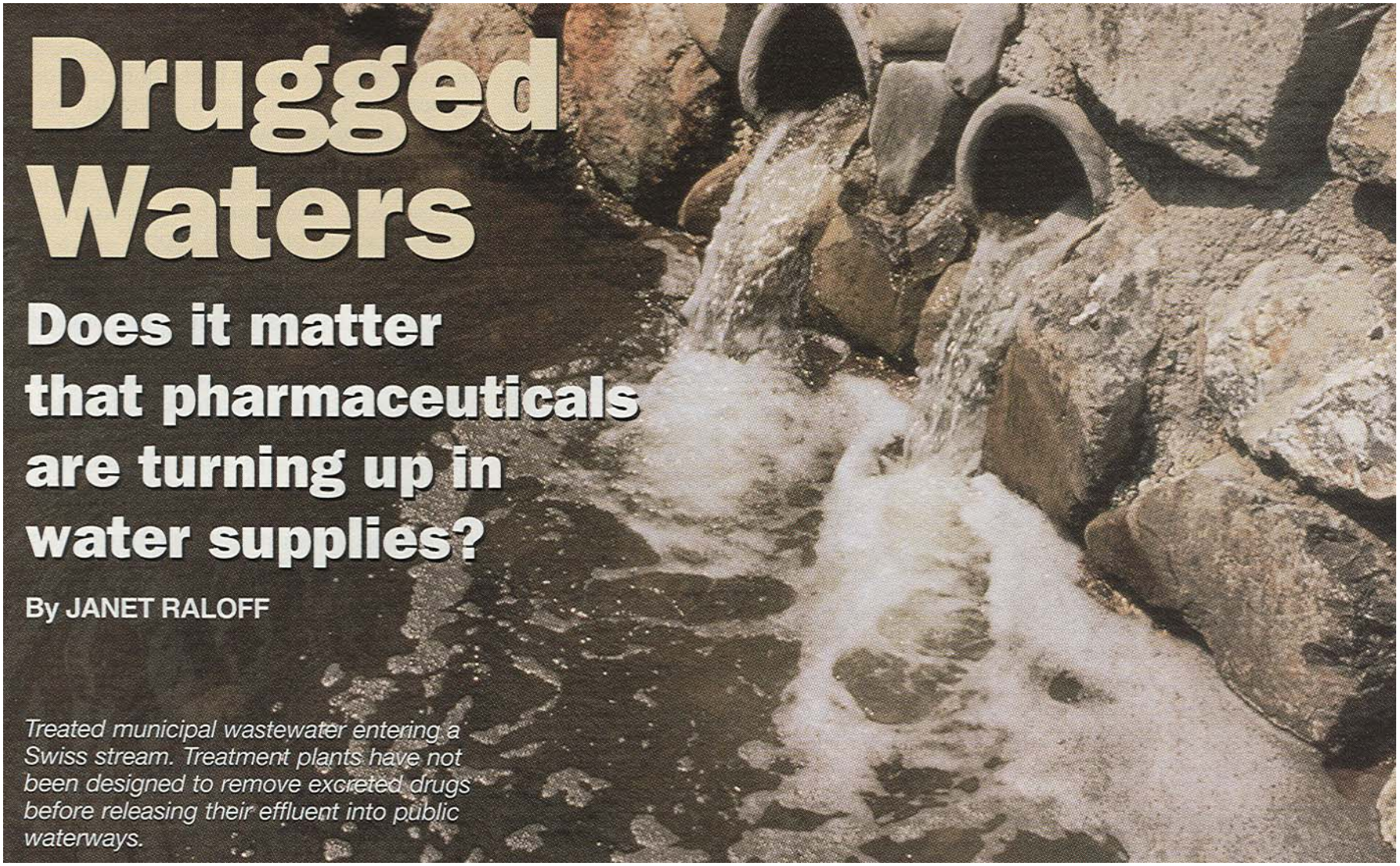
COMMUNITY SERVICE ENVIRONMENT


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 "UHH"?
Jim Day '08
LAS VEGAS REVIEW-JOURNAL

