Day Two: Thursday, October 22, 2009

Application of Biomonitoring Results to Risk Assessment
Coordinators: Perry Cohn, NJ DHSS and Helen Goeden, MDH

Introduction……..Perry Cohn, NJ DHSS and Helen Goeden, MDH

California Biomonitoring Project Update……..……...Bob Howd, OEHHA, CA

Biomonitoring to Evaluate Effectiveness of……..Steve Spayd, NJ GS
Treatment Options for Arsenic in Private Wells

Pilot Study of Perchlorate in Lactating…….……...Marija Borjan, UMDNJ
Women in an Urban Community in New Jersey

Biomonitoring for Perfluorinated Chemicals…….Jean Johnson and Adrienne Kari, MDH

Chromium and Mercury Biomonitoring Studies…….…..Alan Stern, NJ DEP

A Pilot Study of the Endocrine Disruption and ……..David Rich, UMDNJ
Inflammatory Effects of Environmental Toxicants on Fetuses

Round Table Discussion

Overview Talk: High Throughput Testing/Genomics in……Helmut Zarbl, UMDNJ
Toxicology and Risk Assessment

Pharmaceuticals, Personal Care Products, and Unregulated Contaminants
Coordinator: Scott Stoner, NYS DEC

Introduction…….Scott Stoner, NYS DEC

WHO/PHE PPCPs in Drinking Water Project……..Edward Ohanian, HECD/EPA

Strategy for Addressing Contaminants of……..Octavia Conerly, HECD/EPA
Emerging Concern in Water: An Update

New York's Continued Progress on Pharmaceuticals…….Scott Stoner, NYS DEC

Overview of PPCP Research in Pennsylvania……...Rhonda Manning, PA DEP

Pharmaceuticals and Endocrine Disrupting……. Mark Ferrey, MPCA
Compounds in Minnesota Lakes

Green Pharmacy: Opportunities to Green …….Nick Anastas, Poseidon's Trident, LLC
Each Phase in PPCP Lifecycle

Pharmaceutical Disposal Issues and……..Virginia Thompson, EPA Region 3
Actions Across the United States

Research on Occurrence and Treatment Removal of ……Eileen Murphy, NJ DEP
Unregulated Contaminants from Drinking Water

USGS Studies on PPCPs in Water……..Jeff Fischer, USGS

Round Table Discussion

Application of Biomonitoring Results to Risk Assessment

Introduction: Perry Cohn
New Jersey Department of Health & Senior Services
(609) 588-3120
perry.cohn@doh.state.nj.us

Please contact the speaker for more information.

Dr. Perry Cohn and asked that the attendees who were not at the meeting the previous day to introduce themselves. The following attendees introduced themselves:

- Julius Nwosu, EPA Region 10
- Jeff Fischer, U.S. Geological Survey
- Amy Juchatz, Suffolk County, New York, Department of Environment and Energy
- Debra Hammond, New Jersey DEP, Water Quality Standards
- Gary Buchanan, New Jersey DEP, Office of Science
- David Rich, University of Medicine and Dentistry of New Jersey (UMDNJ)
- Marija Borjan, UMDNJ

Dr. Cohn then introduced the session on biomonitoring:

Basically, I wanted to just very briefly go over the mountain peaks of biomonitoring. The big biomonitoring program, certainly here in the United States, there are actually a number of them around the world, and I'm not going to be able to touch on them all. The big one in the United States is the National Health and Nutrition Examination Survey (NHANES). It is run by the Centers for Disease Control and Prevention (CDC). They test all kinds of different chemicals and physiological measures, blood enzymes, lipoproteins, and so forth, and take all kinds of detailed information about the people who are being sampled. Their databases are frequently used by other people to do all kinds of different analyses. They add things as they go along. Somewhere around the year 2001–2002, they added perchlorate, for example. They've also, around that same time, started adding the perfluoro-alkyl chemicals, and so forth. They tend to stay pretty up to date on chemicals.

There's been a long history, I think several decades at this point, looking at organochlorines and mercury in various biological samples in all different kinds of populations, both general and targeted populations, including people who fish. Certainly a lot of this stuff goes on in various ways around the world. Some of them are bigger studies, others smaller. One of the ones that I also wanted to mention is, and Bob Howd is going to discuss it a little more, California recently started initiating its biomonitoring program.

California Biomonitoring Program

Robert Howd
California Environmental Protection Agency
Office of Environmental Health Hazard Assessment
(510) 622-3168
bhowd@oehha.ca.gov

Visuals follow. Please contact the speaker for more information.

California Biomonitoring Program

The California Environmental Contaminant Biomonitoring Program (CECBP), established by SB1379 in 2006, is intended to:

- Determine levels of environmental chemicals in a representative sample of Californians
- Establish trends in the levels of these chemicals over time
- Assess the effectiveness of public health efforts and regulatory programs to decrease exposures to specific chemicals

What is Biomonitoring?

Biomonitoring is the measurement of chemicals (or their metabolites) in a person's body fluids or tissues, such as blood or urine. It tells us the amount of the chemical that actually gets into people from all sources (for example, from air, soil, water, dust, and food) combined. Because of this, biomonitoring can provide useful information on how much exposure to toxic chemicals a person has had.

Biomonitoring Program Components

Scientific Guidance Panel

- Nine members from outside of State government, with expertise in key scientific disciplines

Department of Public Health

- Environmental Health Investigations Branch
- Environmental Health Laboratory Branch

Department of Toxic Substances Control

- Environmental Chemistry Laboratory

Office of Environmental Health Hazard Assessment

- Reproductive and Cancer Hazard Assessment Branch

Public Participation

Program Funding Status

- Base Funding, 3 departments, approx $2 million, plus 2.65 million in 5-yr cooperative agreement with CDC
- Toxic Substances Control Account
- Funded state positions: 13 FTE
- In-kind contributions
  - State staff ~4 FTE
  - Fellows: Association of Public Health Laboratories; Council of State and Territorial Epidemiologists
- Workload adjustments due to state budget

BIOMONITORING PROGRAM MEETINGS

CECBP Meetings are open to the public and public comment is encouraged electronically and during webcast meetings when feasible. Public comments are recorded in the transcript of the SGP meetings, and are available in the public record.

Meeting agendas, materials, transcripts, and webcasts are announced via the Biomonitoring Listserv at: http://www.oehha.ca.gov/multimedia/biomon/agendas.html

Meetings of the Scientific Guidance Panel to date:

- October 6, 2009, Sacramento
- July 28-29, 2009, Oakland
- March 2-3, 2009, Sacramento
- December 4-5, 2008, Sacramento
- October 24, 2008, Oakland
- June 10, 2008, Oakland
- December 17, 2007, Sacramento

Workshop on Chemical Selection

- June 9, 2008, Oakland

Public Input Sessions on Chemical Selection

- April 23, 2008, Fresno
- April 3, 2008, Oakland
- March 23, 2008, Los Angeles

Dept of Public Health Activities

- Overall guidance provided through Environmental Health Investigations Branch
  - Seeking collaborators and funding sources
  - Developing field data collection instruments, outreach plan
  - Continue laboratory method development
  - Initiate sample analysis
- Laboratory capabilities expanded and enhanced
  - Expand Laboratory Information Management System (LIMS)
  - Enhance Quality Assurance/Quality Control
  - Develop new analytical methods
  - Increase number of samples analyzed
  - Lab staff to be trained by CDC

Dept of Public Health Activities

- Sample Collection:
  - Collaboration with Environmental Health Tracking system
  - Urine and blood samples to be collected from mothers, infants
  - Explore feasibility of obtaining samples from existing repositories (e.g., newborn blood spots, maternal serum, Kaiser)

Environmental Health Laboratory Activities - DPH

- Completed training of three staff at CDC
- Quality control methods established
- Proficiency Testing Program developed
- Continuing analytical method development
- Establishing collaborations

Example of Methods Development:

OP-specific Metabolite: 3,5,6-Trichlorpyridinol (TCP)

- Optimized the sample preparation
- Adapted instrumental (LC-MS) analysis method
- Completed method validation (20 batches)
- -Good linearity (9 point calibration curve)
- -Good precision (CV< 15%) and accuracy
- Completed QC pool characterization
- Method will be ready ~September 2009

Other Methods Under Development

- Pyrethroid metabolite: 3-phenoxybenzoic acid
- Phthalate metabolites: mono-ethyl phthalate, mono-(3-carboxypropyl phthalate, mono-butyl phthalate, mono-benzyl phthalate, mono-2-ethylhexyl phthalate
- PAH metabolite: 3-hydroxy phenanthrene
- Validating in-house urine creatinine analysis
- Generating whole-blood reference materials for Pb, Cd, Hg, and Mn

Environmental Chemistry Laboratory – DTSC

Current Activities relevant to project

- Method development for new brominated flame retardants
- Wildlife samples (serum, eggs, adipose) provide testing material
- On-going studies on persistent organic pollutants in human serum
  - OCPs, PCBs, PBDEs, Hydroxy-PCBs,
  - Hydroxy-PBDEs, Triclosan, Phenols
  - Temporal comparisons (1960s vs. 2000s)

DTSC Lab Timetable

- Spring 2009: Set up and training on:
  - – HRGC/MS
  - – LC/MS
  - – Automated sample preparation systems
- June 2009: Staff training at CDC
- July 2009: Start using new equipment:
  - – HRGC/MS system for POPs
  - – LC/MS system for Perfluorinated Chemicals

Office of Environmental Health Hazard Assessment

Chemical Selection – an iterative process, defining priority chemicals, including chemicals designated by CDC, and considering feasibility and resources, to derive list of chemicals for various purposes.

March 2009 SGP meeting added:

- Antimicrobials approved for use in food animal production
- Synthetic hormones approved for use in food animal production
- Cyclosiloxanes

Priority Chemicals List - September 2009

Chemical Name	Lab to do analysis	Biospecimen	Timeline for lab capability	Found in Humans
Metals				
Cadmium	CDPH	Whole Blood	Now	NHANES
Lead	CDPH	Whole Blood	Now	NHANES
Mercury	CDPH	Whole Blood	Now	NHANES
Arsenic	CDPH	Urine	Soon	NHANES
Diesel Exhaust	CDPH	Urine	Later	Other
Tobacco Smoke (cotinine)	CDPH	Blood	Not planned	NHANES
Pyrethroid pesticides				
Allethrin	CDPH	Urine	Later	NHANES
Cyfluthrin	CDPH	Urine	Later	NHANES
Cypermethrin	CDPH	Urine	Now	NHANES
cis-Cypermethrin	CDPH	Urine	Later	NHANES
trans-Cypermethrin	CDPH	Urine	Later	NHANES
Deltamethrin	CDPH	Urine	Now	NHANES
Permethrin	CDPH	Urine	Now	NHANES
cis-Permethrin	CDPH	Urine	Later	NHANES
trans-Permethrin	CDPH	Urine	Later	NHANES
Natural Pyrethrin 1	CDPH	Urine	Later	NHANES
Resmethrin	CDPH	Urine	Later	NHANES
Organophosphate Pesticides				
Acephate	CDPH	Urine	Soon	NHANES
Azinphos Methyl	CDPH	Urine	Soon	NHANES
Chlorethoxyphos	CDPH	Urine	Soon	NHANES
Chlorpyrifos	CDPH	Urine	Now	NHANES
Chlorpyrifos Methyl	CDPH	Urine	Soon	NHANES
Coumaphos	CDPH	Urine	Soon	NHANES
Diazinon	CDPH	Urine	Soon	NHANES
Dichlorvos (DDVP)	CDPH	Urine	Soon	NHANES
Dicrotophos	CDPH	Urine	Soon	NHANES
Dimethoate	CDPH	Urine	Soon	NHANES
Disulfoton	CDPH	Urine	Soon	NHANES
Ethion	CDPH	Urine	Soon	NHANES
Fenitrothion	CDPH	Urine	Soon	NHANES
Fenthion	CDPH	Urine	Soon	NHANES
Isazophos-methyl	CDPH	Urine	Soon	NHANES

Priority Chemicals List - continued

Chemical Name	Lab to do analysis	Biospecimen	Timeline for lab capability	Found in Humans
Malathion	CDPH	Urine	Soon	NHANES
Methamidophos	CDPH	Urine	Soon	NHANES
Methidathion	CDPH	Urine	Soon	NHANES
Methyl parathion	CDPH	Urine	Soon	NHANES
Naled	CDPH	Urine	Soon	NHANES
Oxydemeton-methyl	CDPH	Urine	Soon	NHANES
Parathion	CDPH	Urine	Soon	NHANES
Phorate	CDPH	Urine	Soon	NHANES
Phosmet (Imidan)	CDPH	Urine	Soon	NHANES
Pirimiphos-methyl	CDPH	Urine	Soon	NHANES
Sulfotepp	CDPH	Urine	Soon	NHANES
Temephos	CDPH	Urine	Soon	NHANES
Terbufos	CDPH	Urine	Soon	NHANES
Tetrachlorvinphos	CDPH	Urine	Soon	NHANES
Other Pesticides				
DDT (DDE)	DTSC	Blood	Now	NHANES
para-Dichlorobenzene (1,4-DCB)	CDPH	Urine	Not planned	NHANES
2,4-Dichlorophenoxyacetic acid (2,4-D)	CDPH	Urine	Not planned	NHANES
Environmental phenols				
2,4,4'-Trichloro-2'-hydroxyphenyl ether (Triclosan)	CDPH	Urine	Soon	NHANES
Bisphenol A	CDPH	Urine	Soon	NHANES
Brominated and Chlorinated Organic Chemical Compounds used as Flame Retardants				
Polybrominated Diphenyl Ethers (PBDEs)				
2,2',4'-Tribromodiphenyl ether (BDE 17)	DTSC	Serum	Now	NHANES
2,4,4'-Tribromodiphenyl ether (BDE 28)	DTSC	Serum	Now	NHANES
2,2',4,4'-Tetrabromodiphenyl ether (BDE 47)	DTSC	Serum	Now	NHANES
2,3',4,4'-Tetrabromodiphenyl ether (BDE 66)	DTSC	Serum	Now	NHANES
2,2',3,4,4'-Pentabromodiphenyl ether (BDE 85)	DTSC	Serum	Now	NHANES
2,2',4,4',5-Pentabromodiphenyl ether (BDE 99)	DTSC	Serum	Now	NHANES
2,2',4,4',6-Pentabromodiphenyl ether (BDE 100)	DTSC	Serum	Now	NHANES
2,2',4,4',5,5'-Hexabromodiphenyl ether (BDE 153)	DTSC	Serum	Now	NHANES
2,2',4,4',5,6'-Hexabromodiphenyl ether (BDE 154)	DTSC	Serum	Now	NHANES
2,2',3,4,4',5',6-Heptabromodiphenyl ether (BDE 183)	DTSC	Serum	Now	NHANES
2,2',3,3',4,4',5,5',6,6'-Decabromodiphenyl ether (BDE 209)	DTSC	Serum	Now	NHANES
2,2'4,4',5,5'-Hexabromobiphenyl (PBB 153)	DTSC	Serum	Not Planned	NHANES

