Prioritization of Chemical Contaminants

Shane Snyder, Ph.D.

Professor & Co-Director

University of Arizona

Visiting Professor

Nat. Uni. Singapore

“We are swimming in a sea of chemicals…”

Oct 27, 2010 By Wendy Koch, USA TODAY

USA TODAY

Study: Scented consumer products emit toxic chemicals

Frizz or formaldehyde? Trendy 'do poses a hairy dilemma

Testing finds compound in Brazilian Blowout (but it sure makes hair look fabulous)

By Diane Mapes
msnbc.com contributor
updated 10/21/2010 8:29:04 AM ET

msnbc.com

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Top stories:

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Check out the videos that are making news and igniting conversation today

Rep. Anthony Weiner
Democratic Rep. Anthony Weiner to resign after pressure from DNC over sexting-and-lying scandal

Arab Unrest
Dictators across the Middle East and North Africa fighting to maintain control of their countries

Casey Anthony
Defense begins in Casey Antho

Portland draining reservoir after man urinates in it

http://news.blogs.cnn.com/2011/06/16/portland-draining-reservoir-after-man-urinates-in-it/

Reservoir drained after a wee problem

Nick Allen
June 20, 2011 - 10:00AM

theage.com.au
THE AGE

Man caught urinating in city reservoir
The city of Portland, Oregon has been forced to drain eight million gallons of water after a 21 year old man was caught on CCTV urinating in a reservoir.
Video feedback | Video settings

Eight million gallons of water had to be drained from a US reservoir in Oregon after a man urinated in it.

8,000,000 gal = 30,283,000 L
Bladder holds ≈ 0.3 L
Pee in reservoir ≈ 10 ppb
Male pee ≈ 10 ug/L Estradiol
Theoretical E2 in reservoir:

0.1 ng/L E2 in reservoir

Fish LOEL ≈ 0.1 ng/L
EPA CCL3 risk ≈ 0.9 ng/L

http://www.theage.com.au/world/reservoir-drained-after-a-wee-problem-20110620-1ganj.html

Drinking Water News
For America's Small Communi

Chemicals in Water Alter Gender of Fish

CBSNEWS

Pollution Brings Worrying Signs for Fish Populations; Worse, Most U.S. Drinking Water Comes from the Same Sources

Tap water contaminant 'castrates' frogs

Updated 3/1/2010 9:24 PM | Comments 214 | Recommend 27 E-mail | Save | Print | Reprints & Permissi

By Liz Szabo, USA TODAY

Share

URINE FOR A SURPRISE

A recent Michigan State University study indicates that hormone-laden human urine, not industrial chemicals, could be triggering reproductive abnormalities in male fish near Lake Mead, Nevada. Researchers testing the waters of

They're in the water

Meds lurk in drinking water

AP probe found traces of meds in water supplies of 41 million Americans

By Jeff Donn, Martha Mendoza and Justin Pritchard

The Associated Press

updated 8:06 a.m. PT, Mon., March. 10, 2008

azdailysun.com
Serving Flagstaff and northern Arizona

Is Flag's drinking water at risk?

CYNDY COLE Sun Staff Reporter | Posted: Tuesday, October 18, 2011 5:30 am

“About two years ago, very small traces of an antibiotic, an anti-seizure medication and a possible cancer-causing agent appeared in four groundwater wells in northwest Tucson.

All of the wells are located downstream of the local sewage treatment plant, which releases its treated sewage water into a riverbed.

When tested, some of Flagstaff's drinking water wells downstream of the Rio de Flag wastewater treatment plant have also shown tiny traces of other pharmaceuticals and hormones, which have an ability to influence growth in amphibians.”

IS IT SAFE?


Priorities

US Regulatory History

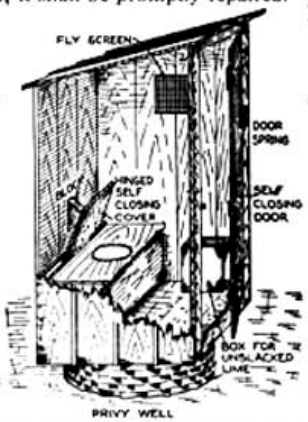
Department of Public Health and Charities

RULES GOVERNING THE SANITARY MAINTENANCE OF PRIVY VAULTS AND PRIVY HOUSES IN THE CITY OF PHILADELPHIA

1. The occupants of premises will be held responsible for the maintenance of privy houses or closets in a sanitary condition and free from damage, except such as result from ordinary use.
2. Privy houses or closets shall be maintained in a clean and sanitary condition.
3. All openings in seats shall be provided with covers. A block shall be so arranged that the seat covers will fall into place when seat is not in use.
4. Wash water, garbage, kitchen slops, etc., shall not be emptied into privy wells.
5. The discharges from any person suffering from typhoid fever, dysentery, or other serious bowel disease, shall not be deposited in any privy well without being previously disinfected in the manner prescribed by the Bureau of Health.
6. Privy wells shall be cleaned, when their contents come to within three (3) feet of the ground level, and at other times when deemed necessary by the Bureau of Health, and shall be frequently treated with lime to prevent their becoming foul.
7. When a privy well is in need of cleaning, it shall be immediately reported by the tenant to the owner or agent and to the Bureau of Health.
8. Doors of privy houses and closets shall not be left open. They shall be so arranged that they will return into the closed position.
9. Doors shall be securely attached by hinges of such size as to properly support the weight of the door at all times.
10. All other openings in the privy houses or closets, except the doors, shall be tightly screened with screens not less than fourteen (14) meshes to the inch.
11. A supply of unslacked lime shall be kept on hand in each privy house or closet and shall be frequently applied to the contents of the privy well.
12. The privy house or closet shall be kept in good repair, and if any part shall become decayed or broken, it shall be promptly repaired.

This Privy MUST be abandoned when Sewer is accessible.