Drugged Waters

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

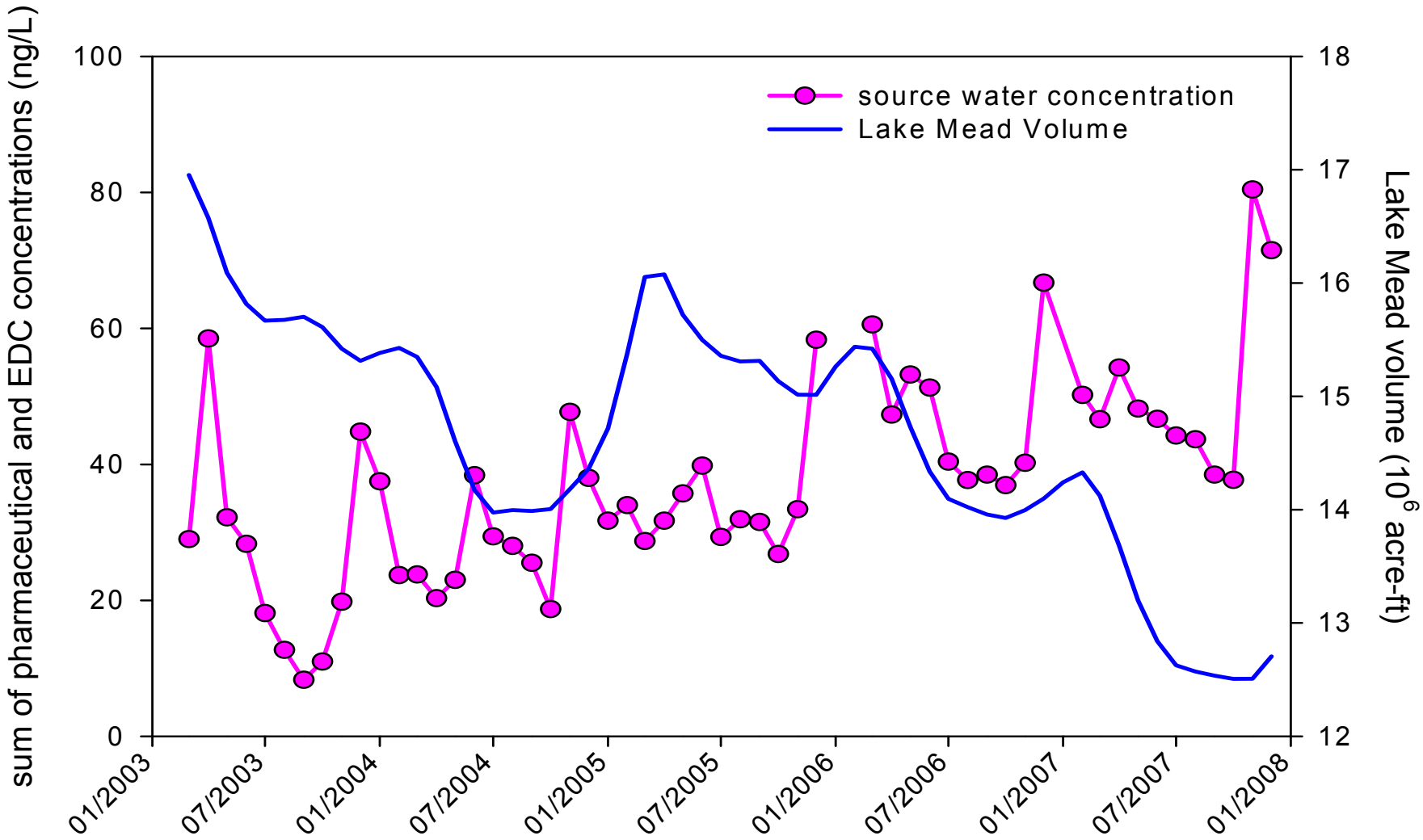
By JANET RALOFF



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

Drought

Effect on Pharmaceutical and EDC Concentrations



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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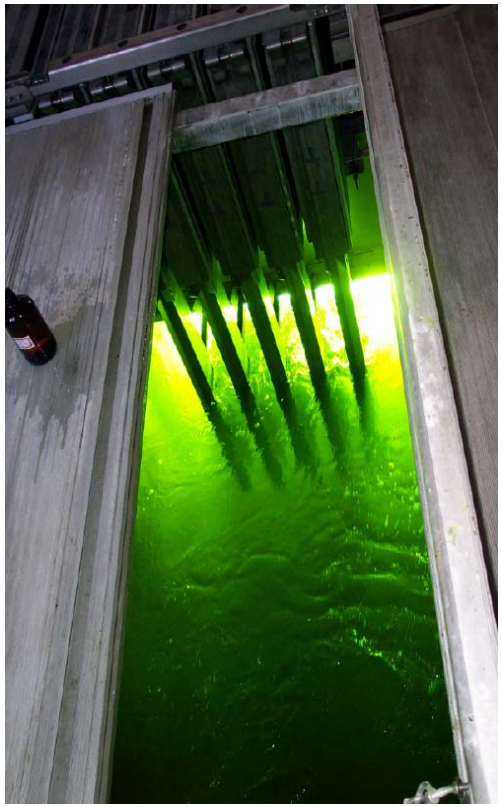