Priority Chemicals List - continued

Chemical Name	Lab to do analysis	Biospecimen	Timeline for lab capability	Found in Humans
Other				
Bis(2-ethyl-1-hexyl) tetrabromophthalate (TBPH)	DTSC	Serum	Soon	Not yet known
Bis(hexachlorocyclopentadieno)cyclooctane (Dechlorane Plus)	DTSC	Serum	Not planned	Not yet known
1,2-Bis(2,4,6-tribromophenoxy)ethane (BTBPE)	DTSC	Serum	Soon	Not yet known
Decabromodiphenylethane (DBDPE)	DTSC	Serum	Soon	Not yet known
1,2-Dibromo-4-(1,2-dibromoethyl)cyclohexane (TBECH)	DTSC	Serum	Soon	Not yet known
2-Ethyl-1-hexyl-2,3,4,5-tetrabromobenzoate (TBB)	DTSC	Serum	Soon	Not yet known
Hexabromocyclododecane (HBCD)	DTSC	Serum	Later	Not yet known
Hexachlorocyclopentadienyl-dibromocyclooctane	DTSC	Serum	Not planned	Not yet known
Pentabromoethylbenzene (PBEB)	DTSC	Serum	Soon	Not yet known
Short-chain chlorinated paraffins	DTSC	Serum	Not planned	Not yet known
Tetrabromobisphenol A (TBBPA)	DTSC	Serum	Soon	Not yet known
Tris(1,3-dichloro-2-propyl)phosphate	DTSC	Serum	Not planned	Not yet known
Tris(2-chloroethyl)phosphate	DTSC	Serum	Not planned	Not yet known
2,3-Dibromopropyl-2,4,6-tribromophenyl ether (DPTE)	DTSC	Serum	Soon	Not yet known
Hexabromobenzene (HBB)	DTSC	Serum	Soon	Not yet known
Pentabromotoluene (PBT)	DTSC	Serum	Soon	Not yet known
Tris(1-chloro-2-propyl)phosphate (TCPP)	DTSC	Serum	Not planned	Not yet known
Tris(2,3-dichloro-1-propyl)phosphate	DTSC	Serum	Not planned	Not yet known
Tetrakis(2-chloroethyl)dichloroisopentyldiphosphate	DTSC	Serum	Not planned	Not yet known
Tetrabromophthalic anhydride	DTSC	Serum	Not planned	Not yet known
Tetrabromobisphenol A bis(2,3)dibromopropyl ether	DTSC	Serum	Not planned	Not yet known
N-N-Ethylene-bis(tetrabromophthalimide)	DTSC	Serum	Not planned	Not yet known
Chlorendic acid	DTSC	Serum	Not planned	Not yet known
Bis(2-hydroxyethyl ether) TBBPA	DTSC	Serum	Not planned	Not yet known
2,2-Bis(bromomethyl)-1,3-propanediol	DTSC	Serum	Not planned	Not yet known
2,2-Bis(chloromethyl)trimethylene bis[bis(2-chloroethyl)phosphate]	DTSC	Serum	Not planned	Not yet known
2, 4, 6-Tribromophenol	DTSC	Serum	Not planned	Not yet known
Perchlorate	CDPH	Urine	Soon	NHANES
Phthalates				
Dimethyl phthalate (DMP)	CDPH	Urine	Not planned	NHANES
Diethyl phthalate (DEP)	CDPH	Urine	Soon	NHANES
Dibutyl phthalate (DBP)	CDPH	Urine	Soon	NHANES
Benzylbutyl phthalate (BzBP)	CDPH	Urine	Soon	NHANES
Dicyclohexyl phthalate (DCHP)	CDPH	Urine	Not planned	NHANES
Di-2-ethylhexyl phthalate (DEHP)	CDPH	Urine	Later	NHANES
Di-n-octyl phthalate (DOP)	CDPH	Urine	Soon	NHANES
Di-isononyl phthalate (DiNP)	CDPH	Urine	Later	NHANES

Priority Chemicals List - continued

Chemical Name	Lab to do analysis	Biospecimen	Timeline for lab capability	Found in Humans
Perfluorinated compounds4				
Perfluorooctanoic acid	DTSC	Serum	Soon	NHANES
Perfluorooctane sulfonic acid	DTSC	Serum	Soon	NHANES
Perfluorohexane sulfonic acid	DTSC	Serum	Soon	NHANES
N-Ethyl-perfluorooctane sulfonamide	DTSC	Serum	Soon	NHANES
N-Methyl-perfluorooctane sulfonamide	DTSC	Serum	Soon	NHANES
Perfluorodecanoic acid	DTSC	Serum	Soon	NHANES
Perfluorobutane sulfonic acid	DTSC	Serum	Not planned	NHANES
Perfluoroheptanoic acid	DTSC	Serum	Soon	NHANES
Perfluorononanoic acid	DTSC	Serum	Soon	NHANES
Perfluorooctane sulfonamide	DTSC	Serum	Not planned	NHANES
Perfluoroundecanoic acid	DTSC	Serum	Soon	NHANES
Perflurododecanoic acid	DTSC	Serum	Soon	NHANES
Cyclosiloxanes5	**DTSC**	**Serum**	**Later**	**Other**
Octamethylcyclotetrasiloxane (D4)	DTSC	Serum	Later	Other
Decamethylcyclopentasiloxane (D5)	DTSC	Serum	Later	Other
Dodecamethylcyclohexasiloxane (D6)	DTSC	Serum	Later	Other
Polycyclic Aromatic Hydrocarbons4				
6-Hydroxychrysene	CDPH	Urine	Later	NHANES
3-Hydroxyphenanthrene	CDPH	Urine	Soon	NHANES
3-Hydroxybenzo[a]pyrene	CDPH	Urine	Later	NHANES

Questions

Q. Eileen Dooley: Do you have any plans for a repository of the residual samples?

A. Bob Howd: There will be a repository of residual samples with the intent of keeping some aside to the best of our ability for going back and doing other things as the methods develop. For the blood spot analysis, for the heel sticks for infants, that's particularly a big question because there is so little sample. That's the big deal. We've been talking with the people at CDC for a long time about methods development on this. I mean there are millions of those.

Q. Eileen Dooley: Then from NHANES, have you thought about prioritizing what is found across the general population and maybe picking certain chemicals from a group according to what NHANES has found?

A. Bob Howd: Yes, that's been a major aspect of the development of the priority chemical list here. There has been close collaboration with CDC on that.

Q. Eileen Dooley: Would it be too expensive to do Buccal cells because looking at DNA and genetic arrays would be too expensive?

A. Bob Howd: There aren't going be genetic arrays and DNA analysis for this project. This is just analyzing the chemicals.

Q. Alan Stern: How are you identifying your study population? What is your structure for selecting people to be sampled and how are you recruiting them? How many are you actually anticipating?

A. Bob Howd: I haven't the faintest idea, I'm sorry to say. The Health Investigations Branch is responsible for selecting the samples and trying define just who should be sampled, how and when. OEHHA is mainly involved in the development of the Priority Chemicals List. That's a critical issue, and I'm sorry that I can't better address that issue.

Q. Gary Ginsberg: I know of parties that are looking at baby heel sticks for metals. There was that paper published on mercury in baby heel stick blood, which looks like a very promising methodology. Are you guys looking to analyze drops of blood for pyrethroids, PFOA, and those kinds of compounds?

A. Bob Howd: I doubt it. I think it will be those simpler things like metals. I know that Ben Blount was working on a method for perchlorate in heel stick blood and that actually works, and that's quite low levels, so I don't know how many things we'll be capable of measuring in the heel stick blood. But metals and perchlorate (which surprised me)—there must be other things but the pyrethroid-metabolites are quite difficult. Well maybe some phthalates you could probably measure there, but I don't know. This is coming along in such a slow fashion because of the difficulty of developing all those sources of the samples and then making sure that the methods work and are reliable in each of those different matrices.

Biomonitoring to Evaluate Effectiveness of Treatment Options for Arsenic in Private Wells

Steven Spayd
New Jersey Department of Environmental Protection / New Jersey Geological Survey
(609) 633-1039
steve.spayd@dep.state.nj.us

Visuals follow. Please contact the speaker for more information.

BACKGROUND: Thousands of people in New Jersey and millions worldwide have been affected by arsenic contamination of drinking water from wells. Special water treatment systems can remove arsenic from drinking water and can be configured to treat all the water in the home (point-of-entry) or water at only a single tap for drinking and cooking (point-of-use).

OBJECTIVE: To compare the effectiveness of point-of-entry and point-of-use arsenic water treatment systems in reducing arsenic exposure from well water using biomonitoring.

METHODS: A biomonitoring study was conducted with 51 subjects having elevated arsenic in their residential home well water in New Jersey. The subjects obtained either point-of-entry or point-of-use arsenic water treatment. The mean arsenic concentration in untreated water was 44 µg/L. Prior ingestion exposure to arsenic in well water was determined by testing arsenic concentrations in the well water and obtaining water-use histories for each subject, including years of residence with the current well and amount of water consumed from the well per day. A series of urine samples were collected from the subjects starting before water treatment was installed. Urine samples were analyzed for inorganic-related arsenic concentrations. Propensity scores were calculated to reduce bias resulting from the non-random assignment of water treatment systems. Generalized estimating equations were used to examine the association between urinary arsenic and urinary arsenic reduction, by treatment group, at nine months after subjects stopped drinking the water or obtained water treatment, while adjusting for correlation among family members by using the propensity score as a covariate.

RESULTS: After nine months of water treatment, the adjusted mean ± SE of the urinary inorganic-related arsenic concentrations, after adjusting for propensity score, prior cumulative arsenic ingestion exposure per body weight, and family correlations, were significantly lower ($p < 0.0005$) in the POE treatment group (2.5 ± 0.6 µg/g creatinine) than in the POU treatment group (7.2 ± 0.8 µg/g creatinine).

CONCLUSIONS: These results suggest that point-of-entry arsenic water treatment systems provide a more effective reduction of arsenic exposure from well water than that obtained by point-of-use treatment.

Biomonitoring to Evaluate Effectiveness of Treatment Options for Arsenic in Private Wells

Steven Spayd, PhD, MPH, PG

New Jersey Geological Survey
NJ Department of Environmental Protection
PO Box 427
Trenton, New Jersey 08625

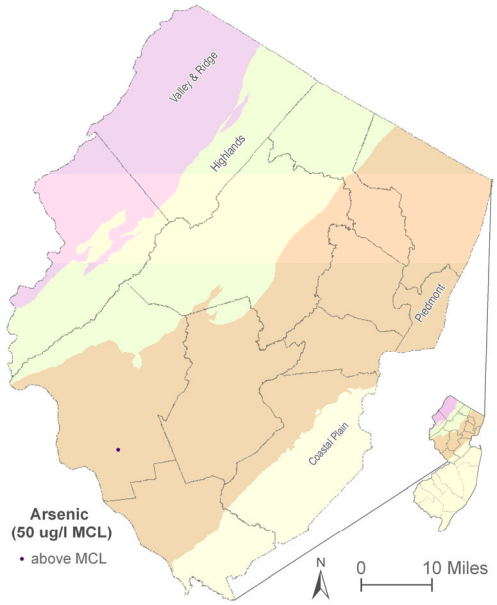
email: steve.spayd@dep.state.nj.us
phone: 609-633-1039

Residential Well

NJ's Arsenic Drinking Water Standard of 5 ug/L is the Most Protective in the World

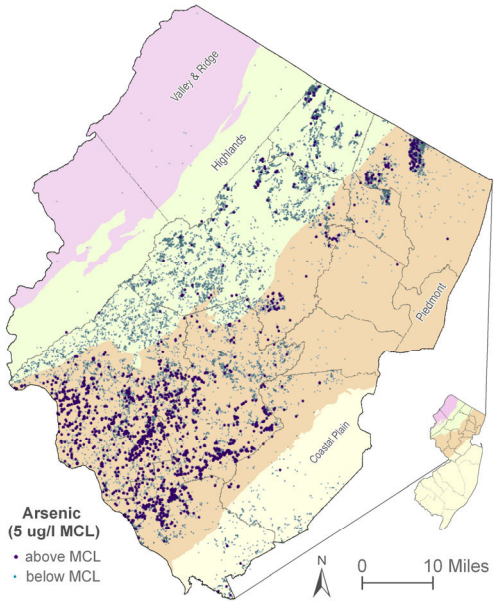
- NJ's new standard took effect in January 2006.
- USEPA's national standard is 10 ug/L.
- NJ's PWTA included arsenic when it started in 2002.

Wells Known to Exceed the Arsenic MCL in 1999



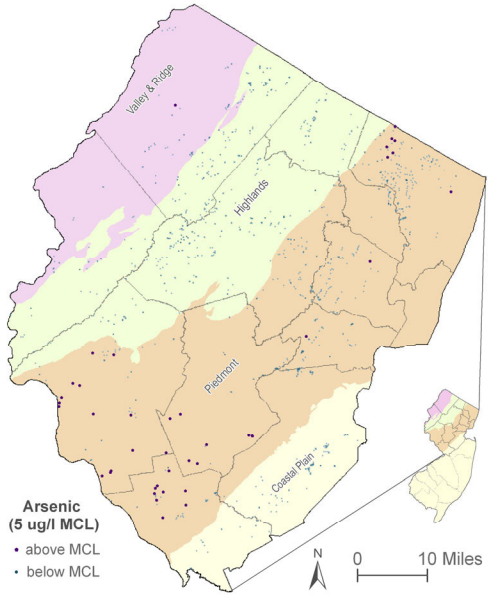
1999

NJ Private Well Testing Act Arsenic Results



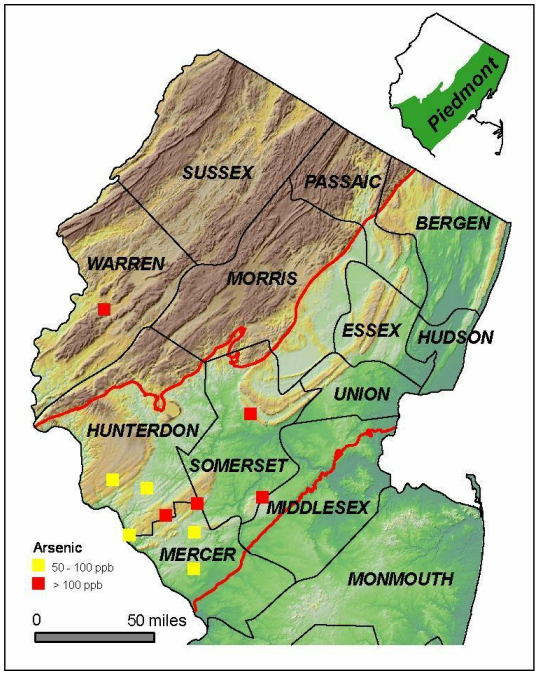
2002-2007

NJ Public Wells - Arsenic Results



Highest Arsenic Concentrations in NJ Well Water

Found in Residential Wells



Common Arsenic Species			
Arsenic Species	**Name**	**Chemical Formula**	**Where Found**
As^{III}	Arsenite	H_3AsO_3	Water
As^{V}	Arsenate	H_3AsO_4	Water
MMA^{III}	Monomethylarsonous Acid	$CH_3As(OH)_2[CH_3AsO]_n$	Metabolite
DMA^{III}	Dimethylarsinous Acid	$(CH_3)_2AsOH[((CH_3)_2As)_2O]$	Metabolite
MMA^{V}	Monomethylarsonate	$CH_3AsO(OH)_2$	Metabolite
DMA^{V}	Dimethylarsinate	$(CH_3)_2AsO(OH)$	Metabolite, Mushrooms
AsB	Arsenobetaine	$(CH_3)_3As^+CH_2COO^-$	Seafood & Fish
AsC	Arsenocholine	$(CH_3)_3As^+CH_2CH_2OH$	Seafood & Fish
Arsenosugars I-XV	Dimethylarsinoylribosides		Seaweed & Scallops

Common Arsenic Species

Arsenic Species	Name	Chemical Formula	Where Found
As^{III}	Arsenite	H_3AsO_3	Water
As^{V}	Arsenate	H_3AsO_4	Water
MMA^{III}	Monomethylarsonous Acid	$CH_3As(OH)_2[CH_3AsO]_n$	Metabolite
DMA^{III}	Dimethylarsinous Acid	$(CH_3)_2AsOH[((CH_3)_2As)_2O]$	Metabolite
MMA^{V}	Monomethylarsonate	$CH_3AsO(OH)_2$	Metabolite
DMA^{V}	Dimethylarsinate	$(CH_3)_2AsO(OH)$	Metabolite, Mushrooms
AsB	Arsenobetaine	$(CH_3)_3As^+CH_2COO^-$	Seafood & Fish
AsC	Arsenocholine	$(CH_3)_3As^+CH_2CH_2OH$	Seafood & Fish
Arsenosugars I-XV	Dimethylarsinoylribosides		Seaweed & Scallops