By order of the
Board of Health

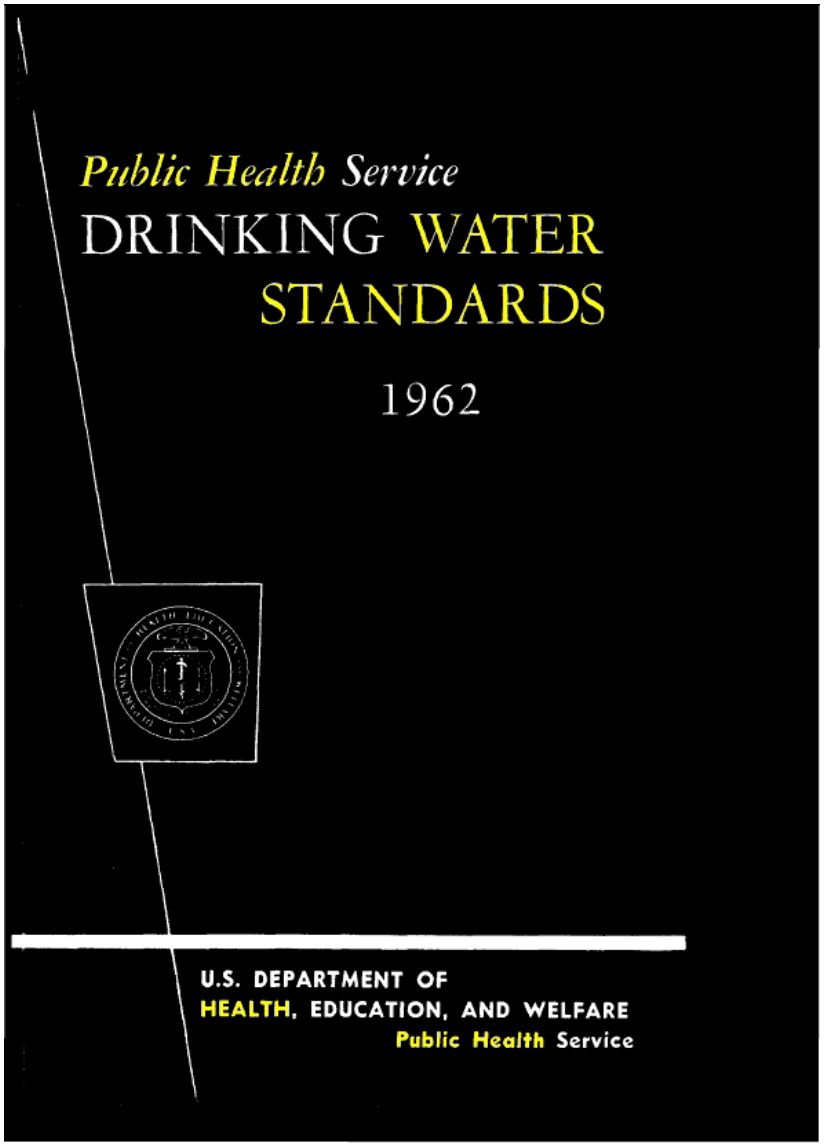


THESE RULES WILL BE STRICTLY ENFORCED BY THE DIVISION OF SANITATION

FOR FURTHER INFORMATION CALL AT THE
Division of Sanitation
615 CITY HALL

THIS CARD MUST NOT BE REMOVED OR DEFACED

11373 10-15-1315



US Regulatory History

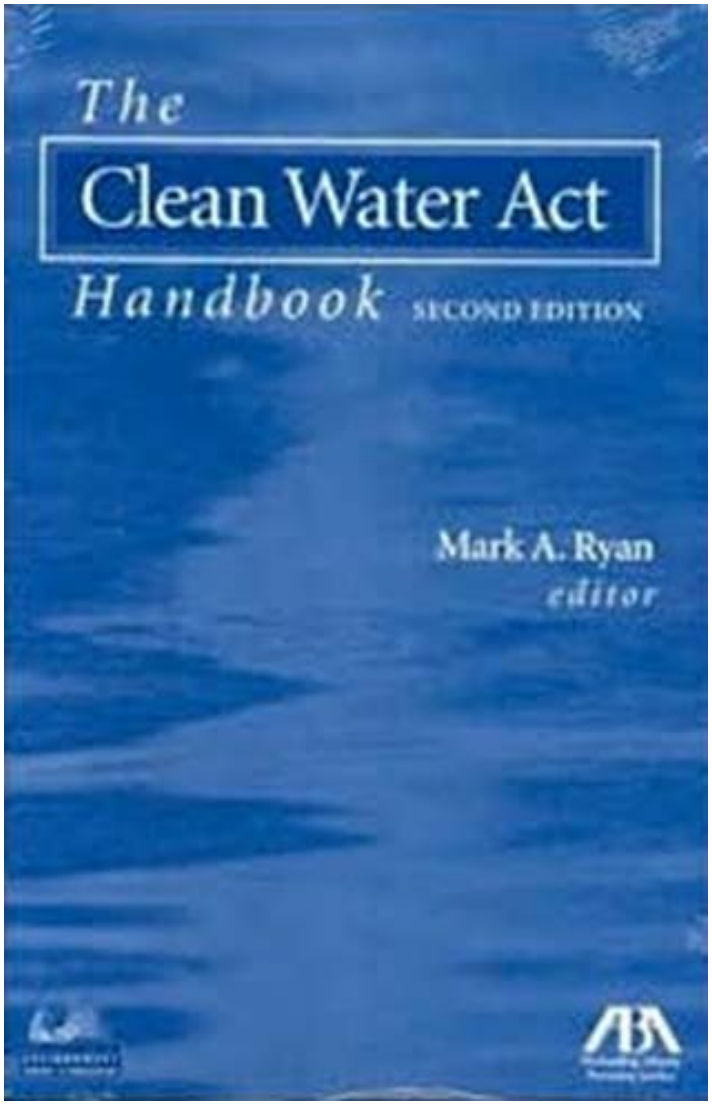
1962: 28 discrete "chemical" contaminants regulated

5.21 The following chemical substances should not be present in a water supply in excess of the listed concentrations where, in the judgment of the Reporting Agency and the Certifying Authority, other more suitable supplies are or can be made available.

Substance	*Concentration in mg/l*
Alkyl Benzene Sulfonate (ABS)	0.5
Arsenic (As)	0.01
Chloride (Cl)	250.
Copper (Cu)	1.
Carbon Chloroform Extract (CCE)	0.2
Cyanide (CN)	0.01
Fluoride (F)	(See 5.23)
Iron (Fe)	0.3
Manganese (Mn)	0.05
Nitrate [1] (NO_3)	45.
Phenols	0.001
Sulfate (SO_4)	250.
Total Dissolved Solids	500.
Zinc (Zn)	5.

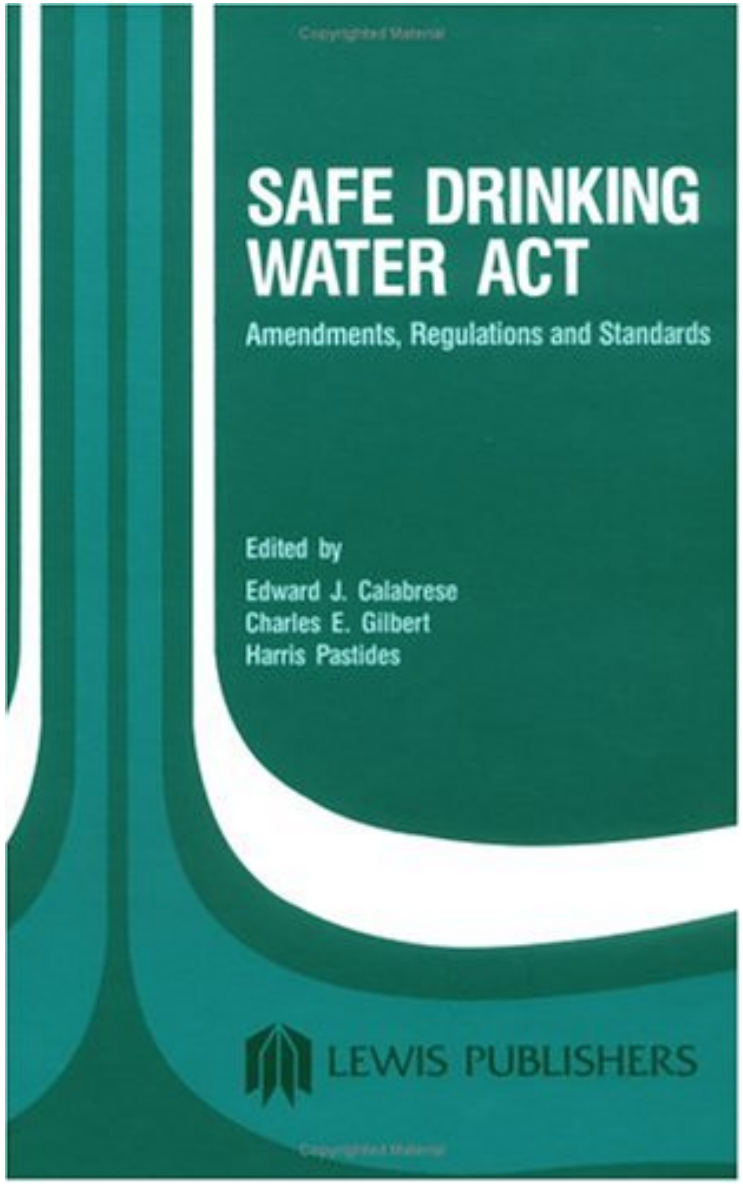
US Regulatory History

- Federal Water Pollution Control Act
  - Originally enacted in 1948
  - Totally revised in 1972
  - Became "Clean Water Act" in 1977
    - Required permit to discharge a pollutant to navigable waters
    - Generally technology driven
    - TMDLs (total loading)
    - State enforcement (generally)



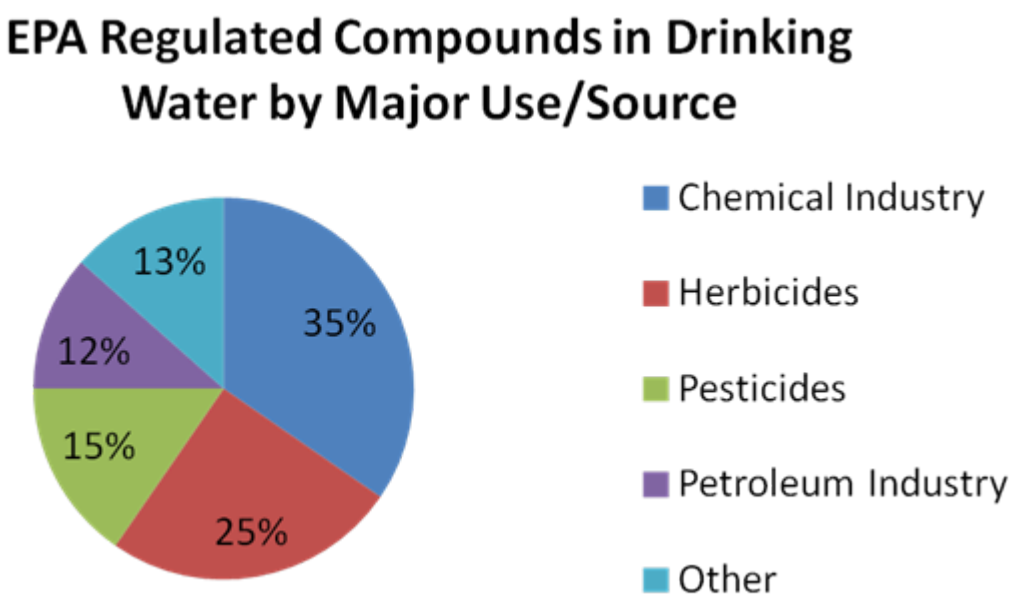
US Regulatory History

- EPA created in 1970
- Safe Drinking Water Act (SDWA)
  - Promulgated in 1974
    - Amended in 1986 and 1996
  - Established National Standards
  - MCLs and MCLGs
    - "no" risk vs. feasible risk
  - Amendments established:
    - CCL Process
    - UCMR Process