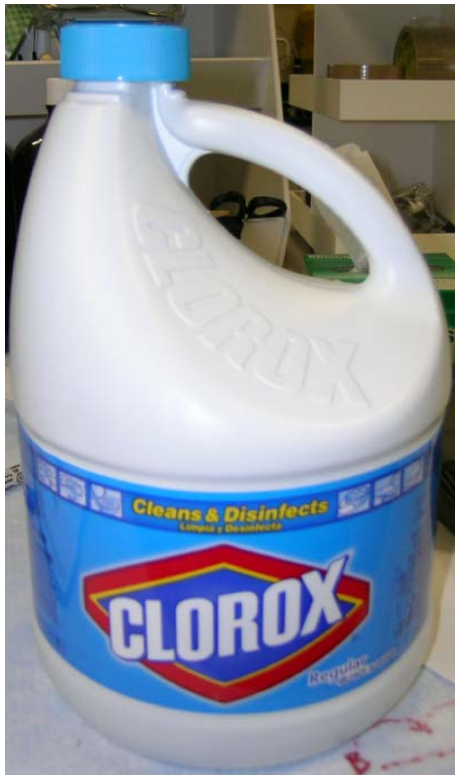
Cleans & Disinfects
CLOROX

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

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WATEREUSE FOUNDATION

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

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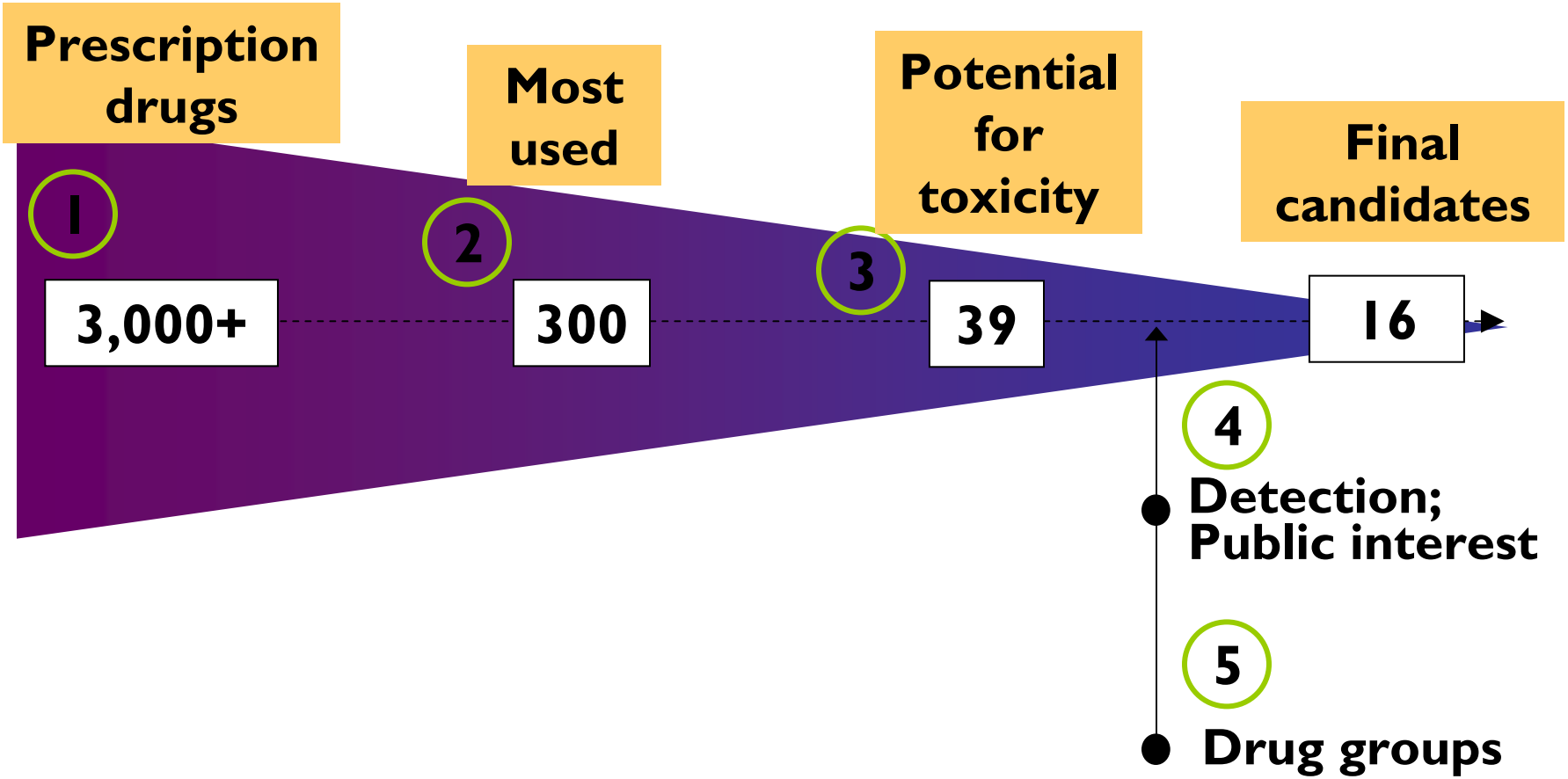
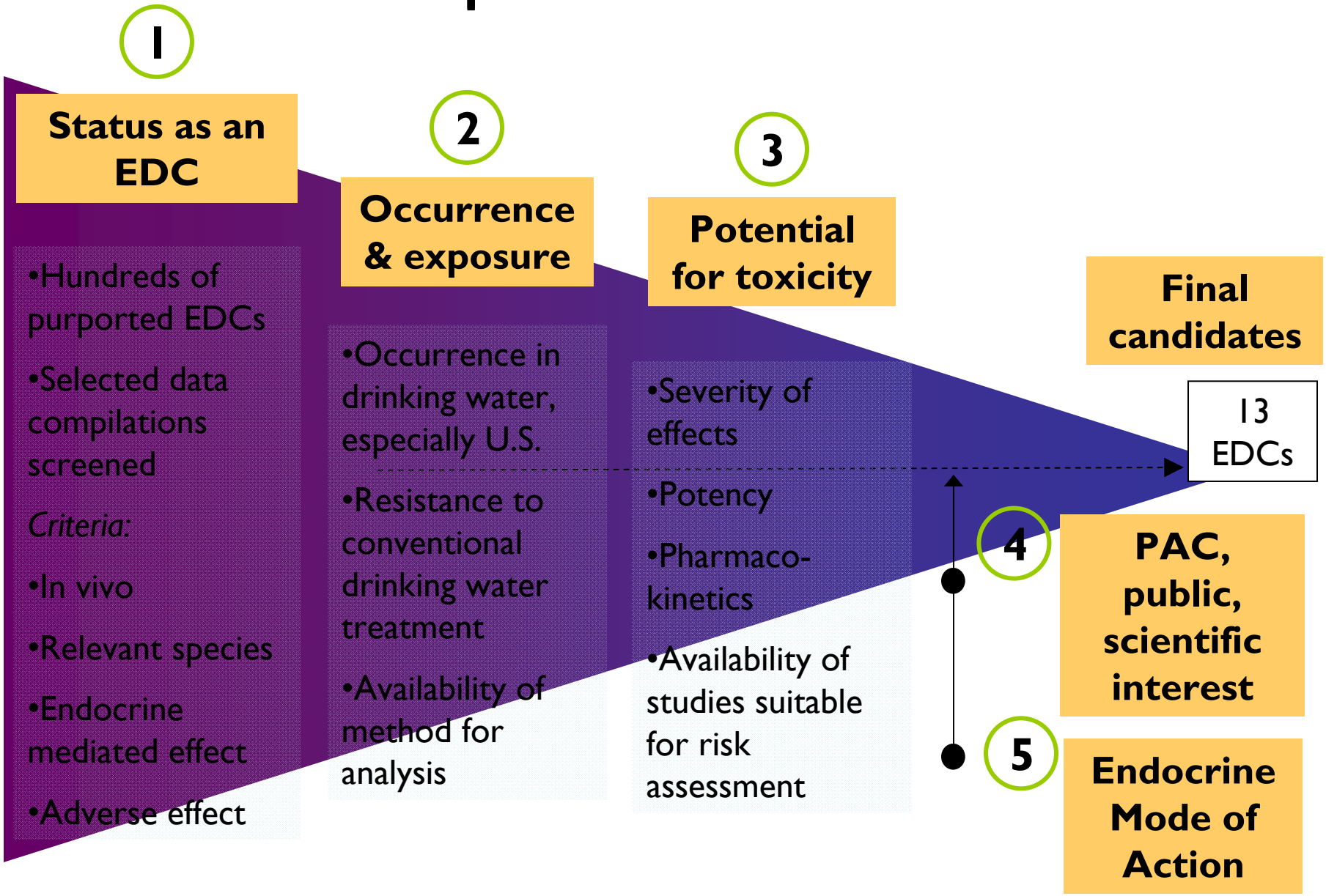
Pharmaceuticals