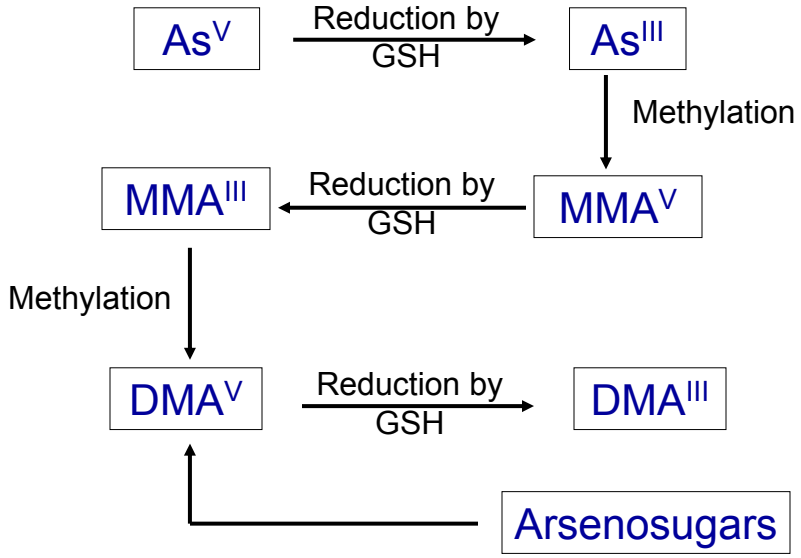
Common Arsenic Species

Arsenic Species	Name	Chemical Formula	Where Found
As^{III}	Arsenite	H_3AsO_3	Water
As^{V}	Arsenate	H_3AsO_4	Water
MMA^{III}	Monomethylarsonous Acid	$CH_3As(OH)_2[CH_3AsO]_n$	Metabolite
DMA^{III}	Dimethylarsinous Acid	$(CH_3)_2AsOH[((CH_3)_2As)_2O]$	Metabolite
MMA^{V}	Monomethylarsonate	$CH_3AsO(OH)_2$	Metabolite
DMA^{V}	Dimethylarsinate	$(CH_3)_2AsO(OH)$	Metabolite, Mushrooms
AsB	Arsenobetaine	$(CH_3)_3As^+CH_2COO^-$	Seafood & Fish
AsC	Arsenocholine	$(CH_3)_3As^+CH_2CH_2OH$	Seafood & Fish
Arsenosugars I-XV	Dimethylarsinoylribosides		Seaweed & Scallops

Toxicology of Arsenic

MMA^{III}	[Most Toxic]
As^{III}	↓
As^{V}	
DMA^{III}	
MMA^{V}	
DMA^{V}	
AsB	
AsC	
Arsenosugars	[Least Toxic]

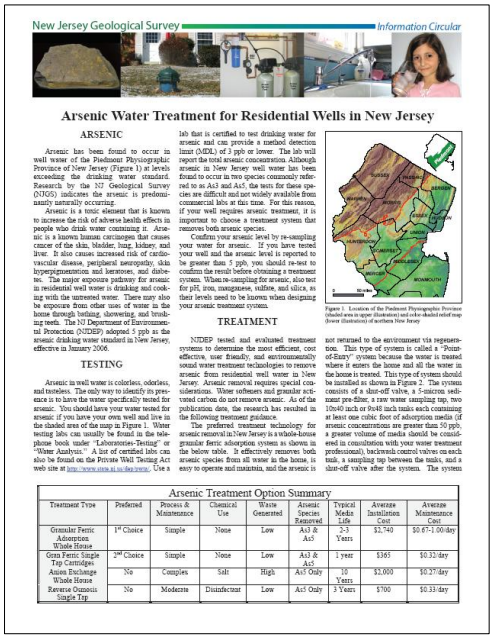
Metabolism of Arsenic



Inorganic-Related Arsenic

The sum of:

$As^{V} + As^{III} + MMA^{III} + MMA^{V} + DMA^{V} + DMA^{III}$



New Jersey Geological Survey — Information Circular

Arsenic Water Treatment for Residential Wells in New Jersey

ARSENIC

Arsenic has been found to occur in well water of the Piedmont Physiographic Province of New Jersey (Figure 1) at levels exceeding the drinking water standard. Research by the NJ Geological Survey (NJGS) indicates the arsenic is predominantly naturally occurring.

Arsenic is a toxic element that is known to increase the risk of adverse health effects in people who drink water containing it. Arsenic is a known human carcinogen that causes cancer of the skin, bladder, lung, kidney, and liver. It also causes increased risk of cardiovascular disease, peripheral neuropathy, skin hyperpigmentation and keratoses, and diabetes. The major exposure pathway for arsenic in residential well water is drinking and cooking with the untreated water. There may also be exposure from other uses of water in the home through bathing, showering, and brushing teeth. The NJ Department of Environmental Protection (NJDEP) adopted 5 ppb as the arsenic drinking water standard in New Jersey, effective in January 2006.

TESTING

Arsenic in well water is colorless, odorless, and tasteless. The only way to identify its presence is to have the water specifically tested for arsenic. You should have your water tested for arsenic if you have your own well and live in the shaded area of the map in Figure 1. Water testing labs can usually be found in the telephone book under "Laboratories-Testing" or "Water Analysis." A list of certified labs can also be found on the Private Well Testing Act web site at http://www.state.nj.us/dep/gwqa/. Use a lab that is certified to test drinking water for arsenic and can provide a method detection limit (MDL) of 3 ppb or lower. The lab will report the total arsenic concentration. Although arsenic in New Jersey well water has been found to occur in two species commonly referred to as As3 and As5, the tests for these species are difficult and not widely available from commercial labs at this time. For this reason, if your well requires arsenic treatment, it is important to choose a treatment system that removes both arsenic species.

Confirm your arsenic level by re-sampling your water for arsenic. If you have tested your well and the arsenic level is reported to be greater than 5 ppb, you should re-test to confirm the result before obtaining a treatment system. When re-sampling for arsenic, also test for pH, iron, manganese, sulfide, and silica, as their levels need to be known when designing your arsenic treatment system.

Figure 1. Location of the Piedmont Physiographic Province (shaded area in upper illustration) and color-shaded relief map (lower illustration) of northern New Jersey

TREATMENT

NJDEP tested and evaluated treatment systems to determine the most efficient, cost effective, user friendly, and environmentally sound water treatment technologies to remove arsenic from residential well water in New Jersey. Arsenic removal requires special considerations. Water softeners and granular activated carbon do not remove arsenic. As of the publication date, the research has resulted in the following treatment guidance.

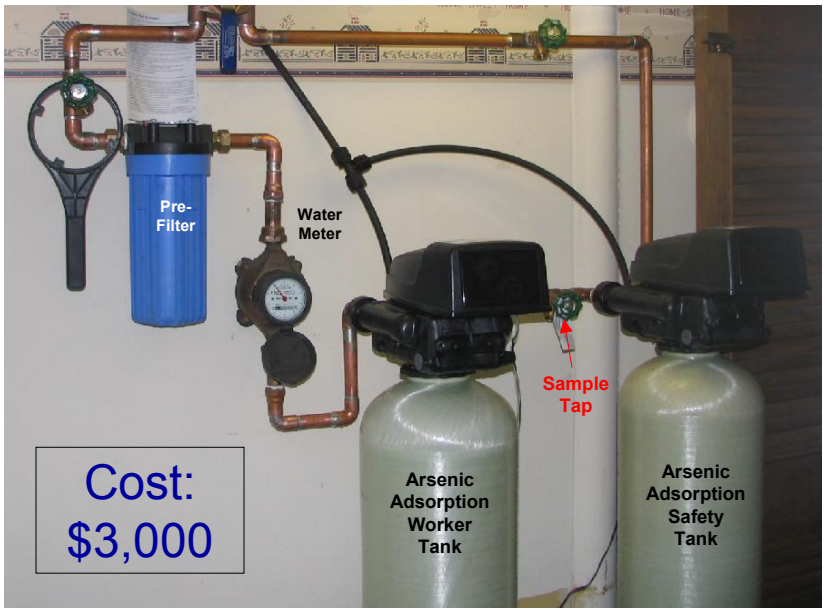
The preferred treatment technology for arsenic removal in New Jersey is a whole-house granular ferric adsorption system as shown in the below table. It effectively removes both arsenic species from all water in the home, is easy to operate and maintain, and the arsenic is not returned to the environment via regeneration. This type of system is called a "Point-of-Entry" system because the water is treated where it enters the home and all the water in the home is treated. This type of system should be installed as shown in Figure 2. The system consists of a shut-off valve, a 5-micron sediment pre-filter, a raw water sampling tap, two 10x40 inch or 9x48 inch tanks each containing at least one cubic foot of adsorption media (if arsenic concentrations are greater than 50 ppb, a greater volume of media should be considered in consultation with your water treatment professional), backwash control valves on each tank, a sampling tap between the tanks, and a shut-off valve after the system. The system

Arsenic Treatment Option Summary

Treatment Type	Preferred	Process & Maintenance	Chemical Use	Waste Generated	Arsenic Species Removed	Typical Media Life	Average Installation Cost	Average Maintenance Cost
Granular Ferric Adsorption Whole House	1st Choice	Simple	None	Low	As3 & As5	2-3 Years	$2,740	$0.67-1.00/day
Gran Ferric Single Tap Cartridges	2nd Choice	Simple	None	Low	As3 & As5	1 year	$365	$0.32/day
Anion Exchange Whole House	No	Complex	Salt	High	As5 Only	10 Years	$2,000	$0.27/day
Reverse Osmosis Single Tap	No	Moderate	Disinfectant	Low	As5 Only	3 Years	$700	$0.33/day

http://www.state.nj.us/dep/pwta/Arsenic_Treatment.pdf

Whole House (POE) Water Treatment



Cost:
$3,000

Point-of-Use (POU) Water Treatment

Cost:
$400

The Study

- The NJDEP arsenic water treatment study.
- Institutional Review Board Approval.
- Subject Recruitment:

  53 Exposed Subjects Total (31 POE and 22 POU).
  - 24 Subjects in the Pre-Post Subset.
  - Mean arsenic concentration in untreated well water was 44 ug/L.
- Added 5 Control Subjects with < 5 ug/L water arsenic.

Water Use Questionnaire

- Calculation of Cumulative Arsenic Ingestion Dose, before installation of arsenic water treatment, in mg.
- As in Water (mg/L) x ingestion (L/day) x days
- Also collected dietary information.

Protocol for Collection of Urine and Blood Samples

- A series of urine samples were collected from the subjects starting before water treatment was installed.
- Subjects asked to avoid seafood and fish for four days prior to biomonitoring sample collection. Compliance was poor.

Analysis of Urine and Blood Samples

Urine samples were analyzed for:

- Total Arsenic
- Inorganic-Related Arsenic
- Creatinine

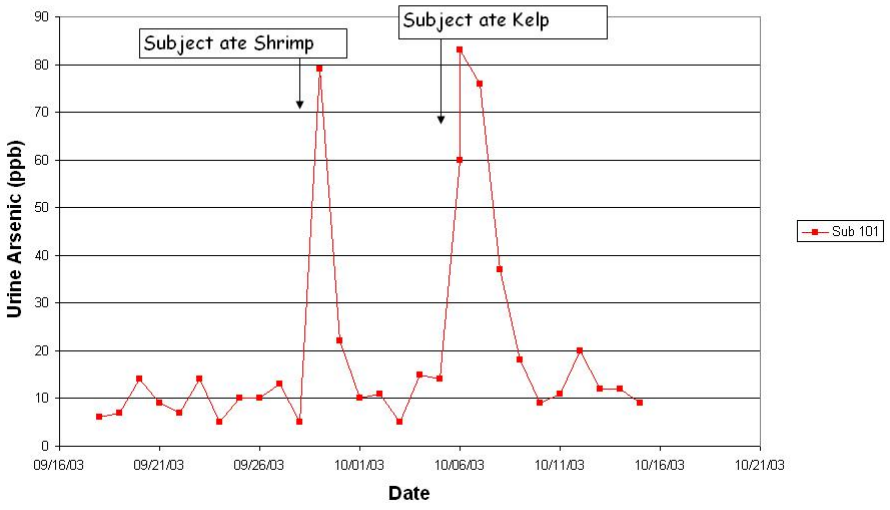
Blood samples were analyzed for:

- Total Arsenic

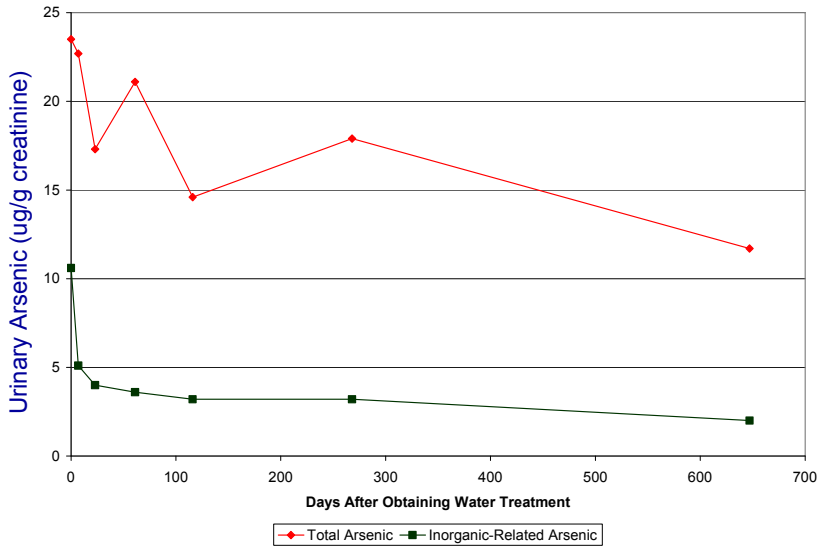
How Much Arsenic in the Diet?

From FDA Total Diet Study	
Food	**Total Arsenic Mean Concentration (mg/Kg)**
haddock, pan cooked	5.540
tuna, canned in oil	0.929
tuna, canned in water	0.878
fish sticks, frozen	0.736
shrimp, boiled	0.678
fish sandwich on bun	0.501
Salmon	0.469
clam chowder	0.141
crisped rice cereal	0.139
tuna noodle casserole	0.112
mushrooms, raw	0.081
white rice, cooked	0.071
rice, infant cereal	0.042
chicken, fried fast food	0.024

Dietary Arsenic Confounding



Total and Inorganic-Related Arsenic in Urine of Pre-Post Group Over Time



Comparison of Study Data to NHANES 2003-2004 Urine Data

Inorganic-Related Arsenic Data (µg/L)			Selected Percentiles			
Groups	**Sample Size**	**Geometric Mean**	**25**	**50**	**75**	**95**
NHANES	2557	N/A	<LOD	6.0	N/A	18.9
Controls	5	3.9	2.5	3.6	6.6	7.6
Pre-Post Time Period 0	24	17.5	12.0	15.5	28.8	138.8
Pre-Post Time Nine-Months	24	6.7	3.5	7.0	13.4	28.7

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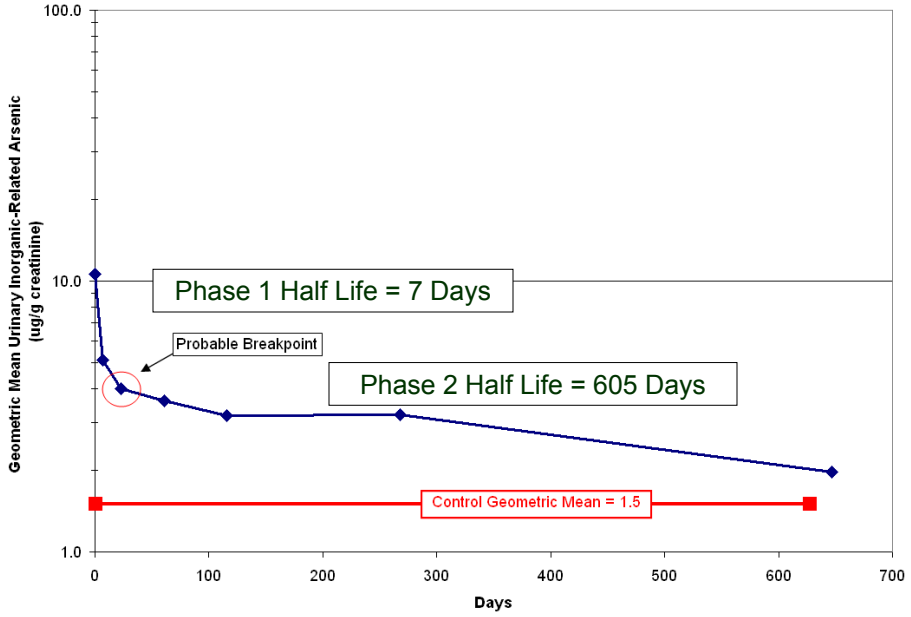
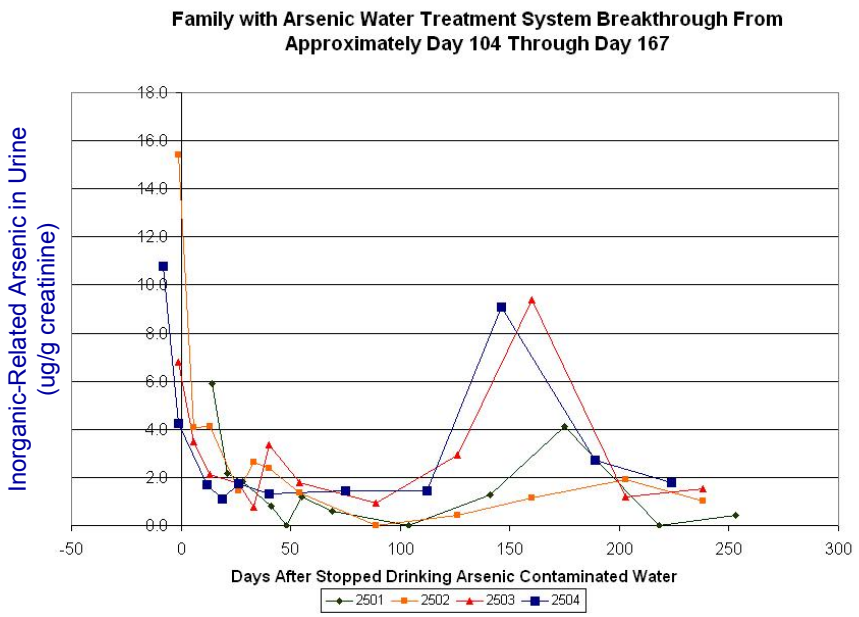
Clearance of Inorganic-Related Arsenic from Urine





Statistical Analyses

- Student T-Test
  - Comparing Independent and Paired Means.
- Propensity Scores
  - Conditional probability of being in a specific treatment group.
  - Calculated to reduce bias from non-random assignment of treatment type (POE vs POU).
- Analysis of Covariance
  - Between groups analysis comparing POE and POU, while controlling for propensity score and prior cumulative arsenic exposure per body weight.
- Generalized Estimating Equations
  - In addition to controlling for covariates, allows adjustment for correlation within families.