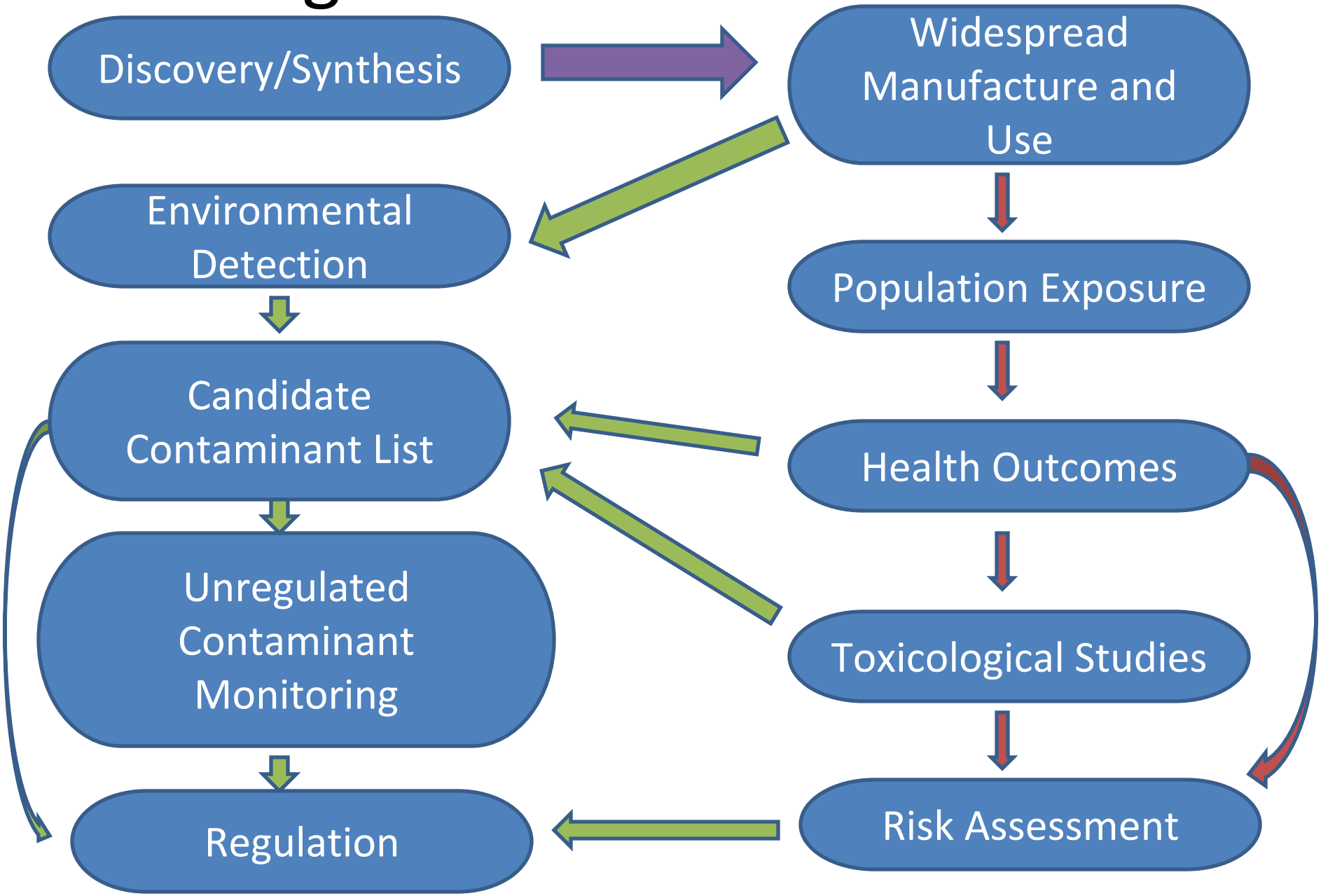


EPA Drinking Water Regulations

- Approximately 90 Contaminants Currently Regulated in Drinking Water
  - 52 are Organic Pollutants



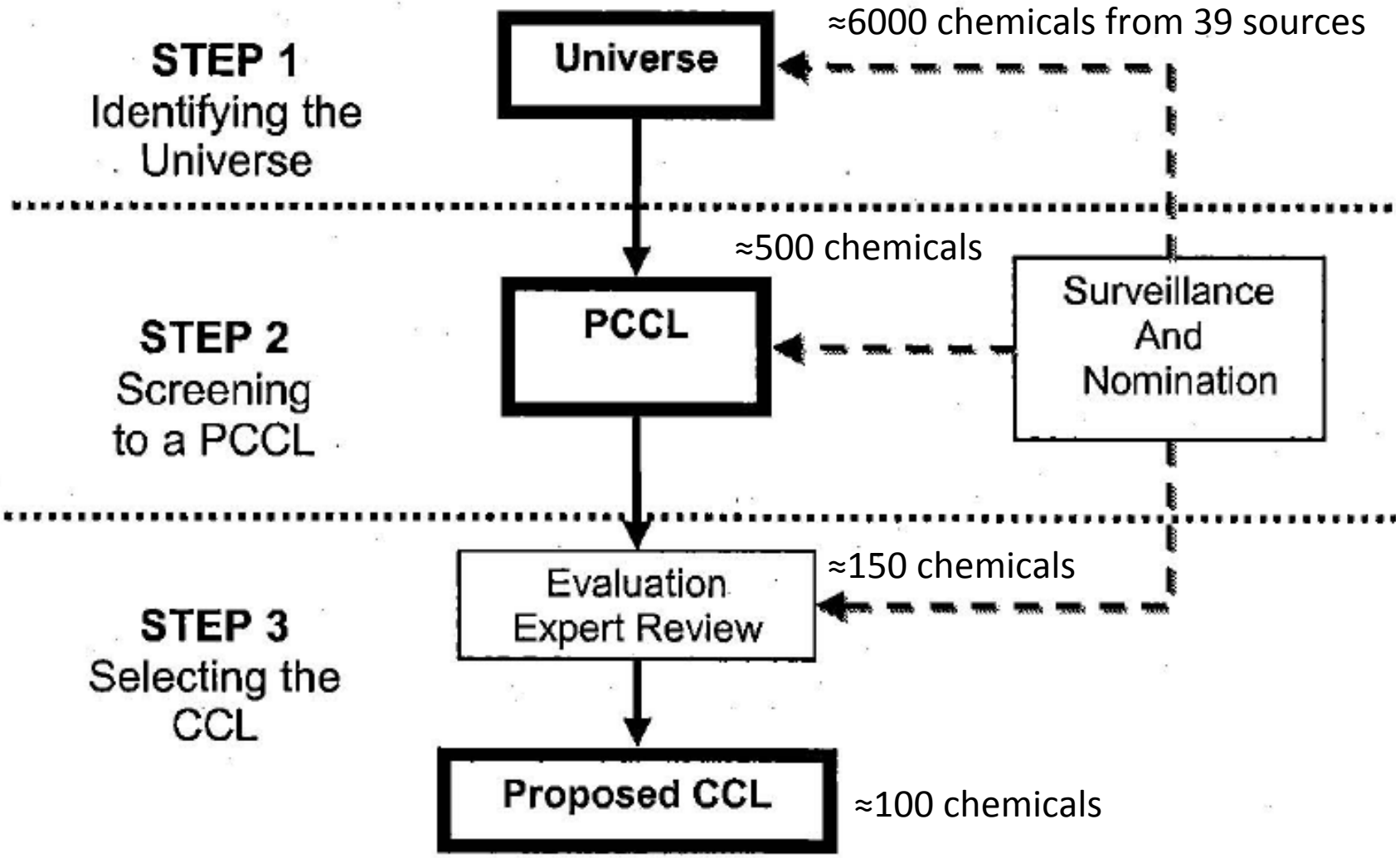
Regulation Flow Schematic



Third Candidate Contaminant List (CCL3)

- The SDWA Amendments of 1996
- Drinking water contaminants known/anticipated that may require future regulation
- CCL must address contaminants that are:
  - Not currently regulated
  - May have adverse health effects
  - Known/anticipated occurrence
- EPA may select up to 30 contaminants from CCL for UCMR
  - However, this is not always the case
  - May include additional analytes that are “included in an analytical suit”

CCL Process


STEP 1
Identifying the Universe
Universe
≈6000 chemicals from 39 sources
≈500 chemicals
STEP 2
Screening to a PCCL
PCCL
Surveillance And Nomination
STEP 3
Selecting the CCL
Evaluation Expert Review
≈150 chemicals
Proposed CCL
≈100 chemicals

CCL3 – Key Highlights

- 12 microbiological pathogens
- 104 chemicals or chemical groups
- 22 were carry-overs from CCL 2
  - i.e., MTBE, perchlorate, solvents
- N-nitroso compounds are prominant
- Nine hormones added
- Perfluro-octanoic acid and sulfonic acid
- 1,4-Dioxane
- Cyanotoxins (but not cyanobacteria)

Contaminant:	Estradiol (17-beta estradiol)

Attribute Scores			
Potency	Severity	Prevalence	Magnitude
8	8	10	5

3-model Categorical Prediction
L
HRL Ratio(s)
NC HRL/Kolpin MAX: 1.75 CAR HRL/Kolpin MAX: 0.0045

Health Reference Level (HRL)[2] cancer	0.0009 ug/L

Water Data	% Detects	Maximum value of Detects	Median value of Detects	90% of Detects	Units for Mag data
Snyder, et al., 2007 FINISHED	0.0	Not detected	Not detected	Not detected	ug/L
Snyder, et al., 2007 RAW		0.0064			ug/L
Kolpin, et al., 2002	**10.6**	**0.2**	**0.16**		**ug/L**