Suspected EDCs



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

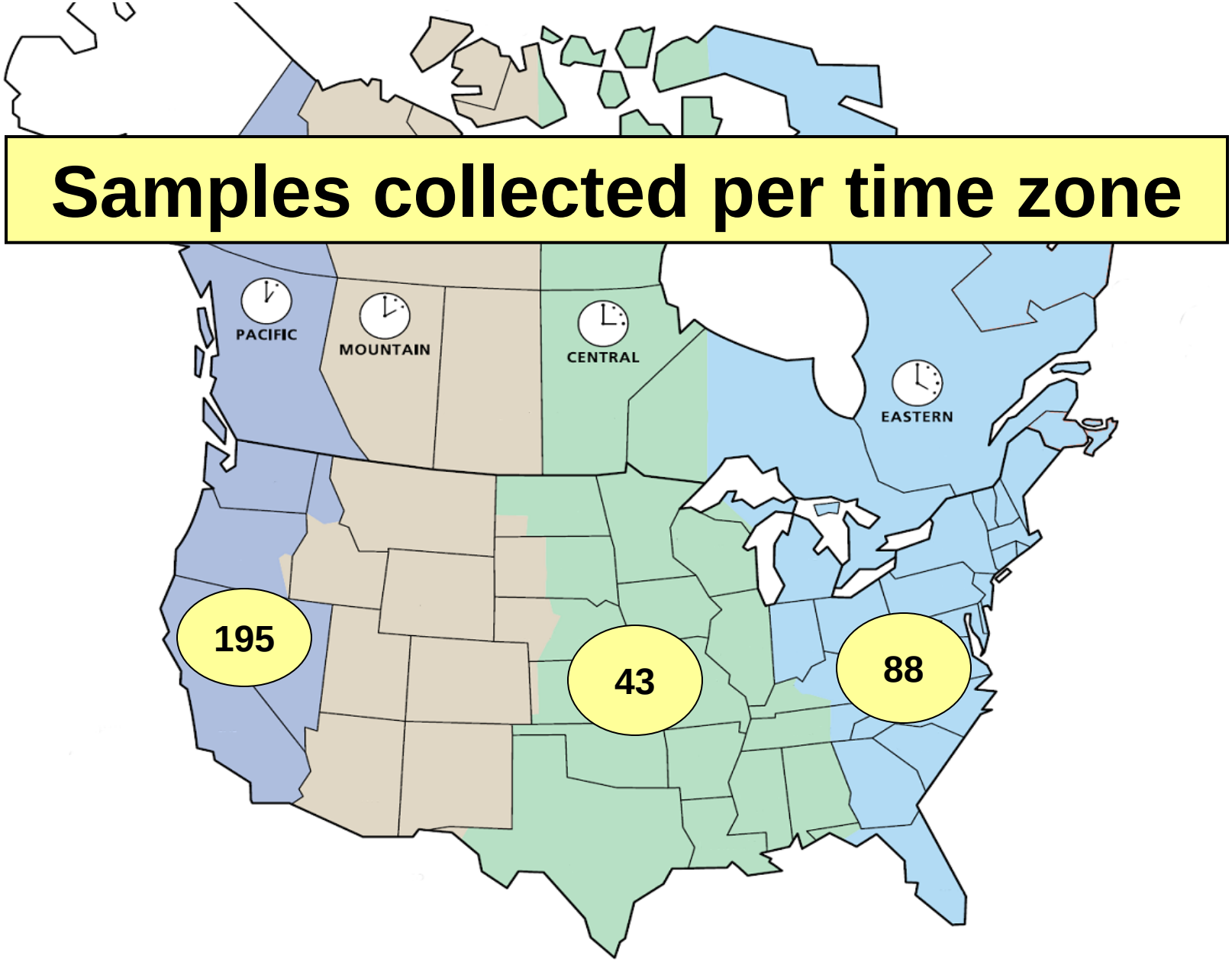
Rebecca A. Trenholm *, Brett J. Vanderford, Janie C. Holady, David J. Rexing, Shane A. Snyder

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

Site Selection

Samples collected per time zone



17 Participating Utilities

Results

Environ. Sci. Technol. **XXXX**, *xxx*, 000–000

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

MARK J. BENOTTI,
REBECCA A. TRENHOLM,
BRETT J. VANDERFORD,
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pharmaceutical at subμg/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 occurrence, 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

51 Compounds since phytoestrogens not included

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

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**

US Drinking Water

Finished Water for 18 Drinking Water Treatment Facilities			
Compound	**Max (ng/L)**	**Median (ng/L)**	**Frequency (%)**
Atrazine	**870**	**49**	**83**
Meprobamate	**42**	**5.7**	**78**
Dilantin (151st – 2007)	**19**	**6.2**	**56**
Atenolol (99th- 2007)	**18**	**1.2**	**44**
Carbamazepine	**18**	**6.0**	**44**
Gemfibrozil	**2.1**	**0.48**	**39**
TCEP	**470**	**120**	**39**
DEET	**93**	**63**	**33**
Metolachlor	**27**	**16**	**33**
TCPP (Fyrol PCF)	**510**	**210**	**28**
Sulfamethoxazole	**3.0**	**0.39**	**22**