Characteristics of Subjects in the Pre-Post Subset by Treatment Group

Water Treatment Groups	POE	POU	Control
General			
Subjects Per Water Treatment Group (n)	16	8	5
Families Per Water Treatment Group (n)	8	4	5
Age in Years, (Mean ± SE)	31 ± 5 *†	61 ± 3*	54 ± 4
Prior Water Ingestion Exposure (Mean ± SE)			
Well Water As (µg/L)	40 ± 8†	45 ± 7†	1.1 ± 0.5
As Water Ingestion Reported (L/d)	0.7 ± 0.1*	1.5 ± 0.4*	1.3 ± 0.6
Years of Exposure	6.8 ± 1.2*	27.0 ± 6.1*†	7 ± 5
As Ingestion Dose (mg)	65 ± 19 *†	482 ± 122*†	3 ± 2
Ingestion Dose per Body Weight (mg/Kg)	1.3 ± 0.5 *†	7.0 ± 1.8*†	0.05 ± 0.03
Dermal Exposure (Mean ± SE)			
Showers per Week at Home	5.1 ± 0.7	6.4 ± 0.6	6.6 ± 0.5
Baths in per Week at Home	0.8 ± 0.4	0.03 ± 0.03	0 ± 0
Teeth Brushing per Week at Home	10.8 ± 1.1 †	14.0 ± 1.3	14.4 ± 0.4
Pool Use per Week During Season	0.4 ± 0.3	0.4 ± 0.3	1.9 ± 1.4
Dietary Exposure (Mean ± SE)			
Seafood and Fish Meals per Week	1.1 ± 0.2	1.8 ± 0.4	1.5 ± 0.4
Mushrooms with Meals per Week	0.5 ± 0.3	0.3 ± 0.2	0.3 ± 0.1
Rice with Meals per Week	1.5 ± 0.2*	0.5 ± 0.2*	2.0 ± 1.3
Poultry with Meals per Week	2.6 ± 0.4	1.6 ± 0.4	2.8 ± 0.6

* $p < 0.05$, significant difference between POE and POU.
† $p < 0.05$, significant difference from Control.
# $p < 0.05$, significant difference within group between initial and final concentration
a Inorganic-related arsenic in final urine adjusted for propensity score and family correlation in GEE.
Control subjects provided only one blood and urine sample.

Characteristics of Subjects in the Pre-Post Subset by Treatment Group

Water Treatment Groups	POE	POU	Control
General			
Subjects Per Water Treatment Group (n)	16	8	5
Urine Biomonitoring (Mean ± SE)			
Creatinine (g/L)	1.6 ± 0.1	1.5 ± 0.2	1.8 ± 0.2
Arsenic in Urine (Geometric Mean ± SE)			
Initial Water Related As (µg/g creatinine)	9.0 ± 1.9 †#	14.8 ± 4.8 †#	1.5 ± 0.4
Inorganic-related As at Nine-Months (µg/g creatinine)	3.4 ± 0.5 †#	2.8 ± 1.4 #	
Inorganic-related As Reduction (Mean µg/g creatinine)	7.3 ± 2.1	13.8 ± 4.9	
Adjusted Arsenic in Urine[a] (Estimated Mean ± SE)			
Inorganic-related As at Nine-Months (µg/g creatinine)	2.5 ± 0.6 *	7.2 ± 0.8 *	
Inorganic-related As Reduction (µg/g creatinine)	10.2 ± 0.4 *	8.1 ± 0.9 *	
Blood Biomonitoring (Geometric Mean ± SE)			
Total Arsenic Initial Blood (µg/L)	10.2 ± 2.4	9.7 ± 1.5	9.2 ± 1.6
Total Arsenic Final Blood (µg/L)	6.2 ± 0.9	5.3 ± 1.7	9.2 ± 1.6

* $p < 0.05$, significant difference between POE and POU.
† $p < 0.05$, significant difference from Control.
\# $p < 0.05$, significant difference within group between initial and final concentration
[a] Inorganic-related arsenic in final urine adjusted for propensity score and family correlation in GEE.
Control subjects provided only one blood and urine sample.

Characteristics of Subjects in the Pre-Post Subset by Treatment Group

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Total Arsenic Initial Blood (µg/L)	10.2 ± 2.4	9.7 ± 1.5	9.2 ± 1.6
Total Arsenic Final Blood (µg/L)	6.2 ± 0.9	5.3 ± 1.7	9.2 ± 1.6

* $p < 0.05$, significant difference between POE and POU.
† $p < 0.05$, significant difference from Control.
\# $p < 0.05$, significant difference within group between initial and final concentration
[a] Inorganic-related arsenic in final urine adjusted for propensity score and family correlation in GEE.
Control subjects provided only one blood and urine sample.

Conclusions

1. Available arsenic water treatment systems are effective in reducing arsenic exposure from well water.

2. After installing arsenic water treatment, urinary inorganic-related arsenic levels reduce 50% in about one week. Total arsenic levels in blood also reduce, but total arsenic in blood is not a good biomarker as it is affected by dietary arsenic from seafood and fish.

Conclusions

3. There is an arsenic body burden developed during chronic exposure to arsenic in well water.

   The clearance appears to have two phases. The first phase has a half-life of 7 days, and the second phase has a half-life of approximately 605 days.

Conclusions

4. Diet and sampling protocol have a significant effect on arsenic concentrations in human urine and blood.

5. HG analytical methods for speciation analysis OR a protocol with a strict one-week restriction of diet from fish, seafood, and seaweed are needed for arsenic biomonitoring.

Conclusions

6. When treating water in a home to remove arsenic, should we treat all the water (POE treatment) or just drinking and cooking water (POU treatment)?

Adjusted Urinary Arsenic After Nine Months (ug/g)		
POU	7.2 ± 0.8	$p < 0.0005$
POE	2.5 ± 0.6	

These results suggest that POE arsenic water treatment systems provide a more effective reduction of arsenic exposure from well water than that obtained by POU.

Recommendations

1. Regulatory agencies should consider requiring or recommending POE arsenic water treatment.

2. A larger randomized study should be conducted to confirm the present findings and determine the exposure pathways for people with POU water treatment systems.

Acknowledgements

- Michael Gochfeld, MD, PhD
- Brian Buckley, PhD
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- Gail Carter
- Many Others at NJDEP, NJGS, EOHSI, and UMDNJ
- The Subjects
- My Wife & Daughters

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National Institute of Environmental Health Sciences (NIEHS) Center of Excellence Grant ES050222

Questions?

Questions

Q. Gloria Post: Basically, you didn't get to really go through the last part but you concluded that people were being exposed besides through what was being treated by the point of use system, probably. But, you're not making any conclusions as to whether their exposure was from drinking from other parts in their house, or inhalation and dermal.

A. Steve Spayd: The study wasn't designed to figure out why. We just wanted to see whether there was a difference. It could be dermal exposure, it could be that it is inconvenient to drink from the tap at the kitchen sink so they are drinking the water from other parts of the house. We really don't know. I'd recommend that we really need a larger study, a more controlled study and one where we also look at, "Gee if the point of use is still higher, why?"

Q. Irene Dooley: What concentration was the treated water generally? Were you monitoring it through the whole test?

A. Steve Spayd: The treated water was usually non-detect at less than 1 µg/L. A couple of times, as in the case where the one system broke through, it was always less than 3 µg/L.

Q. Julius Nwosu: How did you determine the level of exposure for children in this assessment?

A. Steve Spayd: Parents gave us a record of how much water they were drinking at home per day. We had a questionnaire that asked how much water they drank from home per day.

Pilot Study of Perchlorate Exposure in Lactating Women in an Urban Community in New Jersey

Marija Borjan
University of Medicine and Dentistry of New Jersey
School of Public Health
(732) 744-6160
borjanma@umdnj.edu

Visuals follow. Please contact the speaker for more information.

Perchlorate is most widely known as a solid oxidant for missile and rocket propulsion systems and has been detected in drinking water, fruits, vegetables, and milk throughout New Jersey and most of the U.S. Perchlorate interferes with the uptake of iodine into the thyroid and may interfere with the development of the skeletal system and central nervous system of infants who ingest perchlorate. Therefore, it is important to understand the occurrence of perchlorate in breast milk. This study will allow us to acquire valuable information on human exposure to perchlorate through analyses of breast milk, urine, and drinking water. One hundred and six lactating mothers were recruited from the Eric B. Chandler health center in New Brunswick, NJ and provided consent to participate in this study. Each subject was asked to provide three sets of samples and complete a 24-hour dietary recall. Regression analyses showed that diet was the greatest predictor of perchlorate in breast milk and urine and that drinking water was not a major source of perchlorate. The average perchlorate level in drinking water samples was 0.168 ng/mL (n = 253), which is below New Jersey's Maximum Contaminant Level of 5 ng/mL. Perchlorate was detected in all breast milk samples provided (n = 276). The average perchlorate level in breast milk was 6.80 ng/mL. These findings are consistent with widespread perchlorate exposure in lactating women and infants, and shows that breast milk is a viable exposure route for infants. Based on the measured perchlorate levels in breast milk, we estimate that 25% of infants 0-6 months of age would exceed the EPA's reference dose of 0.0007 mg/kg/day. Breast-feeding is important in an infant's growth and development. Therefore, it is important to gain a better understanding of environmental contaminant concentrations in human breast milk and other sources of infant nourishment.

Pilot Study of Perchlorate in Lactating Women in an Urban Community in New Jersey

Marija Borjan, Ph.D., M.P.H.

Perchlorate (ClO_4^-)

- Anion constituent of salt
- Very stable and non-reactive in aqueous environments
- Highly soluble and mobile in water
- Poorly retained in sediment subsurface
- Strong oxidizing agent
  - Widely known as a solid oxidant for missile and rocket propulsion systems
  - Fireworks, road flares

Sodium (Na^+)/Iodide (I^-) Symporter (NIS)

- Protein molecule that mediates the transport of iodide
  - Moves against chemical and electric gradient
  - Transports other ions that have similar shape and charge
    as iodide
  - Perchlorate competes with iodide for NIS-mediated transport
- Present in salivary glands, stomach, and mammary gland

Mode-of-Action

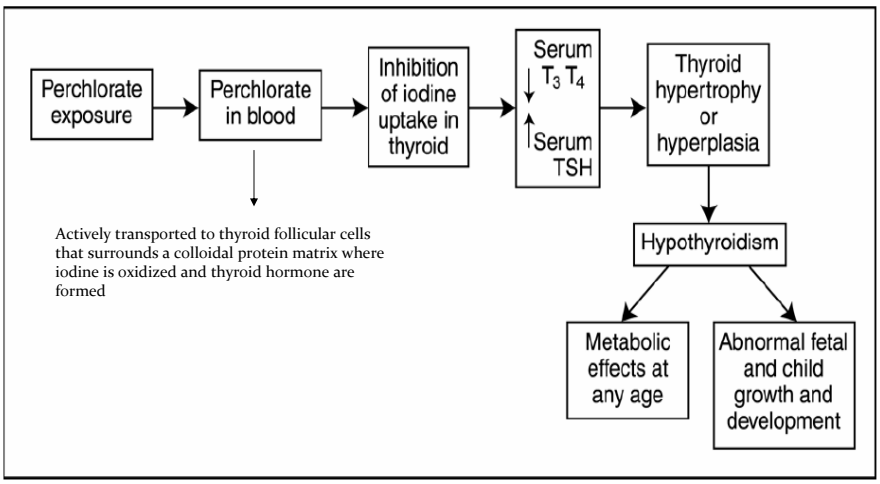


Figure 4-1. Mode of action model for perchlorate toxicity (Adapted from NRC 2005a).

Source: NAS 2005

Populations of Potential Concern

(ITRC 2005)

Potential receptor of concern	Rationale	References
Developing fetus	Thyroid hormones necessary for normal brain development	Haddow et al. 1999, Howdeshell 2002, Heindel and Zoeller 2003, Lavado-Autric et al. 2003, Auso et al. 2003
Nursing infants	Exposure to perchlorate via human milk; brain still developing, thyroid hormones necessary for brain development	Clewell et al. 2003b, Tazebay et al. 2000
Children	Brain still developing; thyroid hormones necessary for brain development, as well as growth and metabolism	Giedd et al. 1999, Sowell et al. 1999, Thompson et al. 2000, Webster et al. 2003
Postmenopausal women	High rates of hypothyroidism	Hollowell et al. 2002, Surks et al. 2004

Reference Dose (RfD)

- Adopted from the National Academy of Sciences review
  - Daily ingestion of up to 0.0007 mg/kg of body weight per day can occur without adversely affecting the uptake of iodine into the thyroid
  - Protective for the most sensitive persons
  - Greer et al. (2002)
    - NOEL 0.007 mg/kg/day
    - Uncertainty factor of 10
  - Still being debated

New Jersey

- NJDEP currently in the process of setting a regulatory standard (MCL) for perchlorate
  - Recommends that water should not be consumed with perchlorate levels greater than 5 ppb
    - Protective drinking water concentration based on the following assumptions (NJ Drinking Water Quality Instit.):

$$\frac{(0.0007 mg/kg/day)\times(67kg)\times(0.2)}{2 Liters/day} = 0.0047 mg/L = 5\mu g/L (or 5 ppb)$$

New Jersey

- Perchlorate detected in drinking water, fruits, vegetables, and milk
- Groundwater and irrigation water
- US FDA (2007)
  - Exploratory survey of 27 types of foods and beverages throughout the U.S. from 2004-2005
  - Sample selection
    - High water content, high consumption
    - Plants irrigated with contaminated water

Food Analyzed	Location of Grower	Perchlorate (ppb)
Romaine lettuce	Blairstown	7.07
	Bridgeton	4.46
	Cedarville	10.1
	Emerson	3.70
	Newfield	14.2
	Toms River	21.6
Tomatoes, Beefsteak	Cedarville	5.58
	Chester	3.36
	Swedesboro	ND
Tomatoes,	Glen Gardener	6.48
Tomatoes	Cherry Hill	ND
	East Brunswick	ND
	Hillsborough	16.4
	Jamesburg	1.04
	Lakewood	2.60
	Long Valley	1.30
	Monmouth Junction	0.38*
	Monroeville	ND
	Thorofare	ND
Spinach	East Windsor	8.15
	Vineland	40.9
	Wayne	6.02
Apple, Gala	Monroeville	ND
Broccoli	East Windsor	6.96
	Hackettstown	3.60
Whole Milk	New Jersey	Range: 3.40-4.85