Contaminant:	Estradiol (17-beta estradiol)

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Potency	Severity	Prevalence	Magnitude
8	8	10	5

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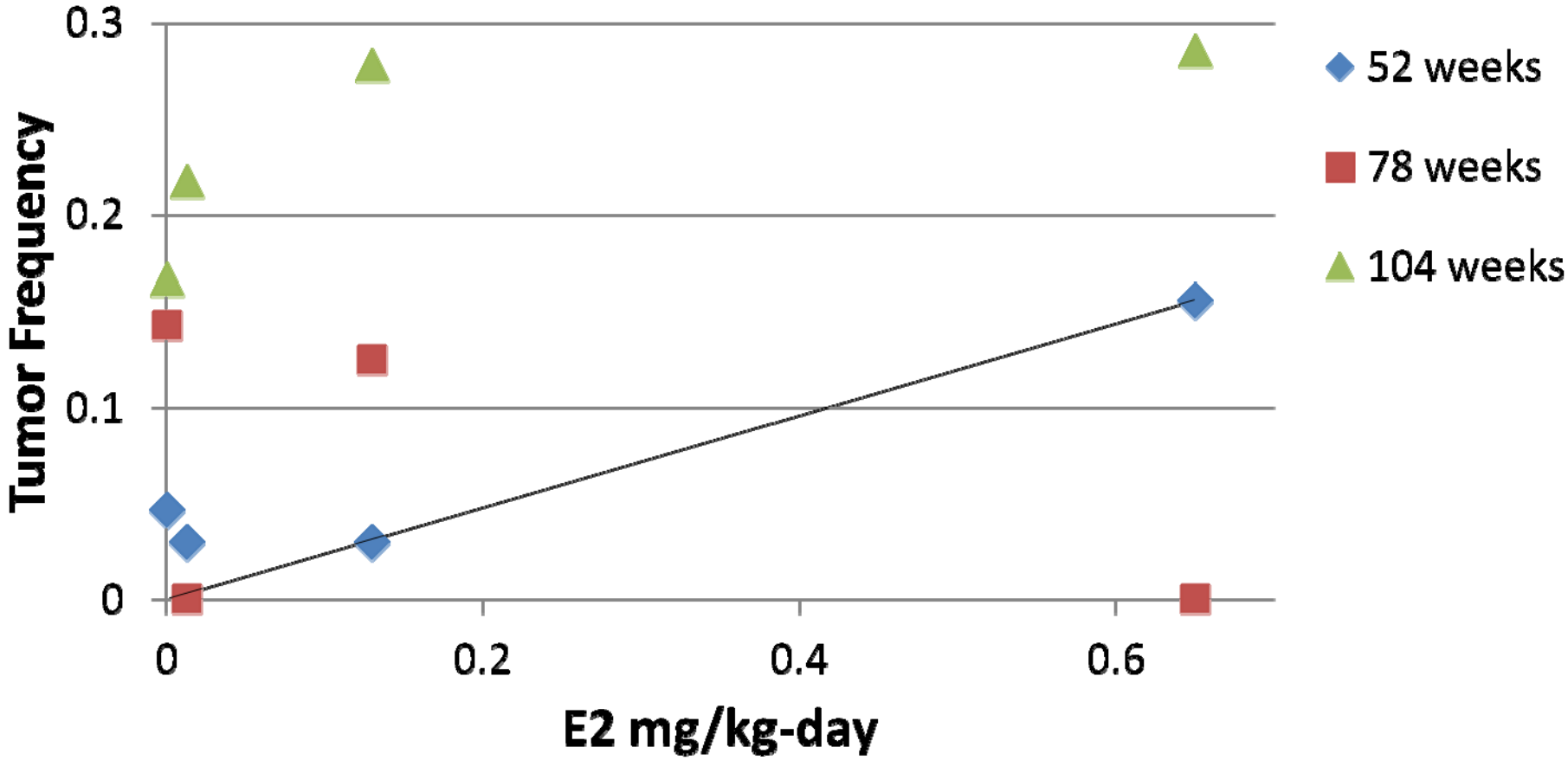


Brief History of the UCMR

UCM-State Rounds 1 & 2 (1988-1997)

- Required public water systems (PWSs) serving more than 500 people to monitor contaminants.
- Round 1 (1988-1993): 62 contaminants in 40 states.
- Round 2 (1993-1997): 48 contaminants in 35 states.

UCMR 1 (2001-2005)

- A redesign of the original UCM Program
- Incorporated a tiered monitoring approach along with EPA implementation
- Required monitoring for 25 contaminants (24 chemicals and 1 bacterial genus) during 2001-2003.

UCMR 2 (2007-2011)

- Managed by EPA
- Established a new set of 25 chemical contaminants sampled during 2008-2010

UCMR 3 (2012-2016)

- Current regulation monitoring for 30 contaminants (28 chemicals and 2 viruses) from 2012-2015

Reference: http://water.epa.gov/lawsregs/rulesregs/sdwa/ucmr/

UCMR 3: 30 Unregulated Analytes and Associated Methods

Assessment Monitoring (List 1 Contaminants)			
1,4-dioxane	1,2,3-trichloropropane	1,3-butadiene	1,1-dichloroethane
chloromethane (methyl chloride)	bromomethane (methyl bromide)	chlorodifluoromethane	bromochloromethane (Halon 1011)
Vanadium	Molybdenum	Strontium	Cobalt
Chromium-6	Chromium-total	chlorate	perfluorooctanesulfonic acid (PFOS)
perfluorooctanoic acid (PFOA)	perfluorononanoic acid (PFNA)	perfluorohexanesulfonic acid (PFHxS)	perfluoroheptanoic acid (PFHpA)
perfluorobutanesulfonic acid (PFBS)			
Screening Survey (List 2 Contaminants)			
estrone	17β-estradiol	estriol	17α-ethynylestradiol
equilin	testosterone	4-androstene-3,17-dione	
Pre-Screen Testing (List 3 Contaminants)			
enteroviruses	noroviruses		

Synthetic Organic Compound (GC/MS) Volatile Organic Compounds (VOCs) (GC/MS) Metals (ICP/MS) Soluble chromate (ion) (IC/UV-VIS) Oxyhalide Anion (IC/Conductivity) Perfluorinated Chemicals (LC/MS/MS) Hormones (LC/MS/MS) Viruses (cell culture & qPCR)

NDMA most frequently detected contaminant in UCMR2 (1188 PWS Tested)

	# Detect	*% Detect*	*Max (ng/L)*	*Ave (ng/L)*
NDMA	305	25.7	630	9
NDEA	24	2.0	100	16
NDBA	5	0.4	21	8
NDPA	0	ND	ND	ND
NMEA	3	0.3	5	4
NPYR	19	1.6	24	5

For NDMA, EPA 10^{-6} cancer risk equates to 0.7 ng/L

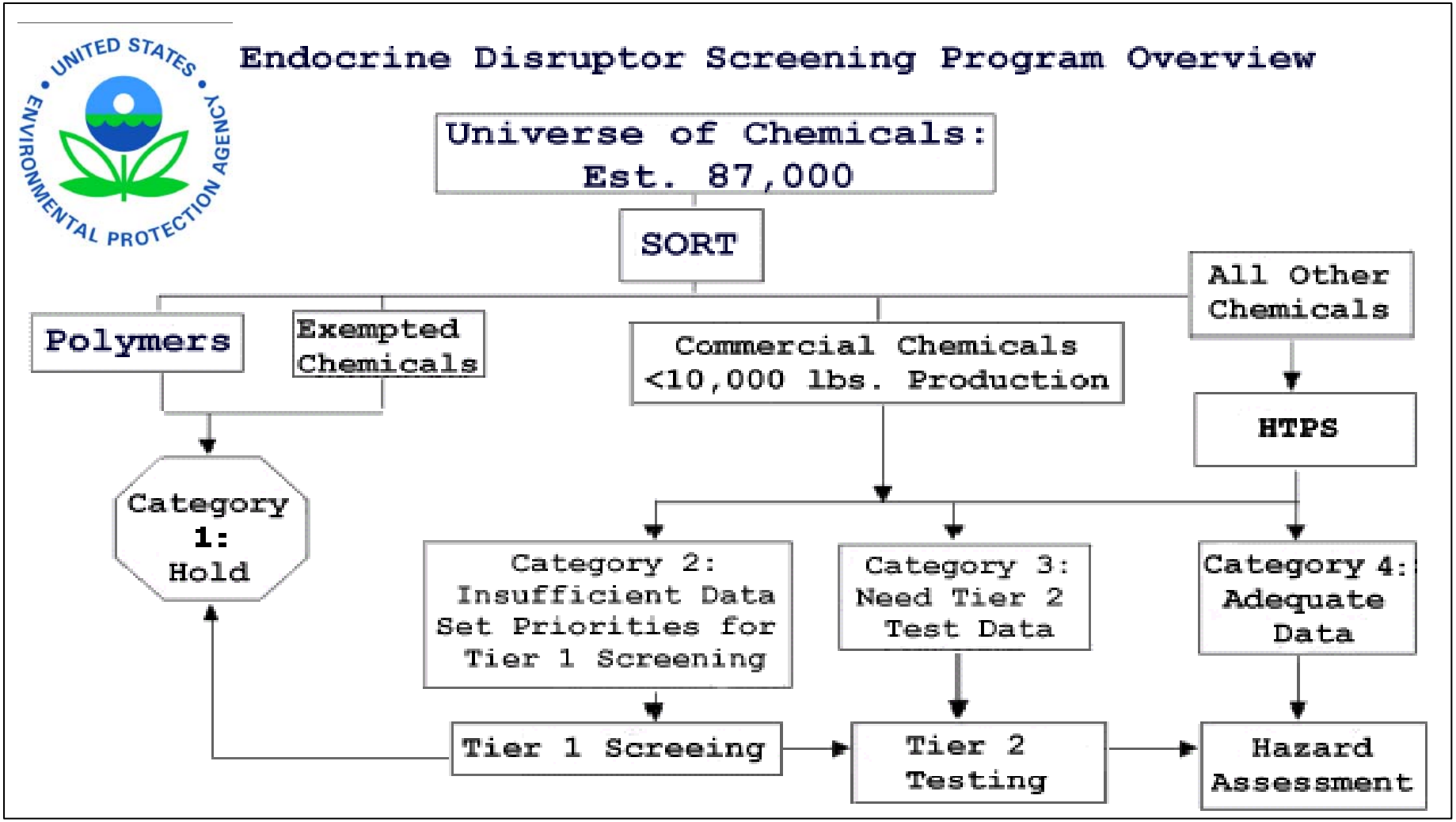
For NDMA, California action level is 10 ng/L & public health goal is 3 ng/L