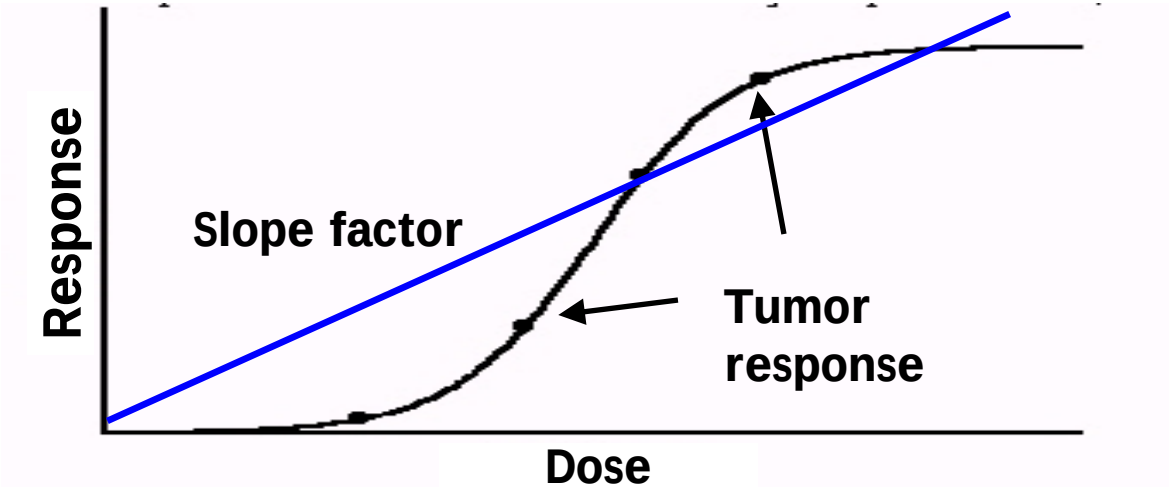
US Drinking Water

Finished Water for 18 Drinking Water Treatment Facilities			
Compound	**Max (ng/L)**	**Median (ng/L)**	**Frequency (%)**
MRL > 1000 ng/L			
MRL > 50 ng/L			
MRL > 20 ng/L			
MRL > 20 ng/L			
MRL > 20 ng/L			
MRL > 10 ng/L			
MRL > 500 ng/L			
MRL > 100 ng/L			
MRL > 50 ng/L			
MRL > 1000 ng/L			
MRL > 10 ng/L			

Risk Assessment

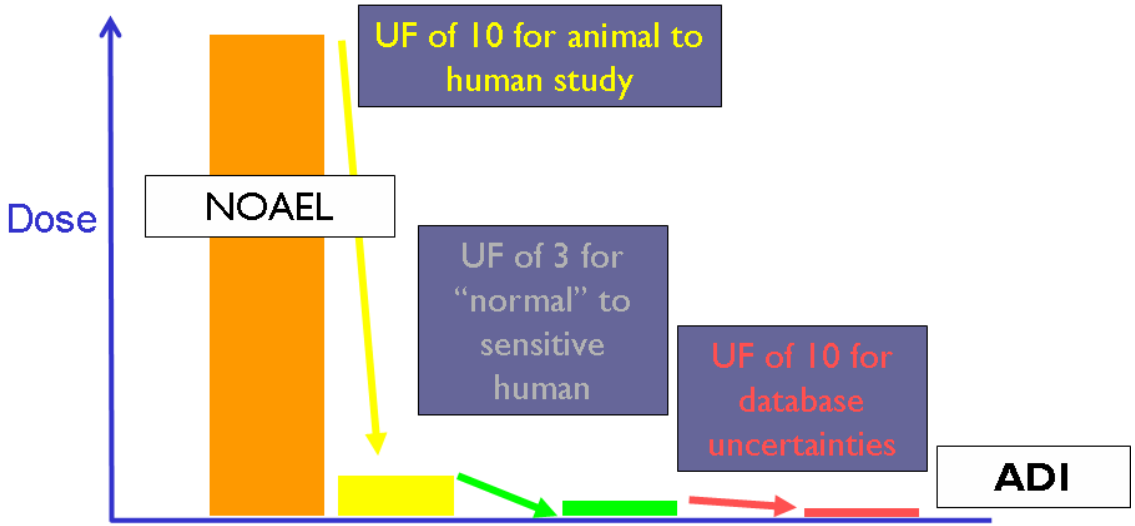
deriving ADIs / screening values

carcinogens



non cancer

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



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 DWELs with max. drinking water concentrations

Drug	Class	DWEL (µg/L)	Max. conc. (µg/L)	Margin of safety	No. of 8-oz glasses to exceed DWEL
Risperidone	Antipsychotic	0.49	0.0029	170	1,400
Phenytoin	Anticonvulsant	6.8	0.032	210	1,800
Carbamazepine	Anticonvulsant	12	0.018	670	5,600
Fluoxetine	SSRI antidepressant	34	0.00082	41,000	350,000
Norfluoxetine	Metabolite	34	0.00077	44,000	370,000
Diazepam	Benzodiazepine tranquilizer	35	0.00033	110,000	900,000
Gemfibrozil	Antilipidemic	45	0.0021	21,000	180,000
Atenolol	Beta-blocker	70	0.026	2,700	23,000
Meprobamate	Antianxiety agent	260	0.043	6,000	51,000
Triclosan	Antibacterial	2,600	0.0012	2,200,000	18,000,000
Sulfamethoxazole	Anti-infective	18,000	0.003	6,000,000	51,000,000

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

EDC DWELs with max. drinking water concentrations

Drug	Class	ADI-DWEL (µg/L)	Max. conc. (µg/L)	Margin of safety	No. of 8-oz glasses to exceed DWEL
Atrazine	Herbicide	180	3.0	60	26
Bisphenol A	Industrial chemical	1,800	0.025	72,000	610,000
Linuron	Herbicide	70	0.0083	8,400	71,000
p-Nonylphenol	Industrial chemical	1,800	0.11	16,000	140,000
Butylbenzyl phthalate	Industrial chemical	3,500	<0.050	>70,000	>590,000
Bis(2-ethylhexyl) phthalate	Industrial chemical	420	<0.10	>4,200	>36,000
17b-Estradiol	Hormone	1.8	<0.00050	>3,600	>30,000
Estrone	Hormone	0.46	<0.00020	>2,300	>19,000
Ethynylestradiol	Synthetic Hormone	0.0035	<0.0010	>3.5	>30
Lindane	Insecticide	20	<0.010	>2,000	>17,000
Methoxychlor	Insecticide	0.70	<0.010	>70	>590
Octylphenol	Industrial chemical	5,300	<0.025	>210,000	>1,8000,000
Vinclozolin	Fungicide	420	<0.010	>42,000	>360,000