ND=Not Detected

*Estimate below limit of quantitation (LOQ) and above limit of detection (LOD)

(FDA 2007)

Public Water Systems Samples Through the UCMR or by BSDW with Results 4 ppb and Greater

PW System Name	County	Township	Date Sampled	(ppb)	Sampled By
St. Marys School	Atlantic	Bueno Vista Twp	4/13/2005	6.8	BSDW
St. Marys School	Atlantic	Bueno Vista Twp	5/10/2005	5.5	BSDW
Park Ridge WD	Bergen	Park Ridge Boro	11/26/2002	5.1	UCMR
Park Ridge WD	Bergen	Park Ridge Boro	7/17/2003	13	UCMR
Park Ridge WD	Bergen	Park Ridge Boro	3/3/2004	5.1	BSDW
Park Ridge WD	Bergen	Park Ridge Boro	3/3/2004	23	BSDW
Park Ridge WD	Bergen	Park Ridge Boro	3/25/2004	5	UCMR
Park Ridge WD	Bergen	Park Ridge Boro	6/17/2004	21	BSDW
Park Ridge WD	Bergen	Park Ridge Boro	6/30/2004	5.6	BSDW
Vineland Water & Sewer Utility	Cumberland	Vineland City	12/3/2003	6	UCMR
Vineland Water & Sewer Utility	Cumberland	Vineland City	7/23/2003	6	UCMR
Montclair Water Bureau	Essex	Montclair Town	5/19/2003	5.3	UCMR
Montclair Water Bureau	Essex	Montclair Town	3/3/2004	6.1	BSDW
Middlesex WD	Middlesex	Woodbridge Twp	5/23/2001	7.1	UCMR
Middlesex WD	Middlesex	Woodbridge Twp	11/27/2001	5.2	UCMR

PW: Public Water
WD: Water Department
UCMR: Unregulated Contaminate Monitoring Regulation (US EPA)
BSDW: Bureau of Safe Drinking Water (NJDEP)

Methods

- 106 lactating mothers recruited from Eric B. Chandler health center, New Brunswick, NJ
- *Inclusion* criteria include the following:
  - Expecting to give birth in less than a month and are planning on breast feeding
  - Have recently given birth and are breast feeding
  - Must be 18 years of age or older.

Methods Cont…

- *Exclusion* criteria include the following:
  - serious medical illnesses not being properly controlled
  - abnormalities of the breast(s)
    - mastitis (inflammation of the breast)
  - inability to understand informed consent
  - mother is about to change health care providers, move out of the area, or is unable to return to the clinic.

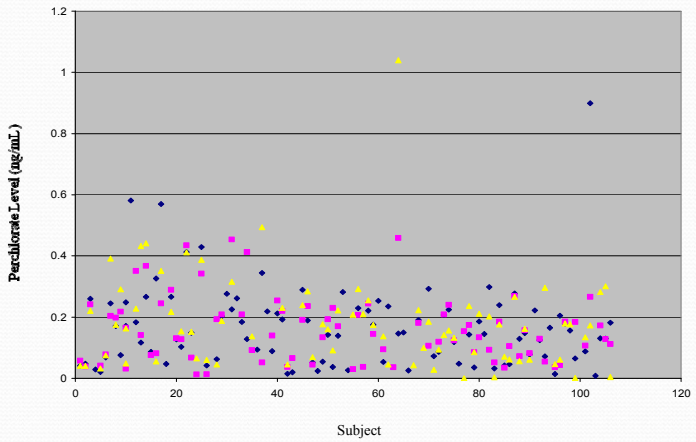
Methods Cont…

- Three sample collections scheduled for each subject
  - Primary drinking water sample
  - Breast milk sample
  - Urine sample
- Samples shipped to CDC laboratories in Atlanta
  - Urine creatinine specimens analyzed on the Roche Hitachi Mod P Chemistry Analyzer, using Creatinine Plus Assay
  - Perchlorate, iodide, nitrate, and thiocyanate measured using ion chromatography and tandem mass spectrometry (Valentin-Blasini et al. 2007)

Demographics

- Race/Ethnicity: > 90% are Hispanic
- Age: range from 18-38 (mean 26)
- Education:
  - 58% had no high school education
  - 11% some high school
  - 10% high school graduate

Perchlorate levels detected in drinking water (ng/mL)



- ◆ Sample Set 1 [range: 0.008-0.900 ng/mL; mean ± SD: 0.168 ± 0.135 ng/mL; n = 96]
- ■ Sample Set 2 [range: 0.012-0.159 ng/mL; mean ± SD: 0.157 ± 0.105 ng/mL; n = 81]
- ▲ Sample Set 3 [range: 0.001-1.040 ng/mL; mean ± SD: 0.182 ± 0.152 ng/mL; n = 76]

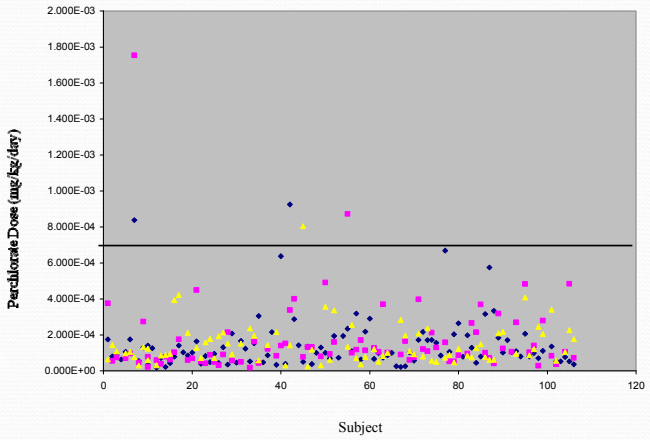
Mother's ClO_4^- Total Dose

$$\frac{(total\ breast\ milk\ \ perchlorate\ mass[mg/day]) + (total\ urine\ \ perchlorate\ mass[mg/day])}{body\ weight\ (kg)}$$

= mother's total perchlorate exposure (mg/kg/day)

- Breast milk produced per day: 700 mL
- Urine produced in adult per day: 2 L
- Body weight for Hispanic woman, 20-39 years of age: 72.0 kg

Mother's total daily perchlorate dose (mg/kg/day)

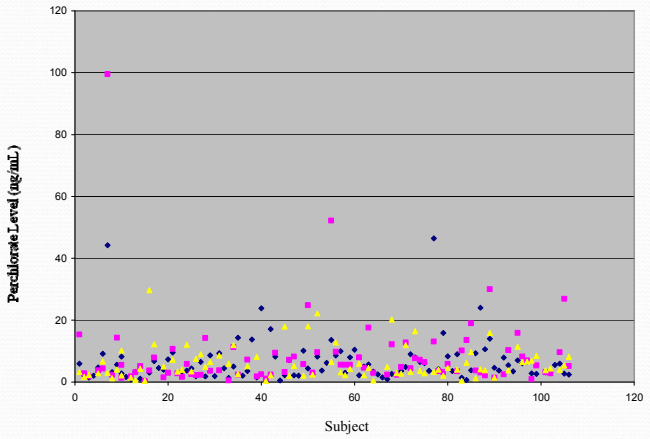


◆ Sample Set 1 [range: 1.800×10^{-5} - 9.250×10^{-4} mg/kg/day, $1.459\times10^{-4} \pm 1.517\times10^{-4}$ mg/kg/day; n = 106]
■ Sample Set 2 [range: 1.800×10^{-5} - 1.753×10^{-4} mg/kg/day, $1.705\times10^{-4} \pm 2.219\times10^{-4}$ mg/kg/day; n = 87]
▲ Sample Set 3 [range: 2.400×10^{-5} - 8.050×10^{-4} mg/kg/day, $1.461\times10^{-4} \pm 1.169\times10^{-4}$ mg/kg/day; n = 83]

Breast Milk

- % infant nutrition from breast feeding
  - 5% breast fed <25% of the time
  - 30% breast fed 25-50%
  - 22% breast fed 50-75%
  - 20% breast fed 100%
- Over 80% used formula
- Type of water used to mix formula
  - Municipal tap water (87%)
  - Bottled water (30%)

Perchlorate levels detected in breast milk (ng/mL)



- ◆ Sample Set 1 [range: 0.420-46.400 ng/mL; mean ± SD: 6.272 ± 6.978 ng/mL; n = 106]
- ■ Sample Set 2 [range: 0.300-99.500 ng/mL; mean ± SD: 8.149 ± 12.469 ng/mL; n = 87]
- ▲ Sample Set 3 [range: 0.320-29.700 ng/mL; mean ± SD: 6.065 ± 5.373 ng/mL; n = 83]

Infant's estimated ClO_4^- dose calculation (breast milk)

$$D = \frac{(C \times IR \times EF)}{BW}$$

D = exposure dose (mg/kg/day)
C = concentration of perchlorate in breast milk (mg/L)
IR = intake rate of breast milk (L/day)
EF = exposure factor (unit less)
BW = body weight (kg)

Average IR:
Breast milk: Infant 0-1 mth: 0.51 L/day
Infant 1-3 mths: 0.72 L/day
Infant 3-6 mths: 0.76 L/day

Average BW:
Infant 0-1 month: 4.8 kg
Infant 1-3 months: 5.6 kg
Infant 3-6 months: 7.4 kg

Estimated breast milk perchlorate doses for infants 0-6 months of age (mg/kg/day)

Sample Set	N	Mean	Percentiles						
			5th	10th	25th	50th	75th	90th	95th
0-1 month									
1	106	6.664×10^{-4}	9.527×10^{-5}	1.540×10^{-4}	2.667×10^{-4}	4.622×10^{-4}	8.508×10^{-4}	1.223×10^{-3}	1.772×10^{-3}
2	87	8.658×10^{-4}	1.211×10^{-4}	1.862×10^{-4}	2.667×10^{-4}	5.143×10^{-4}	1.024×10^{-3}	1.647×10^{-3}	2.769×10^{-3}
3	83	6.444×10^{-4}	5.087×10^{-5}	1.500×10^{-4}	2.901×10^{-4}	4.452×10^{-4}	7.948×10^{-4}	1.334×10^{-3}	1.911×10^{-3}
1-3 months									
1	106	8.064×10^{-4}	1.153×10^{-4}	1.863×10^{-4}	3.227×10^{-4}	5.593×10^{-4}	1.030×10^{-3}	1.479×10^{-3}	2.145×10^{-3}
2	87	1.048×10^{-3}	1.466×10^{-4}	2.253×10^{-4}	3.227×10^{-4}	6.223×10^{-4}	1.239×10^{-3}	1.993×10^{-3}	3.351×10^{-3}
3	83	7.798×10^{-4}	6.156×10^{-5}	1.816×10^{-4}	3.510×10^{-4}	5.387×10^{-4}	9.617×10^{-4}	1.615×10^{-3}	2.311×10^{-3}
3-6 months									
1	106	6.441×10^{-4}	9.209×10^{-5}	1.488×10^{-4}	2.578×10^{-4}	4.468×10^{-4}	8.224×10^{-4}	1.181×10^{-3}	1.713×10^{-3}
2	87	8.369×10^{-4}	1.171×10^{-4}	1.799×10^{-4}	2.578×10^{-4}	4.971×10^{-4}	9.901×10^{-4}	1.592×10^{-3}	2.677×10^{-3}
3	83	6.229×10^{-4}	4.917×10^{-5}	1.450×10^{-4}	2.804×10^{-4}	4.303×10^{-4}	7.682×10^{-4}	1.290×10^{-3}	1.847×10^{-3}

EPA RfD: 0.0007 mg/kg/day

Conclusions

- Detectable levels of perchlorate were found in all urine and breast milk samples collected, which may indicate that the general population is exposed to perchlorate
- For this study population drinking water was a minor source of perchlorate exposure
- For this study population diet was the greatest predictor for perchlorate exposure
- Infants are exposed to perchlorate and breast milk is a viable exposure route
- Important breast milk is monitored for environmental contaminants

Breast Feeding

- Important in an infant's growth and development
- Provides immunologic protection
- Reduces risk of developing illnesses such as:
  - Asthma
  - Diabetes
  - Arthritis
  - Obesity
  - Cardiovascular disease
  - Pneumonia

Recommendations

- Collect food samples from local markets and agricultural areas
- Collecting food samples from the subjects
- Sampling formula
- Perchlorate levels in fore-milk versus hind-milk
- Cumulative effects of perchlorate, thiocyanate, and nitrate
- More data is needed on the toxicological effects of perchlorate on sensitive populations such as infants and on the effects of perchlorate on thyroid function in these sensitive populations

Questions

Q. Ed Ohanian: Would the results from Marija's study have any impact on the relative source contribution value that you have for California?

A. Bob Howd: Yes, if we used this kind of thinking to develop the relative source contribution. What we had done in our PHG was to calculate the relative source contribution if the water were at the PHG level of 6 ppb rather than trying to figure out what it was averaging in California at the time. But, yes, it depends on your thinking.

Q. Gary Ginsberg: It sounds like you collected iodide data as well as perchlorate data in breast milk. There's the Kirk study, which had a correlation between iodide and perchlorate in breast milk, suggesting that the higher the perchlorate level in breast milk, the lower the iodide levels. Did you see that?

A. Marija Borjan: Actually that was one of my study questions and we didn't see that. That's something I'm still looking into because I had assumed that the higher perchlorate there would be in the breast milk and the urine, the lower the iodide levels would be. But they were actually correlated. So, the higher the perchlorate, the higher the iodide. That is still something I'm trying to research. That was one of the interesting facts that came out of my data, but I'm still looking into it.

Biomonitoring for Perfluorinated Chemicals in Minnesota: A Pilot Project

Jean Johnson
Minnesota Department of Health
(651) 201-5902
jean.johnson@state.mn.us

Adrienne Kari
Minnesota Department of Health
(651) 201-3635
adrienne.kari@state.mn.us

Visuals follow. Please contact the speakers for more information.

In 2007, the Minnesota Department of Health began a biomonitoring pilot program for the purpose of describing the distribution of exposure to environmental contaminants in communities that are identified as likely to be exposed. This presentation will describe the results of a pilot project to measure exposure to 7 perfluorochemicals, including PFOA, PFOS, PFHxS, PFBA, and PFNA, in 2 Minnesota communities with PFC contaminated drinking water. Serum specimens were collected in 2008-2009 and analyzed for the 196 adult study participants. All specimens (100%) had detectable levels of PFOA, PFOS, and PFHxS. PFBA was detected in 28% of specimens, and PFNA was detected in 3%. Geometric mean levels of PFOA, PFOS, and PFHxS were elevated compared to levels reported for a 2003-2004 US population (NHANES) sample. Significant associations with male gender, increasing age, and length of residence in the community are reported.