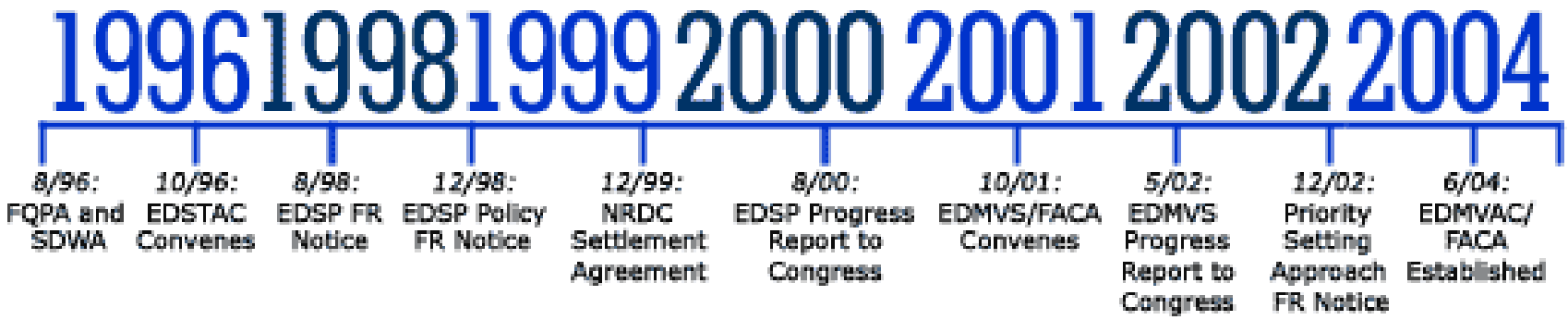
PBDEs least frequently detected contaminant in UCMR2 (3927 PWS Tested)

	# Detect	*% Detect*	*Max (ng/L)*	*Ave (ng/L)*
BDE-47	0	ND	ND	ND
BDE-99	0	ND	ND	ND
BDE-153	0	ND	ND	ND
BDE-100	0	ND	ND	ND

PBDEs not detected in more than 27,000 analyses!
MRLs = 300 to 900 ng/L

Endocrine Disruptor Screening Program Overview





Constituents of Emerging Concern

- *Research Program*

Final Report

Monitoring Strategies for Chemicals of Emerging Concern (CECs) in Recycled Water

Recommendations of a Science Advisory Panel

Panel Members

Paul Anderson, Nancy Denslow, Jörg E. Drewes (*Chair*), Adam Olivieri, Daniel Schlenk, and Shane Snyder

Convened by the

State Water Resources Control Board

June 25, 2010
Sacramento, California

- The State Water Board, in consultation with CDPH convened a "blue-ribbon" advisory panel to guide future actions relating to CECs.
- The panel or a similarly constituted panel shall update the report *every five years*.

CALIFORNIA Water Boards
STATE WATER RESOURCES CONTROL BOARD
REGIONAL WATER QUALITY CONTROL BOARDS

CDPH California Department of PublicHealth

Requirement for Monitoring

Health-relevant CECs

CECs of toxicological relevance to human health

Performance indicator CECs

Useful for monitoring treatment process efficacy

Surrogates

Monitor the efficiency of trace organic compound removal by a treatment process and/or provide an indication of a treatment process failure

Table 8.2. Health-based and performance based indicator CECs and performance surrogates for potable and non-potable reuse practices.

Reuse Practice	Health-based Indicator	MRL (ng/L)	Performance-based Indicator	Expected Removal[8]	MRL (ng/L)	Surrogate	Method	Expected Removal[8]
Groundwater Recharge SAT	17β-estradiol[1]	1	Δgemfibrozil[5]	>90%	10	Δammonia	SM	>90%
	Triclosan[2]	50	ΔDEET[6]	>90%	10	Δnitrate	SM	>30%
	Caffeine[3]	50	ΔCaffeine[3]	>90%	50	ΔDOC	SM	>30%
	NDMA[4]	2	Δiopromide[5]	>90%	50	ΔUVA	SM	>30%
			ΔSucralose[7]	<25%	100			
Direct Injection	17β-estradiol[1]	1	ΔDEET	>90%	10	Δconductivity	SM	>90%
	Triclosan[2]	50	ΔSucralose	>90%	100	ΔDOC	SM	>90%
	Caffeine[3]	50	ΔNDMA	25-50%	2			
	NDMA[4]	2	ΔCaffeine	>90%	50			
Landscape Irrigation	None		None			Turbidity	SM	
						Cl2 Residual	SM	
						Total Coliform	SM	

[1]Steroid hormones; [2]Antimicrobial; [3]Stimulant; [4]Disinfection byproduct; [5]Pharmaceutical residue; [6]Personal care product; [7]Food additive; [8]travel time in subsurface two weeks and no dilution, see details in Drewes *et al*. 2008; SM – Standard Methods


FUTURE
PAST

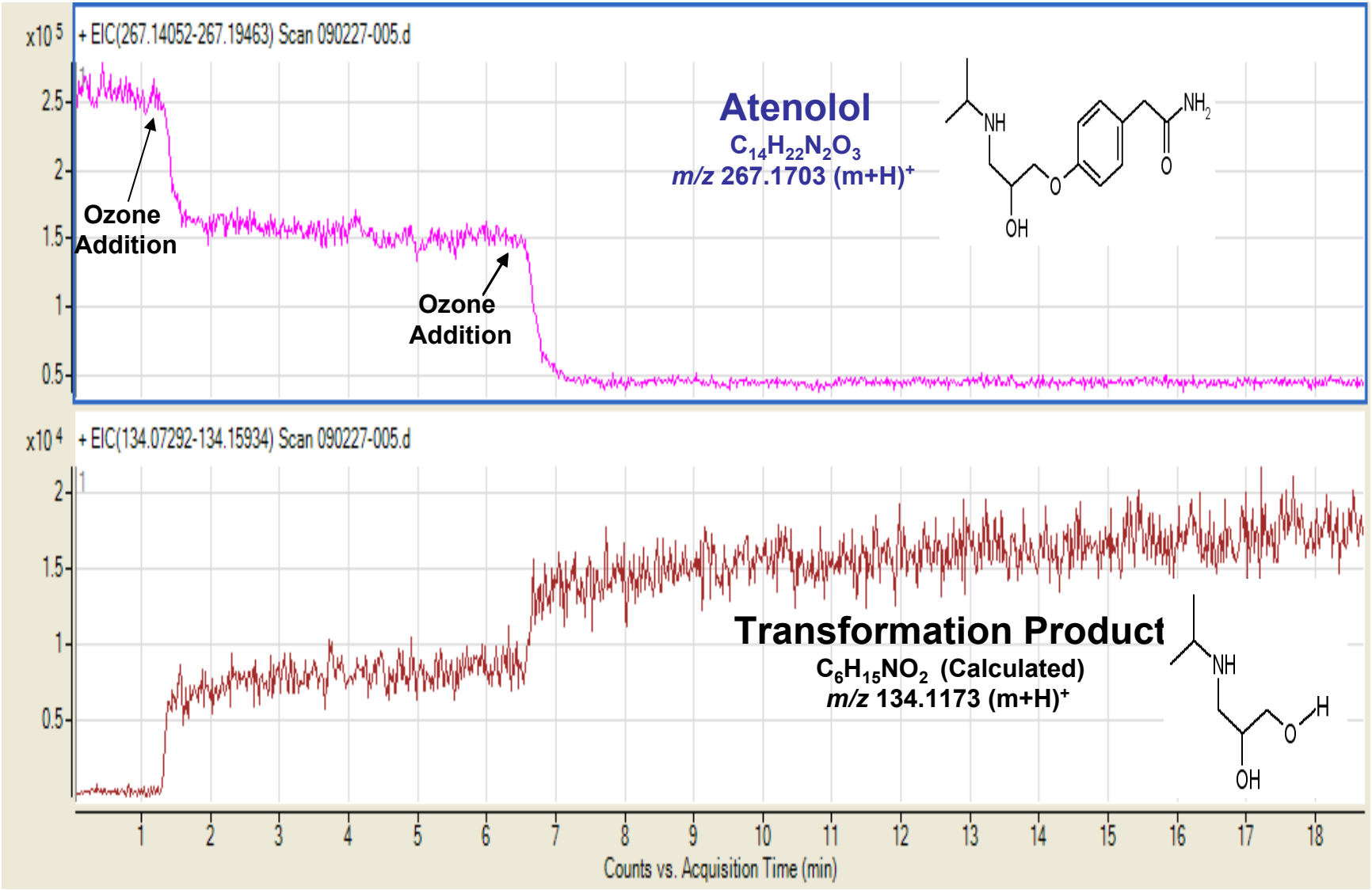
"Americans today are exposed to more chemicals in our products, our environment and our bodies than ever before..…. We are using the best available science to examine a larger list of chemicals and ensure that they are not contaminating the water we drink and exposing adults and children to potential harm." *Lisa Jackson EPA Administrator, 2010*