Method Reporting Limits based on 100x <DWEL				
	Max Drinking Water Conc. (µg/L)	DWEL (µg/L)	Liters per day to meet DWEL	Recommended MRL (µg/L)
Phenytoin	0.032	6.8	430	0.1
Carbamazepine	0.018	12	1,300	0.1
Fluoxetine	0.001	34	68,000	0.3
Diazepam	0.001	35	70,000	0.4
Gemfibrozil	0.002	45	45,000	0.5
Atenolol	0.026	70	5,400	0.7
Meprobamate	0.043	260	12,000	3.0
Bisphenol A	0.025	1,800	144,000	20
4-Nonylphenol	0.11	1,800	33,000	20
Sulfamethoxazole	0.003	18,000	1,200,000	200

"Identifying Hormonally Active Compounds, Pharmaceutical Ingredients, & Personal Care Product Ingredients of Most Health Concern From Their Potential Presence in Water Intended for Indirect Potable Reuse"

WRF 05-005 – Expert Workshop
November 5-6th, 2008

Southern Nevada Water Authority

WATEREUSE FOUNDATION

INTERTOX

Approach

- Gather Data from Published Toxicological Studies
- Use Data to Obtain Uncertainty Factor (UF) and Effect Dose
- Use 7 Methods to Obtain Screening Levels
  - NOAEL/LOAEL, Minimum Therapeutic Dose, 2 TTC-Based Approaches, Cancer Slope Factor (CSF), Maximum Tolerated Dose, and Existing Toxicity Critereon
- Compare Results, Choose Most Conservative (Protective of Public Health)

Describe Methods for Deriving Human Health Risk-Based Screening Levels

Considered Four Approaches:

a) *For noncarcinogenic effects:* No observed adverse effect level (NOAEL) or lowest observed adverse effect level (LOAEL) from toxicology studies in humans, with uncertainty factors applied

b) *For carcinogenic effects:* Tumor incidence data and linear extrapolation models to derive cancer slope factors (SFs) and target levels based on incidence of cancer

c) *For drugs:* Minimum therapeutic dose

d) *Threshold of Toxicologic Concern (TTC)*

Toxicological Data Used to Develop Screening Levels for Noncancer Endpoints for Target PPCPs

Compound	Species/ Gender/ Study duration	Effect dose (mg/kg-d)	Effect	Composite UF [a]	Screening level (µg/kg-d)
Alendronate	Rat/ F /Premating- gestation	0.5 (LOAEL)	Reproductive (protracted parturition)	3,000 (10,3,10,3,3)	0.17
Atenolol	Human/F /Gestation	0.80 (LOAEL)	Developmen l (decreased infant birth weights)	300 (1,3,10,3,3)	2.7

Female rats exposed from before mating through gestation

Lowest observed adverse effect level in database (of 9 studies)

Reproductive effect (protracted birth)

UFs: 10 for animal to human, 3 for sensitive members of population, 10 for LOAEL to NOAEL, 3 for study duration, 3 for lack of a 2-generation study in database

0.0005 µg/kg-d/ 3,000

PPCPs with Evidence of Carcinogenicity and Tumor Data, and Slope Factors (SFs) and Screening Levels

Compound	Evidence	Tumor incidence data	Cancer SF $(mg/kg\text{-}d)^{-1}$	Screening level based on CSF (µg/kg-d)
Fluconazole	Hepatocellular adenomas in rats (M)	CPDB 2007a: 2 yr, rat (M) 0 mg/kg-d= 2/100 2.5 mg/kg-d = 0/50 5.0 mg/kg-d = 4/50 10 mg/kg-d = 5/50	1.1E-02	0.21

Evidence of liver cancer in male rats

Tumor incidence data: 2 year study at 4 dose levels

Cancer slope factor derived using tumor incidence data and EPA Benchmark Dose Model (estimate dose that produces 10% excess risk, then extrapolate to produce upper-bound estimate risk per 1 mg/kg-d of dose

Calculated assuming an acceptable lifetime excess cancer risk of 1 in one million, and that a person is exposed to this dose 365 d/yr for 30 yrs over a 70 yr lifetime
$= (10^6 \times 25{,}550)/ (SF \times 10.950)$

Minimum Therapeutic Doses for Target PPCPs and EDCs, and Corresponding Screening Levels

Compound	Treatment Endpoint	Ther Dose (mg/kg-d)	Traditional UF [a]	Pregnancy Category & Adverse Human Effects at Ther Dose	Adverse Effects in Animals (Relative to Ther Dose)	Proposed Additional UFs	Screening Level (µg/kg-d)
Alendronate	Osteoporosis	0.071	300 (1,3,10,3,3)	C	Cancer; Repro, rat: 1.1x; Devel, rat: 2.3x	3-cancer	0.080
Aten[illegible]ol	Hype[illegible]tension	0.36	300 (1,[illegible]10,3,3)	D (low birth we[illegible]ht)	Canc[illegible]: Repro, rat: 4.2x	3-de[illegible]l; 3-cancer	0.12

Fosamex®

Treatment for osteoporosis (bisphosphate inhibitor of bone resorption)

Minimum therapeutic dose for adults (5 mg/d)

UFs: 1 for animals to humans, 3 for intra-individual variability, 10 for LOAEL to NOAEL, 3 for study duration, 3 for database uncertainties

FDA pregnancy category

Evidence of toxicity in animals: cancer of Harderian gland in mice (not likely relevant to humans) and thyroid in rats; reproductive effects in rats (protracted parturition) at 1.1x therapeutic dose; developmental effects (reduced body weight gain in rat pups) at 2.3x therapeutic dose)

Additional UFs

Threshold of Toxic Concern (TTC)-based Screening Levels for PPCPs

Compound	Structural class*	Genotoxicity test result	Minimum Oral LD50 (mg/kg)	TTC-based screening level (µg/kg-d)	
				Based on scheme of Cheeseman *et al.* (1999)	Based on scheme of Kroes *et al.* (2004)
Alendronate	III	Negative	27,800 (mouse)	0.21	1.3
Aten[illegible]	[illegible]	[illegible]egative	2,00[illegible] (mouse)	[illegible]0.21	[illegible].3
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Fosamex®