Biomonitoring for Perfluorinated Chemicals in Minnesota: A Pilot Project

FSTRAC Meeting
Princeton, NJ
October 22, 2009

Jean Johnson, PhD
Adrienne Kari, MPH

Minnesota Department of Health
Health Promotion and Chronic Disease Division
Chronic Disease and Environmental Epidemiology Section

Biomonitoring in Minnesota

- In 2007, Minnesota passed a law creating the Environmental Health Tracking and Biomonitoring Program
- This law directs MDH to develop four biomonitoring pilot projects in communities "likely to be exposed" to:
  - Arsenic
  - Perfluorochemicals (PFCs)
  - Mercury
  - A fourth chemical (BPA and cotinine selected)
- Advisory Panel represents stakeholders from government, industry, NGOs, university, local government and legislators.
- Limited in scope, the purpose of each pilot is to
  - measure the amount and range of exposure in the community
  - build state capacity to do biomonitoring
  - apply lessons learned to develop an ongoing biomonitoring program for the state

Other activities prescribed in the Legislation

- Pilot projects were to be “community-based”.
- Participants would have the option to receive their individual results.
- Education and interpretation would be provided to the community and area clinicians.
- MDH will establish guidelines for conducting biomonitoring…guided by protocols developed by the CDC National Biomonitoring Program
  - Ensuring privacy
  - Informed consent (NIH)
  - Inclusion of children
  - Storage (banking) of samples
  - Interpretation, communication of results
  - Educational materials
  - Training programs for health care professionals
  - Follow-up support and medical consult
  - Community participation
  - Purpose of the pilots

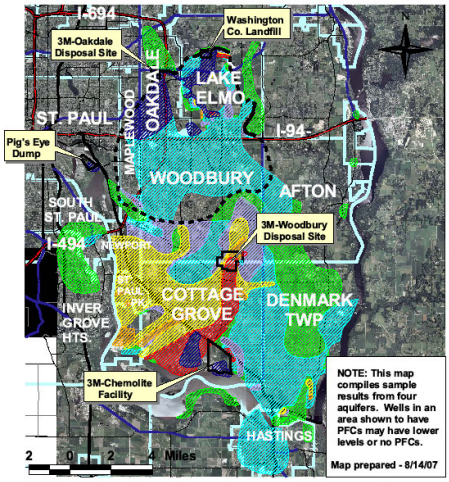
Comparison of four pilot projects

	Study population	**Study community**	**Biospecimen/ Analyte**	**Likely source of exposure**	**Population sample**	**Recruitment goal**
Minneapolis Children's Arsenic Study	Children, 3-10 years old	Urban; geographic community	Urine/ total and speciated arsenic	Ingestion of residential soil contamination, diet, and other exposure routes	Random selection	100
East Metro PFC Biomonitoring Study	Adults, 20 years and older	Suburban; communities based on drinking water source	Blood serum/ 7 PFCs including PFOA, PFOS, and PFBA	Ingestion of contaminated drinking water; diet, and other exposure routes	Random selection	200 (100 from each of 2 communities)
Lake Superior Mercury Biomonitoring Study	Newborns	Rural; geographic community	Newborn dried blood spot/ total mercury	Maternal dietary exposure (fish consumption)	Total population meeting inclusion criteria	1,150 in Minnesota; 600 in Wisconsin and Michigan
Riverside Prenatal Biomonitoring Study	Pregnant women	Urban; clinic-based community	Urine/ Environmental phenols including BPA, and cotinine	Diet and consumer product use (phenols); secondhand smoke (cotinine)	Total population meeting inclusion criteria; stratified by ethnicity	90 (30 from each of 3 ethnic communities)

Background
Perfluorochemicals Analysis in Water

Private and public wells in the Twin Cities east metro area have measurable levels of PFCs.

PFBA, PFOS, and PFOA are the most prevalent.



PFCs in the Southeast Metro Area

- PFCs not detected
- PFBA only, 0.2 - 0.5 ppb
- PFBA only, 0.6 - 0.9 ppb
- PFBA only, 1.0 - 1.5 ppb
- PFBA only, 1.6 - 1.9 ppb
- PFBA only, > 2.0 ppb
- Multiple PFCs detected
- Approximate boundary of northern plumes, dashed where uncertain

East Metro PFC Biomonitoring Pilot Project

Perflurochemicals (PFCs) are a family of chemicals used for decades to make products that resist heat, oil, stains, grease and water.

The biomonitoring project measured these PFCs in the blood of people:

PFOA	Perfluorooctanoic acid*	C8
PFOS	Perfluorooctane sulfonate*	C8
PFBA	Perfluorobutyric acid*	C4
PFHxS	Perfluorohexane sulfonate	C6
PFHxA	Perfluorohexanoic acid	C6
PFPeA	Perfluoropentanoic acid	C5
PFBS	Perfluorobutane sulfonate	C4

*Legislation required 3 specific PFCs be measured.

MINNESOTA MDH DEPARTMENT of HEALTH

Specimens are analyzed at the MDH Public Health Laboratory

•analytic methods are highly sensitive

•MDH limit of detection (LOD) for PFCs in blood is 0.1 ng/ml or parts per billion

•comparable to CDC methods so results are comparable to published NHANES values

PFC Project Communities

- Legislation directed MDH to select 2 exposed communities and sample 100 people in each.
- Communities were defined by their drinking water source.
  - 100 people from households served by Oakdale municipal water supply.
  - 100 people from households with private wells that contain PFCs > 0.1 ppb in Lake Elmo/Cottage Grove.
- To be eligible, participants must :
  - have lived at their current residence since before Jan. 1, 2005
  - be adults, age 20 or older

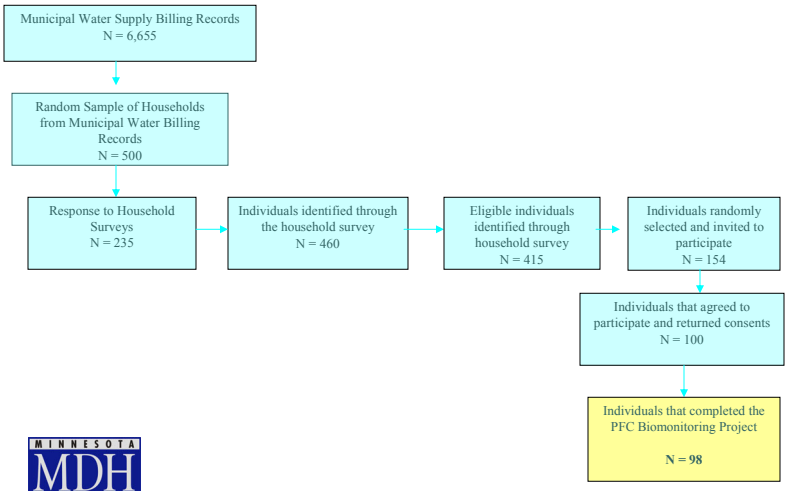
Why was the project limited to adults?

- Adults were more likely to have long term exposure at higher levels.
- Drawing a blood sample is invasive and risky for a young child.
- The project does not provide a health benefit to the child.
  - Federal rules do not allow children to be used in health research unless there is no risk or the study provides a health benefit to the child.
- NHANES does not measure PFCs in children under 12 except in pooled samples.

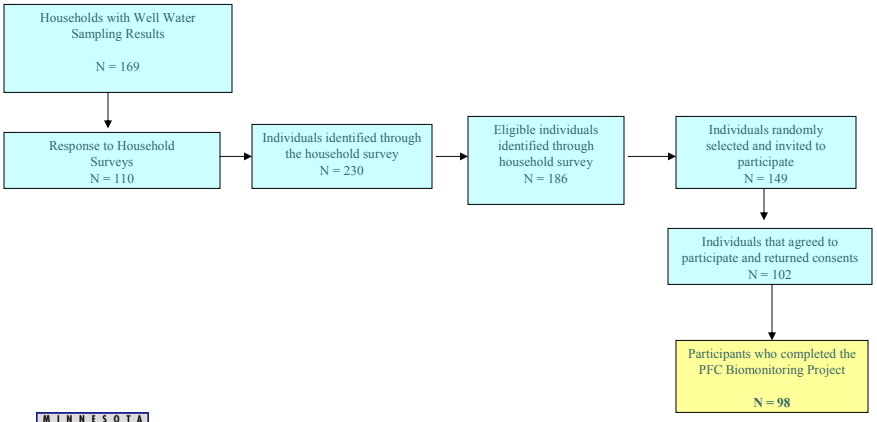
Why is participation limited to people living in their current residence prior to 2005?

- **Alternative water sources were provided to well owners in 2005 and 2006.**
  - **Bottled water**
  - **Granulated Active Carbon (GAC) filters**
- **In 2006, Oakdale installed a large granular activated carbon filter system, removed PFOS and PFOA from city water. PFBA is not entirely eliminated but all contaminants are below levels of health concern.**
- **This limitation assures that the participants will be people with past exposure in the community, some with many years.**

Oakdale Municipal Water Community Recruitment



Private Well Water Community Recruitment



How was the project done?

- Individuals who agreed to participate were asked to go to a local clinic to have 20 cc's of blood drawn.
- They were also asked to answer a short phone questionnaire.
  - any work history at 3M and/or PFC production
  - current drinking water source and length of residence in the home
  - age, gender, ethnicity and general health status

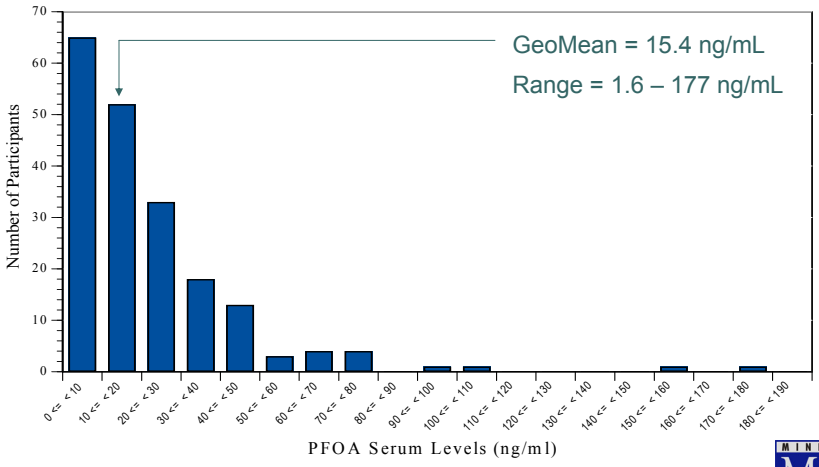
About the participants

Oakdale Municipal (N = 98)	**Mean**	**Range**
Age	53	25 – 85
Residence Time in House	18	4 – 62
Length of Time lived in Oakdale	21	3.5 - 62
Private Well Water (N = 98)		
Age	53	20 -86
Residence Time in House	20	4 – 60
Gender	**Average Age**	**Average Length of Residence**
Male (n=88)	54	19
Female (n=108)	53	19
3M Employment		
Worker (n=30)	59	21
Non Worker (n=166)	53	18

Results

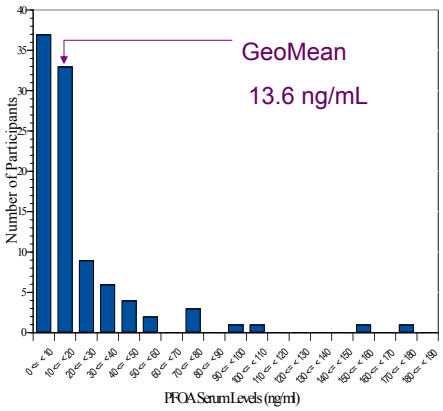
- 3 chemicals were found in all 196 participants
  - PFOA
  - PFOS
  - PFHxS
- PFBA was found in 55 people (28%)
- PFBS was found in 5 people (3%)
- PFHxA and PFPeA were not found in any participants (all below the LOD)

Distribution of PFOA in the East Metro Project Sample

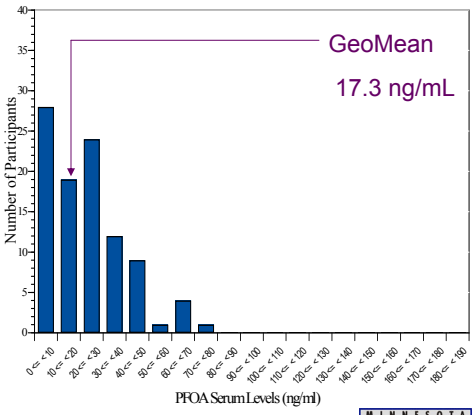


Distribution of PFOA in Private Well and Oakdale Municipal participants

Private Well Participants



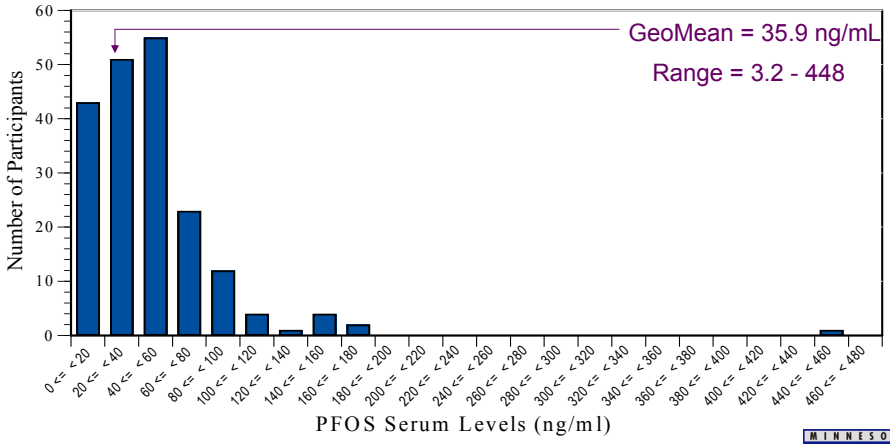
Oakdale Municipal Participants



PFOA: How do we compare to others?

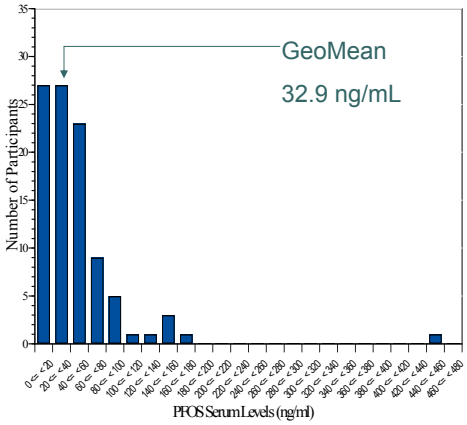
Study and Population (Sample size)	Time period	Geometric Mean ng/mL (ppb)	Range ng/mL (ppb)
E. Metro PFC Biomonitoring Pilot Project (N=196)	Oct 2008 – Jan 2009	15.4	1.6 – 177
US NHANES 2,094 individuals (age 12 to > 60) from a random sample of the US Population	2003 2004	3.9 (3.6 – 4.3)	0.1 – 77.2
Little Hocking, WV (N = 4,465) Community (age 0 to >70) exposed to PFOA contaminated drinking water	2005 2006	197	NA
Arnsberg, Germany 101 Males and 164 females from a community with known PFC water contamination	2006	Female 23.4 Male 25.3	Female 5.4 -99.7 Male 6.1 – 77.5
Occupational Group (N=215) 3M production workers	2000	1130	40 - 12700

Distribution of PFOS in the East Metro Project Sample

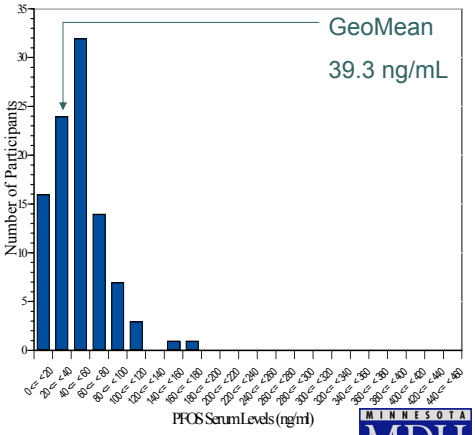


Distribution of PFOS in Private Well and Oakdale Municipal participants

Private Well Participants



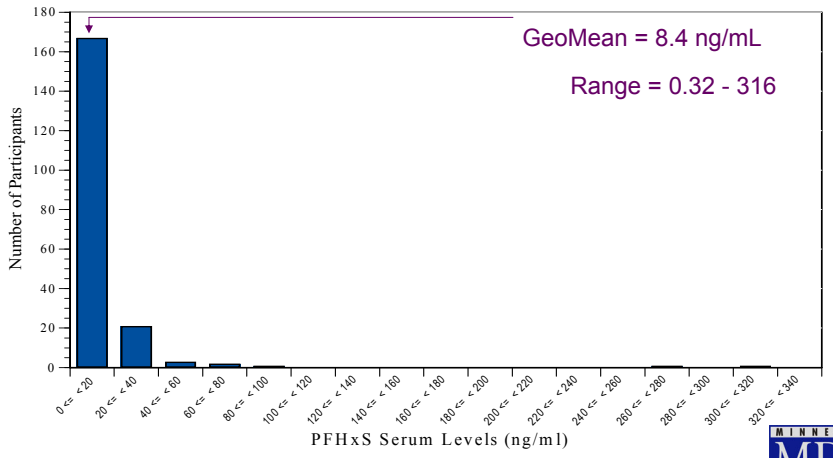
Oakdale Municipal Participants



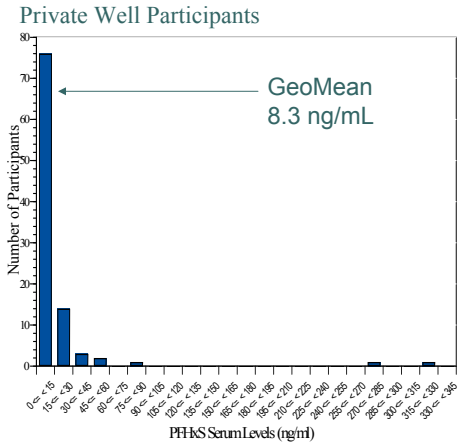
PFOS : How do we compare to others?