- Announced by Lisa Jackson March 22nd, 2010

1. Address contaminants as groups
2. Development of technologies
3. Multiple statutes for drinking water
4. Partner with states to share monitoring data

http://www.webdialogues.net/cs/epa-dwcontaminantgroups-library/download/dlib/1860/EPA_Discussion_Paper.pdf.pdf?x-r=pcfile_d

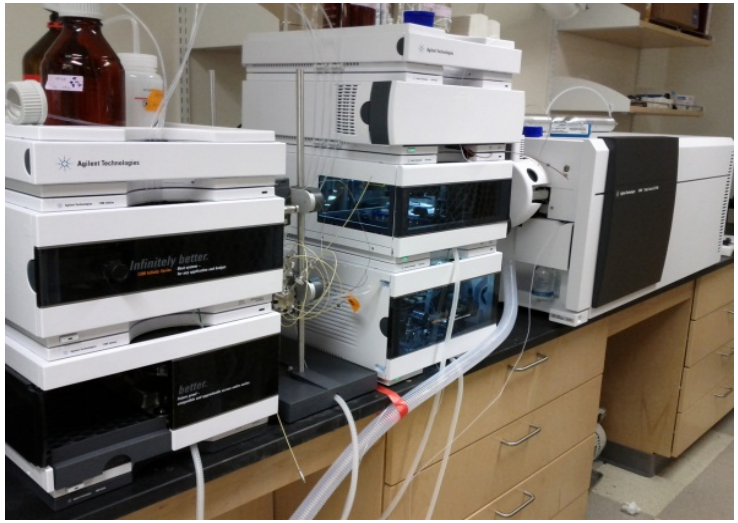
Ozone Reaction Products



Analytical Chemistry VS Bioassay

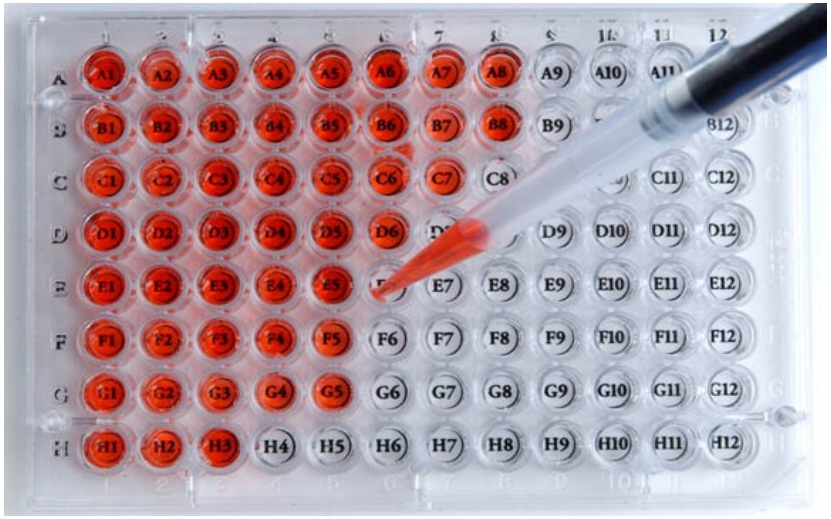
Targeted Analytical

Known compounds
Quantitative
Individual compounds



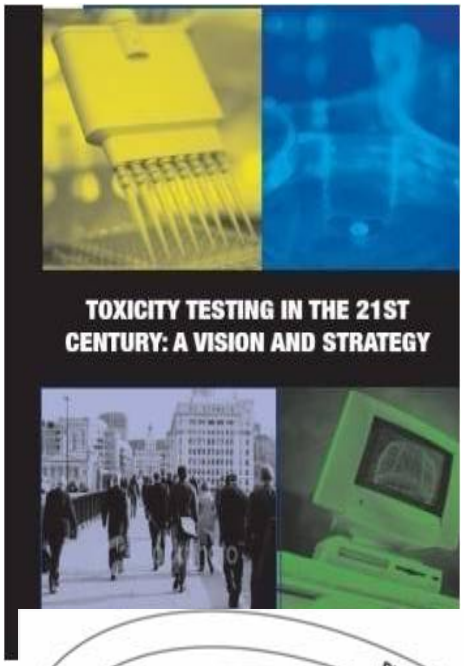
Mechanistic Bioassay

Knowns/unknowns
Semi-quantitative
Synergism/Antagonism



Toxicity Testing in the 21st Century

NRC Report: A Blueprint for Transforming Toxicity Testing



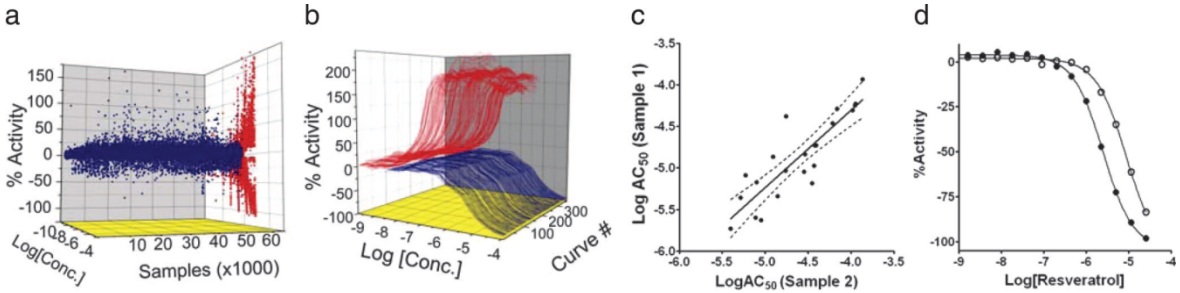
- The current system for toxicity testing is inadequate
  - Expensive ($3B/year)
  - Time-consuming (>2 years to test results)
  - Tests use lots of animals; high dose exposures
  - Results of questionable relevance to humans

- NAS Report: A new toxicity testing paradigm
  - Predictive, high-throughput cell-based *in-vitro* assays
  - Systems biology approach to evaluate pathway perturbations
  - Pharmacokinetic and computational dose-response models enable reliable *in-vivo* to *in-vitro* extrapolation

U.S. Federal Response to Tox 21 Report

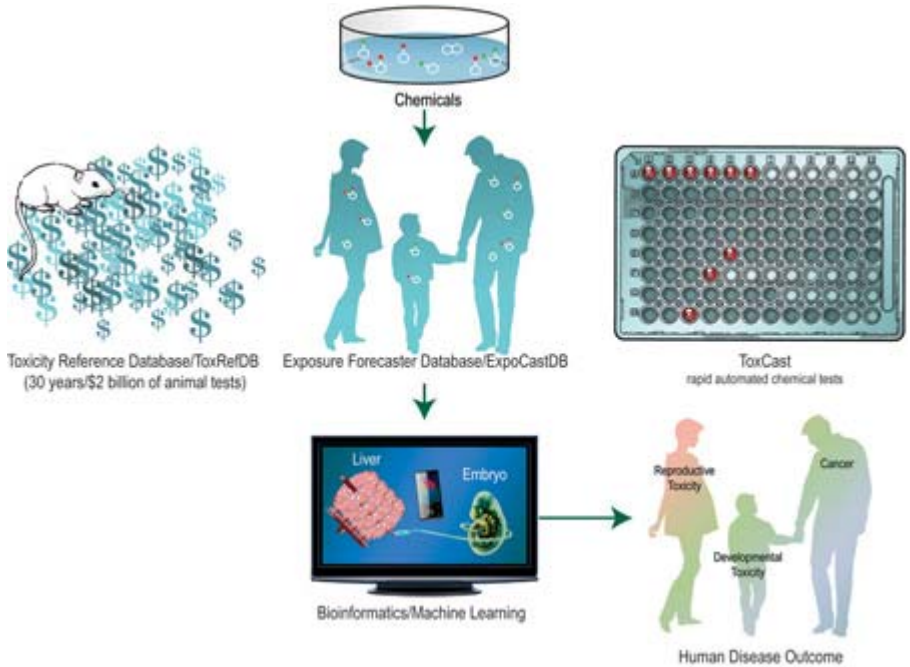
Tox-21 Consortium: MOU Between NIH, EPA &FDA (2008)