Compounds that suggest "significant toxicity"; contains phosphonate groups

Negative in Ames test and in vitro micronucleus assay

Minimum oral lethal dose to 50% of a test population

Compounds with negative genotoxicity tests and no structural alerts

Cramer structural class III compounds

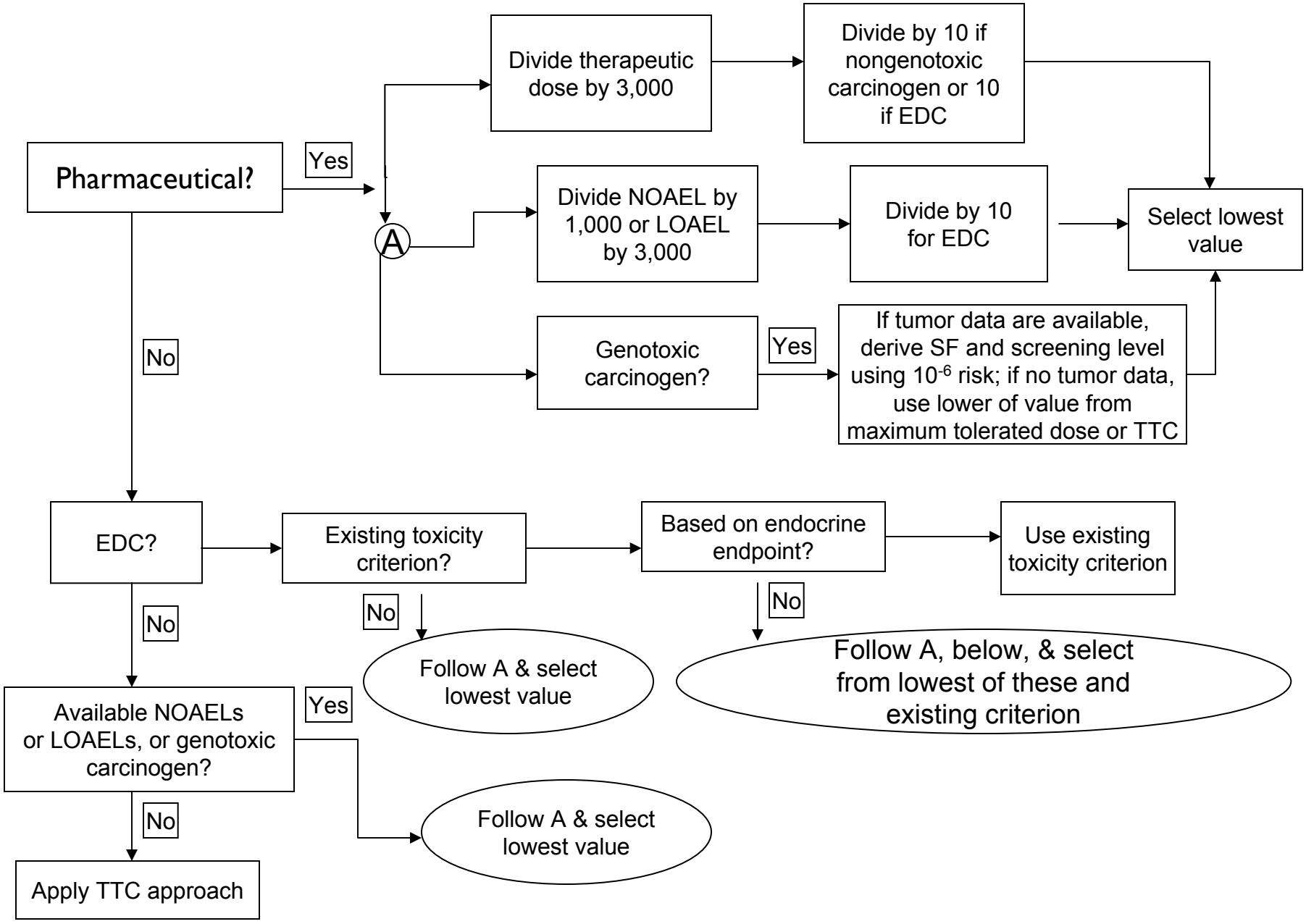
Derived Screening Values From Seven Approaches (µg/kg-d)

	Atenolol	Atrazine	Ethinyl Estradiol	Meprobamate
Based on NOAEL/LOAEL	0.027	0.05	**0.0000033**	75
Based on Minimum Therapeutic Dose	**0.012**	NA	0.00001	2.3
Cheeseman *et al.* (1999) TTC Approach	0.21	0.021	0.43-0.64	**0.021**
Kroes *et al.* (2004) TTC Approach	1.3	1.3	26	1.3
Based on CSF	NA	**0.0043**	0.012	NA
Based on Max. Tolerated, Dose (Carcinogens)	2	0.027	0.00059	NA
Existing Toxicity Criterion	NA	**0.0043**	0.00043	NA

“New” Derivation of Screening Levels

- Based on Blanket Uncertainty Factors:
  - 1,000 if NOAEL Data Are Available
  - 3,000 if only LOAEL Data Are Available
  - Multiply by additional factors of 10 when
    1. Compound is a Non-genotoxic Carcinogen
    2. Compound is a known EDC
- Provides Ease of Use in Process
  - Still Maintains Robust Approach through Multiple Derivations of Screening Levels

DRAFT Decision Tree for Screening Levels (WRF 05-005)



Example Process for NOAEL/LOAEL Approach

	Atenolol	Atrazine	Ethinyl Estradiol	Meprobamate
Description	PPCP	Herbicide & EDC	PPCP & EDC	PPCP
Effect	Developmental (Human)	Developmental (Rat)	Endocrine (Human)	Systemic (Mouse)
Effect Dose (mg/kg-d)	0.8	0.5	0.0001	75
NOAEL or LOAEL	LOAEL	NOAEL	LOAEL	NOAEL
"Old" UF	3000	5000	1000	10,000
Genotoxic?	No	No	No	No
Carcinogenic?	Yes, Thyroid	Yes, Mammary	Yes, Liver	No
"New" UF	3000 x 10	1000 x 10	3000 x 10	1000
New Screening level (µg/kg-d)	0.027	0.05	0.0000033	75