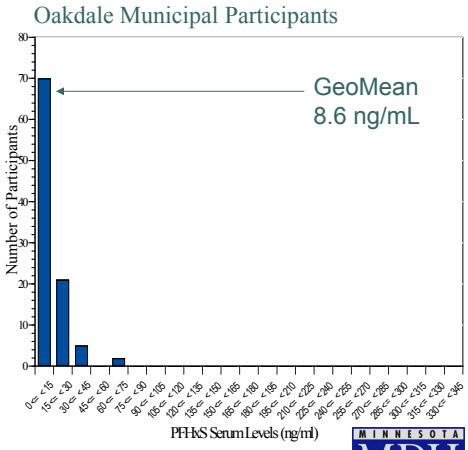
Study and Population (Sample size)	Time period	Geometric Mean ng/mL (ppb)	Range ng/mL (ppb)
MDH E. Metro PFC Biomonitoring Pilot Project (N=196)	Oct 2008-Jan 2009	35.9	3.2 – 448
US NHANES 2,094 individuals (age 12 to > 60) from a random sample of the US Population	2003 - 2004	20.7	0.3 – 435
Germany (N; Males = 101, females = 164) A random sample of individuals from an area with PFC water contamination	2006	Female 5.8 Male 10.5	Females 1.7 – 16.7 Males 2.7 – 36.2
Occupational Group (N=215) 3M production workers	2000	440	10 - 7040

Distribution of PFHxS in the East Metro Project Sample



Distribution of PFHxS Private Well and Oakdale Municipal participants





PFHxS: How do we compare to others?

Study and Population (Sample size)	Time period	Geometric Mean ng/mL (ppb)	Range ng/mL (ppb)
MDH E. Metro PFC Biomonitoring Pilot Project (N=196)	**Oct 2008 – Jan 2009**	**8.4**	**0.32 – 316**
US NHANES **2,094 individuals (age 12 to > 60) from a random sample of the US Population**	**2003 - 2004**	**1.9**	**0.2 - 82**
Arnsberg, Germany (Males = 101, females = 164) **A random sample of individuals from an area with PFC water contamination**	**2006**	**Female 1.1 Male 2.5**	**Females <0.1 – 1.1 Males 0.7 – 2.5**
Occupational Group (N=26) **3M production workers**	**2002 - 2004**	**NA**	**10 - 791**

Relationship of PFCs in blood with gender

(females = 108, males = 88)

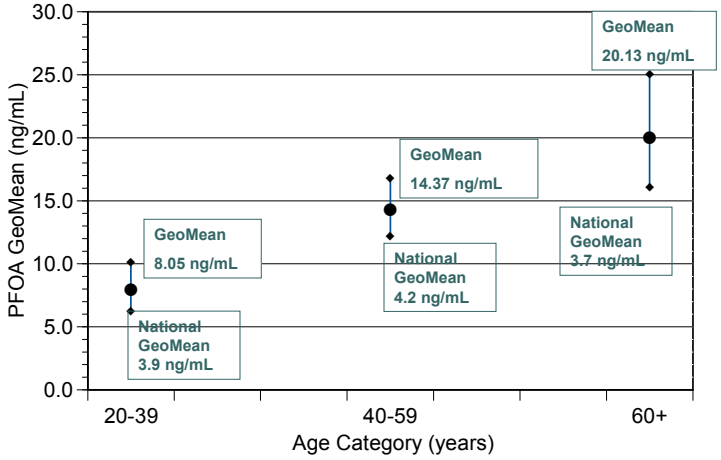
Variable of Interest	Means	P value
PFOA (geomeans, ng/mL)	Males 16.6 Females 14.4	.26
PFOS (geomeans, ng/mL)	Males 43.9 Females 30.5	.001
PFHxS (geomeans, ng/mL)	Males 10.6 Females 7.0	.004

Average blood levels are higher in men compared to women for PFOS and PFHxS.

Relationship of Age and Length of Residence with PFC levels

- We found a significant trend for increasing levels of PFCs with age for PFOA, PFOS, and PFHxS.
- Length of residence was found to be significantly associated with increasing blood levels of PFOA and PFHxS; not with PFOS.
- Age and length of residence are correlated, it is unclear how they impact each other when trying to predict PFC levels.

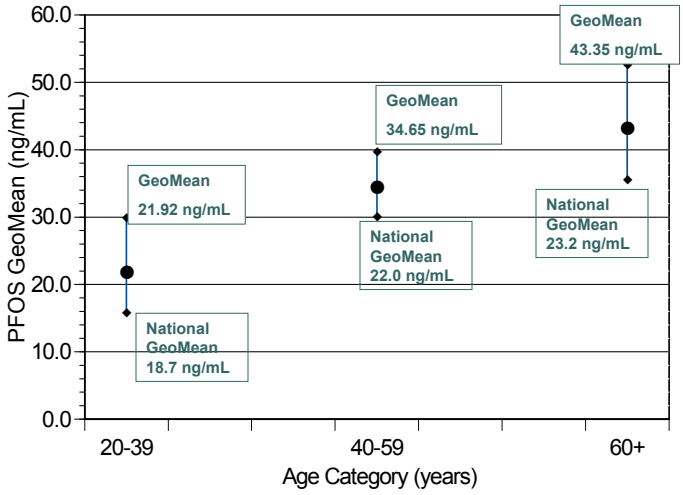
Relationship between Age and PFOA levels



Increasing age associated with an increase in PFOA serum level (ng/mL).

The geomeans are shown with their 95% confidence interval

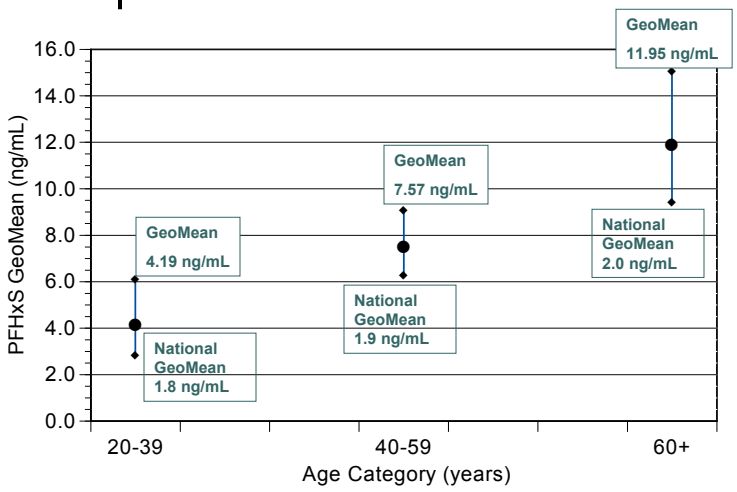
Relationship between Age and PFOS levels



Increasing PFOS level with increasing age. Those 60+ are significantly higher than those in the 20 – 39 category.

The geomeans are shown with their 95% confidence interval

Relationship between Age and PFHxS levels



Increasing age associated with an increase in PFHxS serum level (ng/mL).

The geomeans are shown with their 95% confidence interval

Analyses of Worker Status

(non-workers = 166, workers = 30)

Variable of Interest	Means	P value
PFOA (geomeans, ng/mL)	Workers 17.0 Non Workers 15.1	.52
PFOS (geomeans, ng/mL)	Workers 45.5 Non Workers 34.5	.07
PFHxS (geomeans, ng/mL)	Workers 12.4 Non Workers 7.9	.003

Average levels of PFHxS were higher for people who reported a history of working for 3M compared to Non-workers.

PFBA: How do we compare to others?

Study and Population (sample size)	Bio Specimen	Time Period	50th percentile	75th percentile	95th percentile	99th percentile	Minimum Value	Maximum Value
MDH E. Metro PFC Biomonitoring Pilot Project (N=196) Female (108) Male (88) Well Water Community (98) Municipal Water Supply Community (98)	Serum	Oct 2008 – Jan 2009	< LOD* <LOD* <LOD* <LOD* <LOD*	**.135** **.14** **.12** **.11** **.15**	**.68** **.68** **.42** **1.0** **.52**	**5.6** **5.6** **.53** **5.6** **8.5**	**< LOD*** **<LOD*** **<LOD*** **<LOD*** **<LOD***	**8.5** **8.5** **1.1** **5.6** **8.5**
Occupational Group (N = 28) PFBA and PFBS were measured in employees of the Cordova electronic materials factory.	Serum	2006	8.0	**NA**	**NA**	**NA**	**<0.5**	**56.7**
Occupation Group (N = 177) PFBA was measured in 177 former (127) and current (50) 3M employees from Washington and Dakota Counties.	Serum	Fall 2005 – Spring 2006	<LLOQ	**.5 - <1.0**	**2.0 - <3.0**	**5.0 - < 6.0**	**<LLOQ**	**6.2**

*LOD is the limit of detection = .10 ng/mL

**LLOQ is the lower limit of quantification = .5 ng.mL

PFBS: How do we compare to others?

Study and Population (sample size)	Bio Specimen	Time Period	50th percentile	75th percentile	95th percentile	99th percentile	Minimum Value	Maximum Value
MDH E. Metro PFC Biomonitoring Pilot Project (N=196) Female (108) Male (88) Well Water Community (98) Municipal Water Supply Community (98)	Serum	Oct 2008 – Jan 2009	**<LOD*** **<LOD*** **<LOD*** **<LOD*** **<LOD***	**<LOD*** **<LOD*** **<LOD*** **<LOD*** **<LOD***	**<LOD*** **<LOD*** **<LOD*** **<LOD*** **<LOD***	**.16** **.15** **.18** **.18** **.15**	**<LOD*** **<LOD*** **<LOD*** **<LOD*** **<LOD***	**.18** **.15** **.18** **.18** **.15**
Occupational Group (N = 28) PFBA and PFBS were measured in employees of the Cordova electronic materials factory.[10]	Serum	2006	**7.3**	**NA**	**NA**	**NA**	**0.5**	**128.0**
Occupational Group (N = 6) PFBS was measured in 6 3M employees to measure the half life of the chemical in the body.	Serum	June 2004 - December 2004	**363**	**NA**	**NA**	**NA**	**92**	**921**

*LOD is the limit of detection = .10 ng/mL

How strong is the correlation between blood and water levels?

Private wells were tested between 2005 and 2008 for the same 7 PFCs.

PFOA and PFOS were the only PFCs with a measurable level for greater than 50% of the private well community participants.

For non-detect levels of PFOA or PFOS, an imputed value of LOD/√2.

8 imputed values for PFOA
29 imputed values for PFOS

There was variation in the number of times a private well was sampled and at what frequency. To account for this variability two water measures were created:

1. the highest PFOA/PFOS level ever found in the water
2. the average PFOA/PFOS level found in the water

The average PFOA/PFOS measure was found to account for more of the variability in the water measures and now being used in water to blood PFC concentration models.

Limitations in comparing PFC water concentrations to blood concentrations

Blood PFC levels were measured in fall 2008 and winter 2009.

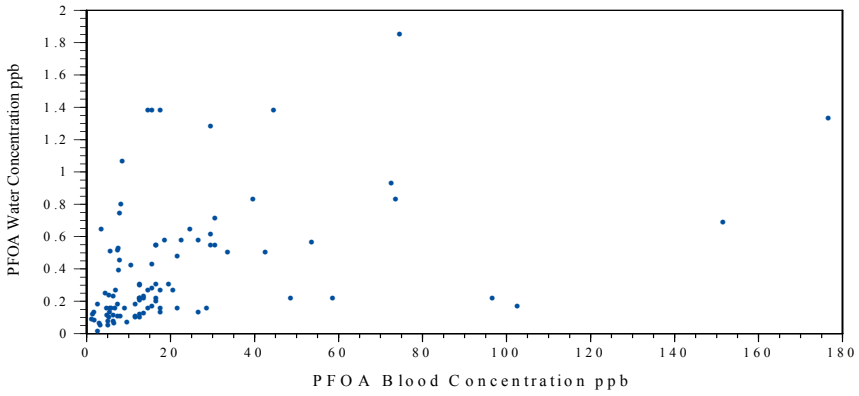
Water PFC levels were measured between 2005 and 2008.

The average number of months between the receipt of a water results letter (drinking water advisory) and a blood draw was 34 months (just under 3 years).

Assuming people stopped drinking the water, this lag in time limits our ability to measure the true association between PFC water levels and PFC blood levels.

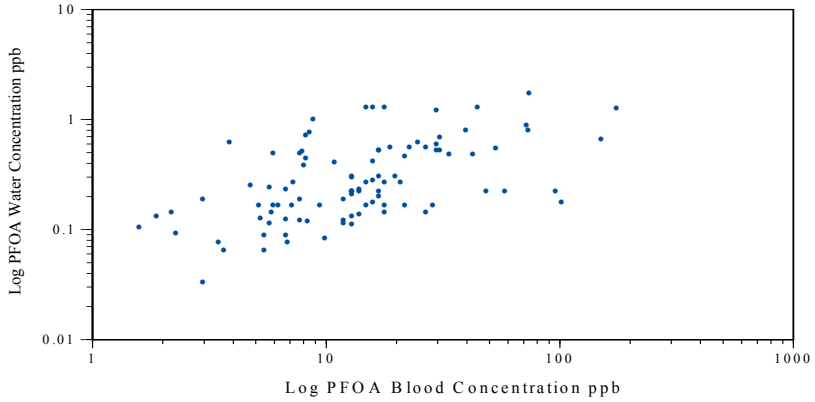
Relationship Between PFOA Water and Blood Levels.

N= 98 private well water drinkers

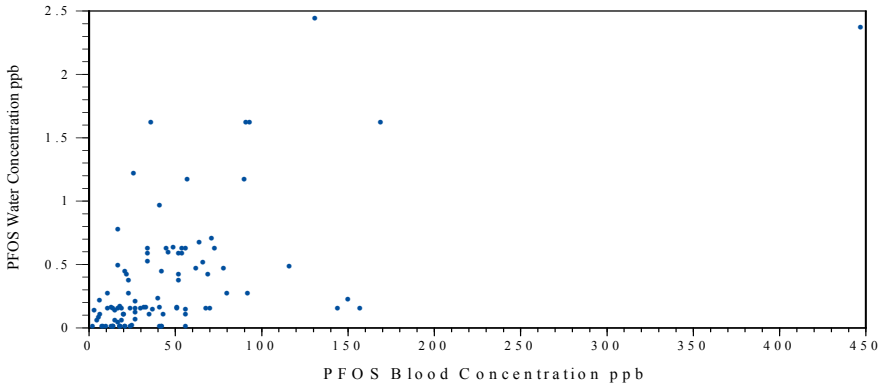


PFOA water to blood levels comparison (log transformation)

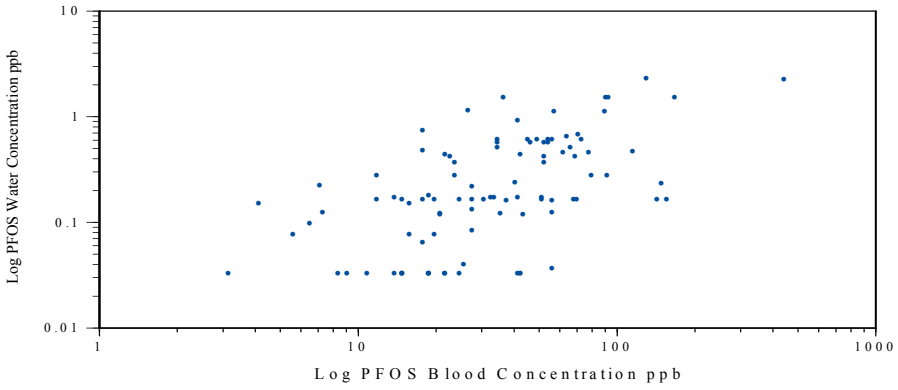
Both the blood and water PFOA concentration distributions were log normal – to correct for normalcy a log transformation was completed.