- NIH-NCGC: Established automated high-throughput screening (HTS), to test thousands of chemicals using a battery of ~700 biochemical and cell-based assays.
- EPA ToxCast: Use *in-vitro* HTS assay data along with *in-vivo* animal toxicity data to develop bioactivity profiles and predictive toxicity signatures
- NIEHS-NTP work with EPA to develop *in-silico* computational models
- FDA provides regulatory guidance



EPA ToxCast Program Has Made Progress

Screening to Prioritize 80,000 Chemicals & Develop Predictive Signatures



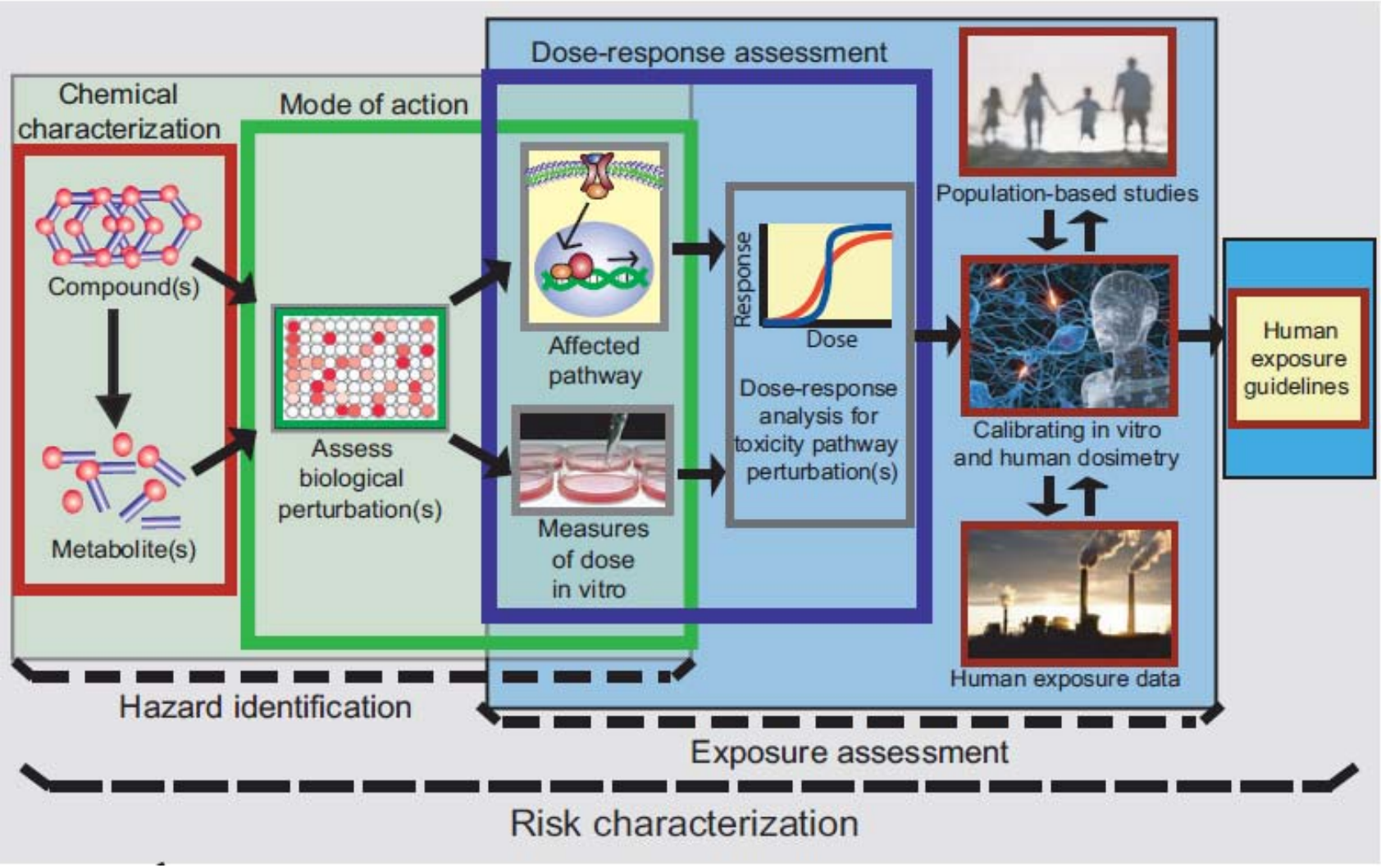
- Toxcast uses high-throughput Tox-21 *in vitro* assay data, *in silico* modeling, and 30 years of animal toxicity test data to understand how humans are impacted by chemical exposures.
- Phase I, completed in 2009 profiled 300 well-studied chemicals (primarily pesticides).
- Phase II (1,000 chemicals) is complete; data analysis in progress.

A recent independent analysis of EPA's ToxCast Phase 1 high-throughput screening data indicates that the assays have a limited capability of predicting *in-vivo* hazard but can separate chemicals based on selectivity (10%).