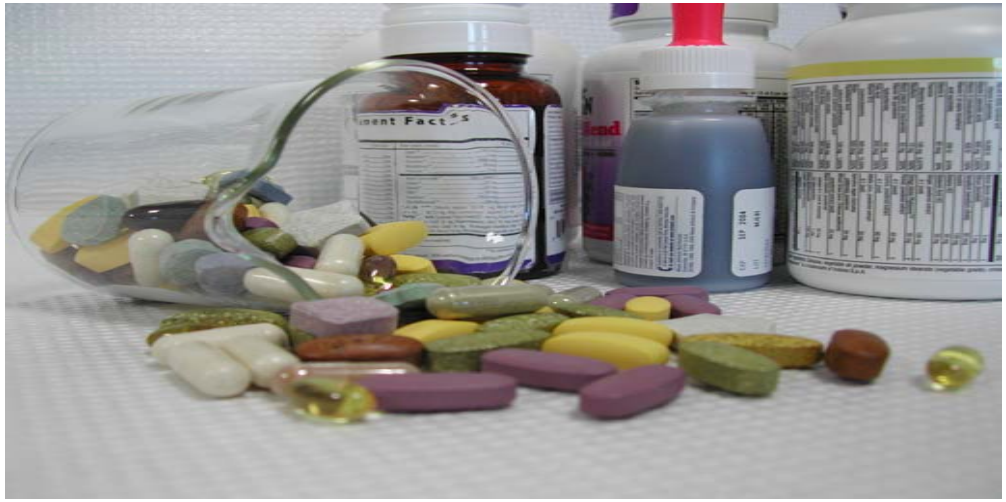
Conclusions

BUT What about the MIXTURES?

WHO – Drinking Water Quality Guidelines

8.2.9 Mixtures

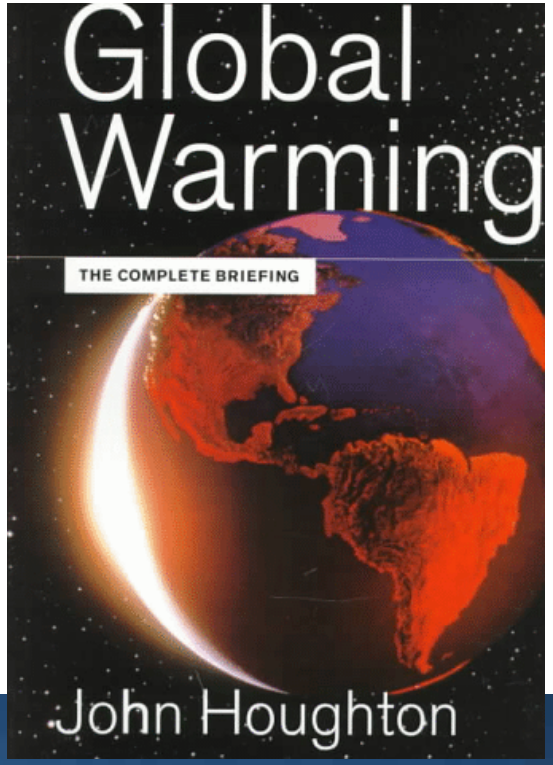
Chemical contaminants of drinking-water supplies are present with numerous other inorganic and/or organic constituents. The guideline values are calculated separately for individual substances, without specific consideration of the potential for interaction of each substance with other compounds present. 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.

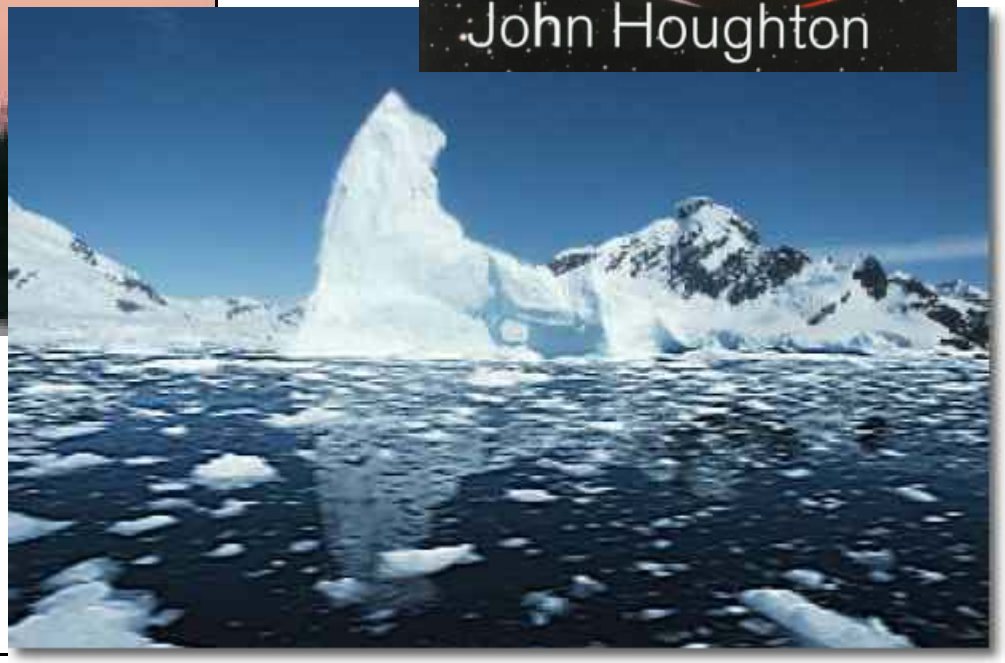


Wounded Waters

The Hidden Side of Power Plant Pollution

February 2004





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.


ZERO

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
  - Pharmaceuticals have the "richest" toxicological data of any environmental contaminants (human data)
  - Conservative uncertainty factors used
  - 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"
- Rapid screening values can be developed to allow a "ball park" assessment of human health relevance from minimal datasets

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