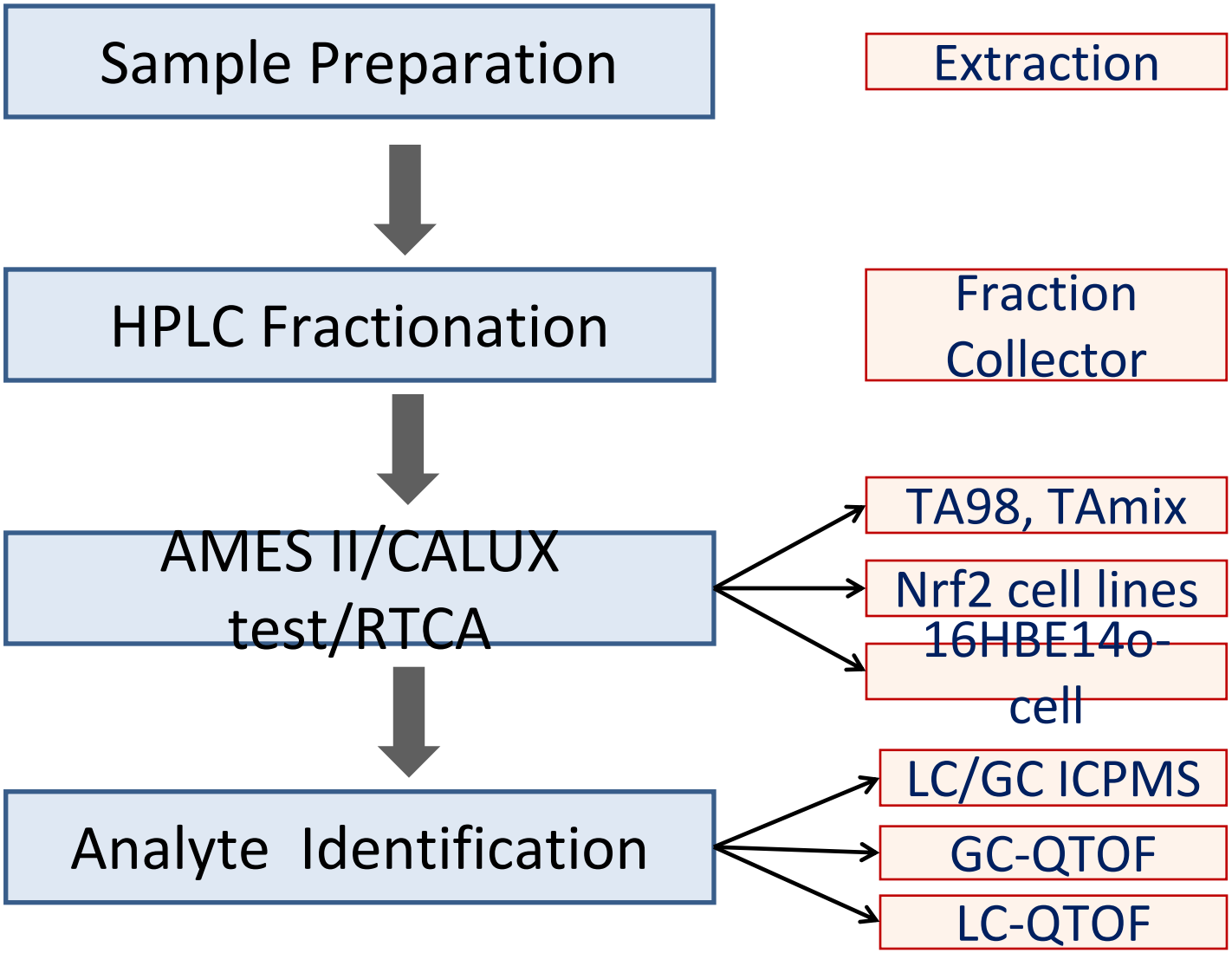
Thomas *et al., Tox Sci.,* 2012

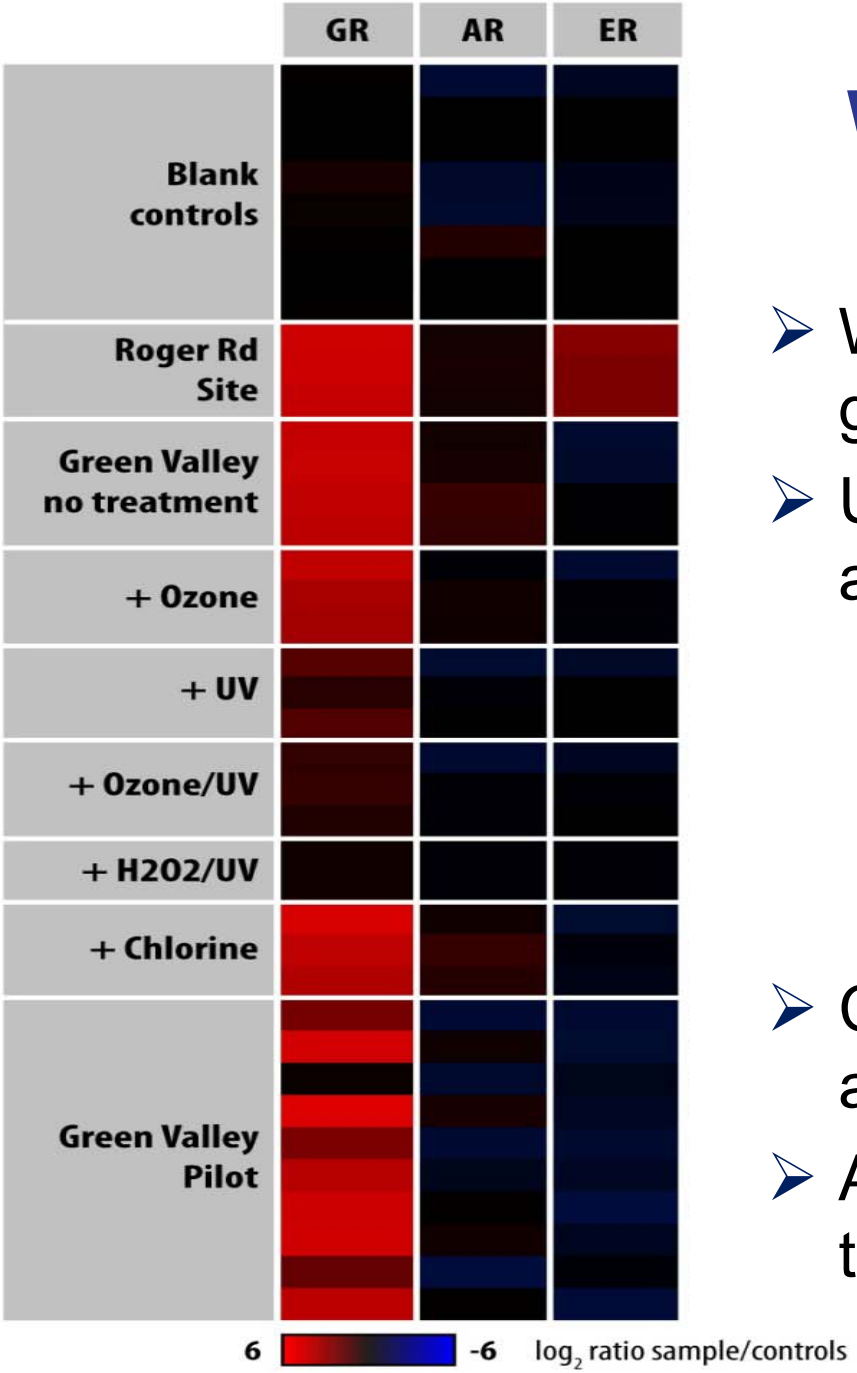
A Map of Toxicity Pathways is the Key

Toxicity Pathway Map Needed to Understand Human Biological Relevance



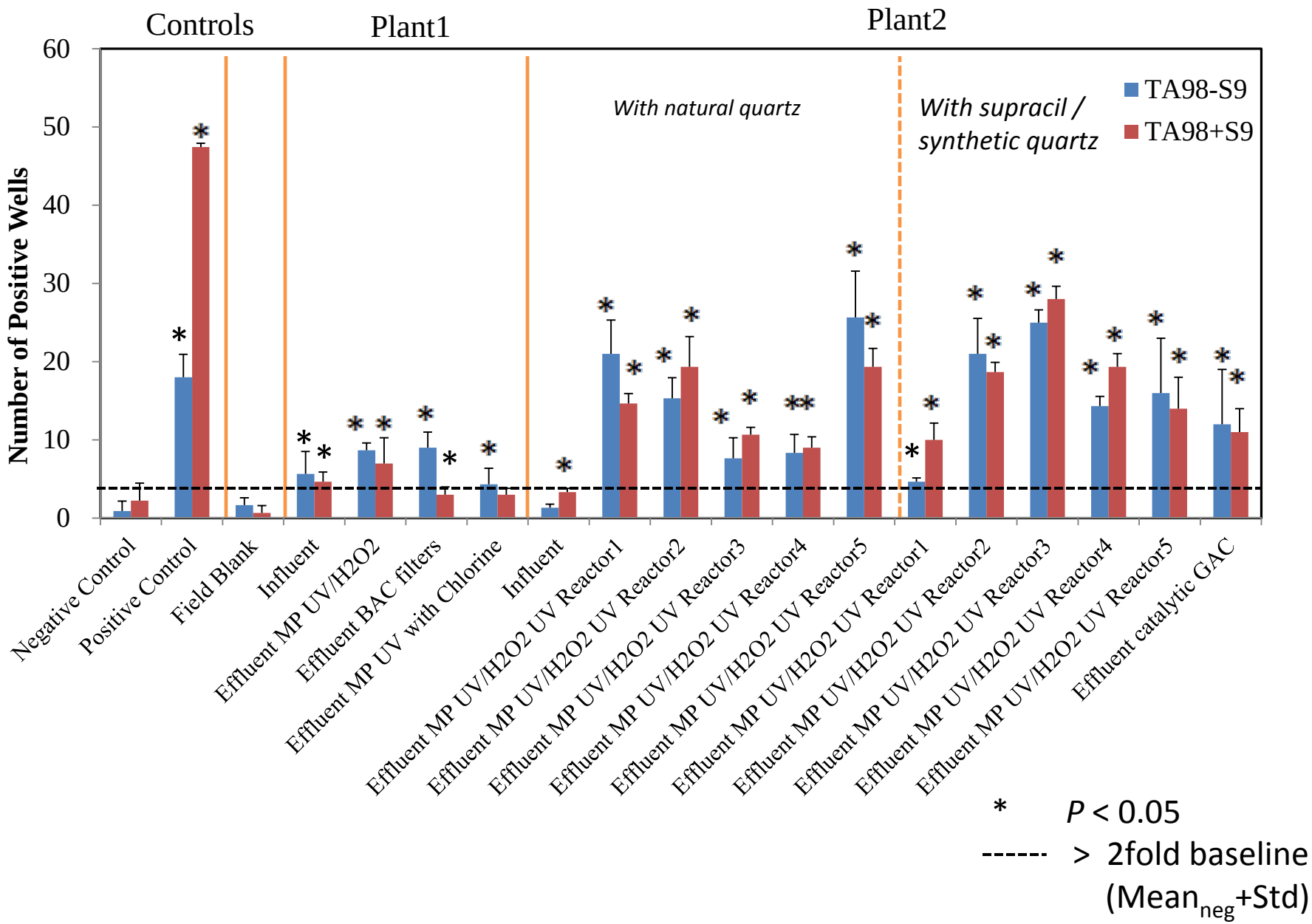
Krewski et al. (2011). New Directions in Toxicity Testing. Ann Rev Public Health, 32, 161-178.


Sample Preparation
Extraction
HPLC Fractionation
Fraction Collector
AMES II/CALUX test/RTCA
TA98, TAmix
Nrf2 cell lines
16HBE14o- cell
Analyte Identification
LC/GC ICPMS
GC-QTOF
LC-QTOF



Results from Ozone & UV Water Reuse Pilot Testing (n=4 seasons)

- WWTP effluent had elevated glucocorticoid (GR) activity
- UV processes are most effective at removing GR activity
  - Agonist appears to be UV sensitive (↑ quantum yield)
  - Guides structural elucidation (i.e., NDMA)
- Chlorine and ozone poor for attenuating GR activity
- Antagonistic ER and AR activity to be investigated


Controls
Plant1
Plant2
With natural quartz
With supracil / synthetic quartz
TA98-S9
TA98+S9
Number of Positive Wells
0
10
20
30
40
50
60
Negative Control
Positive Control
Field Blank
Influent
Effluent MP UV/H2O2
Effluent BAC filters
Effluent MP UV with Chlorine
Influent
Effluent MP UV/H2O2 UV Reactor1
Effluent MP UV/H2O2 UV Reactor2
Effluent MP UV/H2O2 UV Reactor3
Effluent MP UV/H2O2 UV Reactor4
Effluent MP UV/H2O2 UV Reactor5
Effluent MP UV/H2O2 UV Reactor1
Effluent MP UV/H2O2 UV Reactor2
Effluent MP UV/H2O2 UV Reactor3
Effluent MP UV/H2O2 UV Reactor4
Effluent MP UV/H2O2 UV Reactor5
Effluent catalytic GAC
* P < 0.05
------ > 2fold baseline
(Mean$_{neg}$+Std)

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