Relationship Between PFOS Water and Blood Levels.



PFOS water to blood levels comparison (log transformation)



PFOA blood to water ratio

(n=98 private well water participants)

Water PFOA level range: .035355 to 1.869 ppb
Average: .408758 Geomean: 0.29

Blood PFOA level range: 1.6 to 177 ppb
Average: 21.9 Median: 13 Geomean: 13.6

Depending on the measure of center we use:

- the median blood level divided by the average water level (Emmett's method) :
  13ppb/.41ppb = 31.7
- median blood level and geometric mean of water distribution (true measure of center for log normal distribution) and :
  13ppb/.29ppb = 44.8
- geometric mean for the blood level and for the water level:
  13.6ppb/.29ppb = 46.9

Limitations of the pilot project

Relatively small sample size limits the ability to compare subgroups of participants.

The pilot project does not include a local (Minnesota) comparison group collected in the same time period.

The pilot project is not able to identify the specific ways participants were exposed to PFCs.

The pilot project is not able to determine what illnesses were or may be caused by participants' exposure to PFCs.

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Benefits of the pilot project:

Individual participants received information about their own results and ways to reduce exposure.

We have learned how the exposed communities as a whole compared to the US general population, confirms prior assessment.

Community-level information helped inform recommendations for additional actions or follow-up.

- Advisory panel has recommended a follow-up to measure change in levels over time, expected to decrease.
- Calculate half-life.
- Case investigation of highly exposed individuals
- Improved exposure source assessment
- Demonstrate the efficacy of public health actions
- Health study was not recommended by MDH.
  - UM is conducting occupational studies.

MINNESOTA MDH DEPARTMENT of HEALTH

High Individual Serum Concentrations

- High PFOA (177 ng/mL) / High PFOS (448 ng/mL) – same individual
  - Male
  - 3rd age category (60+)
  - 2nd residential category (10 – 19 years)
  - Non-3M employee
  - Describes health as very good
  - Private well owner
- High PFHxS (316 ng/mL)
  - female
  - 3rd age category (60+)
  - 4th residential category (30+ years)
  - Non-3M employee
  - Describes health as good
  - private well owner

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Carin Huset, PhD
Louise Liao, PhD
Paul Swedenborg

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Tannie Eshenaur, MPH
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Rita Messing, PhD
Ginny Yingling, MS

EHTB Advisory Panel Members

EHTB Workgroup Members

East Metro Community Members and Legislators

References

1. Steenland K FT, Savitz D. Status Report: Factors Associated with PFOA Levels in a community surrounding a chemical plant. 2008.

2. Steenland K JC, MacNeil J, Lally C, Ducatman A, Vieira V, and Fletcher T. Predictors of PFOA Levels in a Community Surrounding a Chemical Plant. Environ Health Perspect. In Press ed. Volume In Press, 2009.

3. Calafat AM, Wong LY, Kuklenyik Z, Reidy JA, Needham LL. Polyfluoroalkyl chemicals in the U.S. population: data from the National Health and Nutrition Examination Survey (NHANES) 2003-2004 and comparisons with NHANES 1999-2000. Environ Health Perspect. 2007 Nov;115(11):1596-602.

4. Olsen GW, Mair DC, Church TR, et al. Decline in perfluorooctanesulfonate and other polyfluoroalkyl chemicals in American Red Cross adult blood donors, 2000-2006. Environ Sci Technol. 2008 Jul 1;42(13):4989-95.

5. Wilhelm M, Angerer J, Fromme H, Holzer J. Contribution to the evaluation of reference values for PFOA and PFOS in plasma of children and adults from Germany. Int J Hyg Environ Health. 2007 Dec 24.

6. Holzer J, Midasch O, Rauchfuss K, et al. Biomonitoring of perfluorinated compounds in children and adults exposed to perfluorooctanoate-contaminated drinking water. Environ Health Perspect. 2008 May;116(5):651-7.

7. Olsen GW, Burris JM, Burlew MM, Mandel JH. Epidemiologic assessment of worker serum perfluorooctanesulfonate (PFOS) and perfluorooctanoate (PFOA) concentrations and medical surveillance examinations. J Occup Environ Med. 2003 Mar;45(3):260-70.

8. Sakr CJ, Kreckmann KH, Green JW, Gillies PJ, Reynolds JL, Leonard RC. Cross-sectional study of lipids and liver enzymes related to a serum biomarker of exposure (ammonium perfluorooctanoate or APFO) as part of a general health survey in a cohort of occupationally exposed workers. J Occup Environ Med. 2007 Oct;49(10):1086-96.

9. Olsen GW, Burris JM, Ehresman DJ, et al. Half-life of serum elimination of perfluorooctanesulfonate,perfluorohexanesulfonate, and perfluorooctanoate in retired fluorochemical production workers. Environ Health Perspect. 2007 Sep;115(9):1298-305.

10. Olsen GW, Buehrer, B.D., Cox, R.L., Nunnally, M.C., and Ramm, K. H. Descriptive Analysis of Perfluorobutyrate (PFBA) and Perfluorobutanesulfonate (PFBS) in Sera Collected in 2006 from 3M Cordova Electronic Materials Factory Employees. St. Paul: 3M, 2007 July 30, 2007. Report No.: Epidemiology, 220-6W-08. 1 - 15 p.

PFC analyte correlations

Perfluorochemicals Pearson Correlation (R)	PFOA	PFOS	PFHxS
PFOA	1		
PFOS	.76 ($p < .0001$)	1	
PFHxS	.76 ($p < .0001$)	.81 ($p < .0001$)	1

Questionnaire Responses

Questionnaire Variable	**Responses:**						**N = 196**
Employment	**Yes**	**No**					
Have you ever worked at 3M?	30	166					
Ever worked in PFC Research?	3	27					
Ever worked in PFC production?	2	28					
Water	**Unfiltered Tap**	**Filtered Tap**	**Bottled**	**Other**			
What type of water do you typically drink?	86	66	43	1			
Filtration/Treatment	**None**	**Whole House Carbon**	**Bottled**	**Sink Carbon**	**Kitchen Faucet**	**RO**	**Pitcher Filter**
What type of water filter/treatment is used?	67	23	17	6	14	17	14
Ethnicity	**Non-H White**	**Non-H Black**	**Hispanic**	**Asian American**	**Native American**	**Other**	
How would you describe your ethnicity?	187	0	1	3	1	4	
Health	**Very Good**	**Good**	**Bad**	**Very Bad**			
How would you describe your health?	97	93	6	0			

Questions

Q. Helen Goeden: Before we get to questions, will you and Adrienne be on the phone when we get to the roundtable discussion?

A. Jean Johnson: Sure, we can do that.

C. Helen Goeden: Great, thank you. Any questions?

Q. Lynda Knobeloch: Thank you for excellent presentations. When did 3M stop producing these chemicals? And do you have any idea of what their half-life is in the human body?

A. Jean Johnson: It is my understanding that 3M stopped production in 2002. Regarding the half-life, Helen probably has this is on the tip of her tongue. We're thinking for PFOA it is 3.4 years.

A. Helen Goeden: It is 3.8 years for PFOA. PFOS is 5.4 years, and for PFHxS, it's almost 9 years. These are mean values.

Q. Lynda Knobeloch: Does this help to explain why you see the higher levels in the older age groups?

A. Jean Johnson: I would think so, yes. I think that plus the fact that they have been more likely to have been drinking that water for a long time and have had more time for that level to build up in the body.

A. Helen Goeden: Another thing that could contribute to that is because these are excreted through the kidney, if there are any limitations in renal function, which could be the case in older individuals, their elimination might not be as fast. But we really don't know. Those could be two explanations.

C. Gloria Post: Your study didn't include children, but the other studies that the data are coming out of—with a huge group of people in Ohio and West Virginia—show higher levels in older adults than younger adults and higher levels in children than younger adults also. So the results are similar for PFOA.

C. Helen Goeden: Right, the groups that seem to have the higher levels are the young and the old. Those could be for different reasons.

Chromium and Mercury Biomonitoring Studies

Alan Stern
New Jersey Department of Environmental Protection
(609) 633-2374
alan.stern@dep.state.nj.us

Visuals follow. Please contact the speaker for more information.

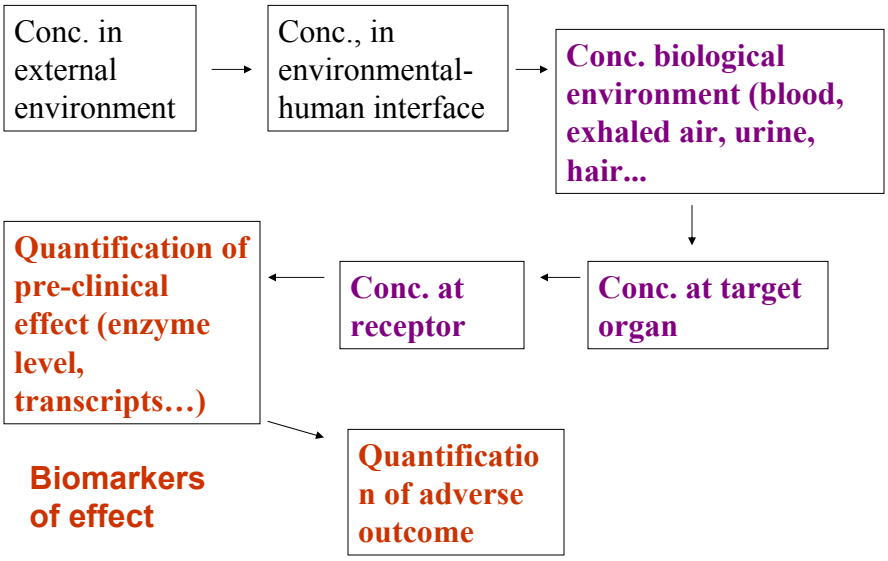
Biomonitoring has a number of important applications in environmental/public health. These include surveillance of status and trends in specific exposure of populations, focused studies of specific sources of exposure in populations at-risk, and construction of dose-response relationships for the derivation of Reference Doses and other standards and guidelines. Biomonitoring for chromium in conjunction with chromate production waste sites in Jersey City, New Jersey and the use of biomarker data from large-scale epidemiological studies to derive the Reference Dose for methylmercury (MeHg) and to estimate the population variability around that dose are presented as two examples of the utility of biomonitoring and biomarkers.

Chromium and Mercury Biomonitoring Studies

Alan H. Stern, Dr.P.H., D.A.B.T.
Office of Science
NJDEP

Biomonitoring 101

Biomarkers of exposure



Biomarkers of effect

- For MeHg and Cr, we have focused on biomarkers of **exposure**
  - as have most others

Uses of biomarkers of exposure

- Status and trends of populations with respect to specific exposures
  - NHANES
- Focused studies of specific sources of exposure
  - our studies of Cr exposure from chromate production waste in Jersey City
  - characterization of exposure parameters
    - who, where, associated factors

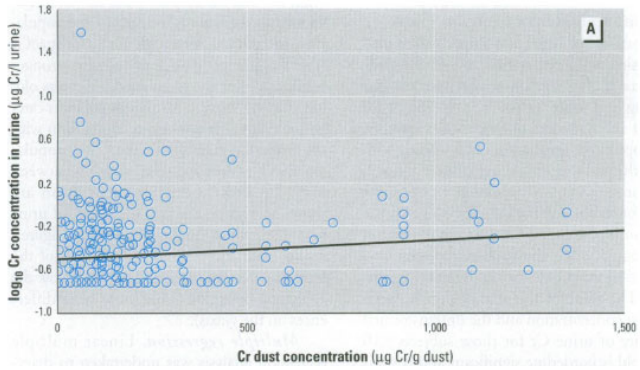
- Construction of dose-response relationships
  - dose defined through biomarkers of exposure and toxicokinetic models relating exposure/intake to biomarker levels
  - MeHg RfD from epidemiological studies of fish-consuming populations
  - IEUBK model for Pb

Cr biomonitoring in conjunction with house dust exposure assessment

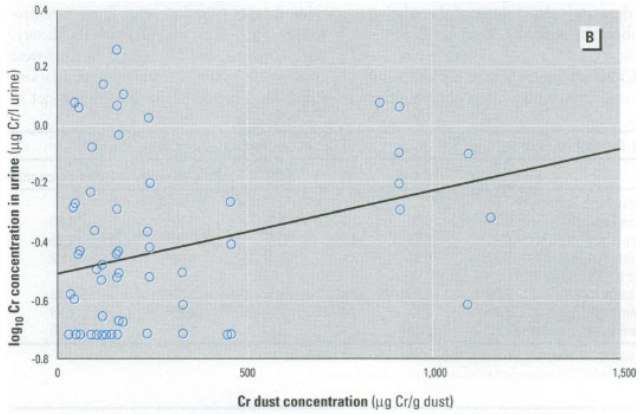
- ~ 160 chromate production waste sites located in Hudson County/Jersey City, NJ
  - Cr^{+6} and Cr^{+3}
    - risk is essentially related to Cr^{+6} exposure
- Studies of total Cr in house dust indicated increased concentration as a function of proximity to waste sites.
  - Now can measure Cr^{+6} in small mass house dust samples

- We combined total urine-Cr biomonitoring with house dust data from same locations
  - Cr^{+6} rapidly reduced to Cr^{+3} in body
    - urine Cr is Cr^{+3}
  - Cr^{+6} absorbed much more readily
  - Cr^{+3} is an essential trace nutrient
    - therefore, there is a dietary background of Cr in urine
    - in environmental (non-occupational) settings cannot generally distinguish dietary variability from environmental exposure

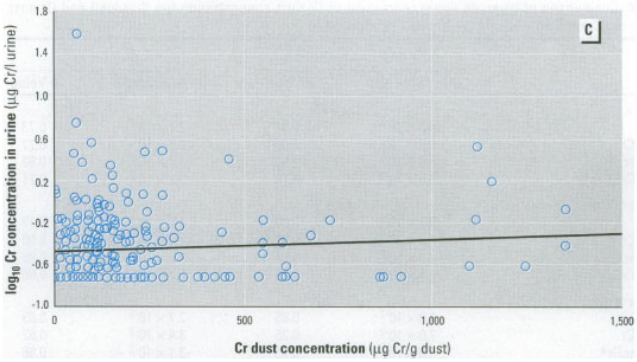
- However, can statistically compare urinary Cr in populations with differing characteristics
  - proximity to waste sites
  - age
- This discrimination is enhanced when a separate pedictor of exposure is used to focus biomonitoring data.
  - Cr concentration in household dust
  - Stern, AH et al. Environ Health Perspect. 1998 Dec;106(12):833-9



Total study population



Study population ≤ 10 yrs old



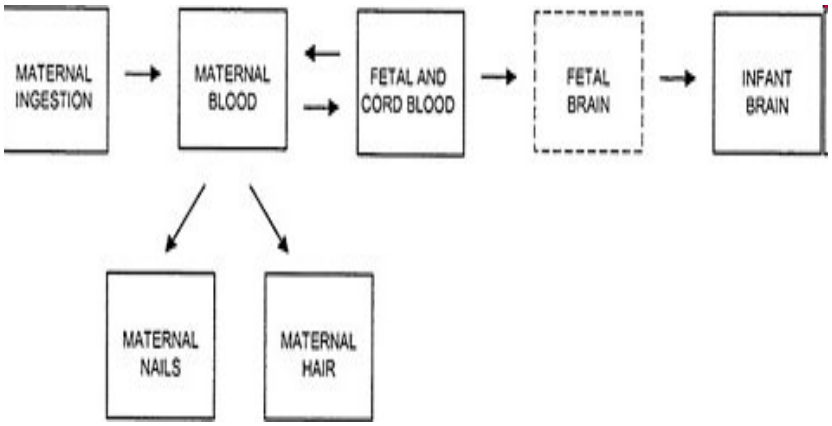
Population > 10 yrs old

- These data provided good evidence for actual exposure
  - previous "environmental sampling" data (house dust) only established the potential for exposure
  - biomarker data showed that those most at risk from exposure (based on location and age) were more likely to show signs of increaed internal absorption of total Cr
    - assumed absorption of Cr^{+6} contained in the totalCr

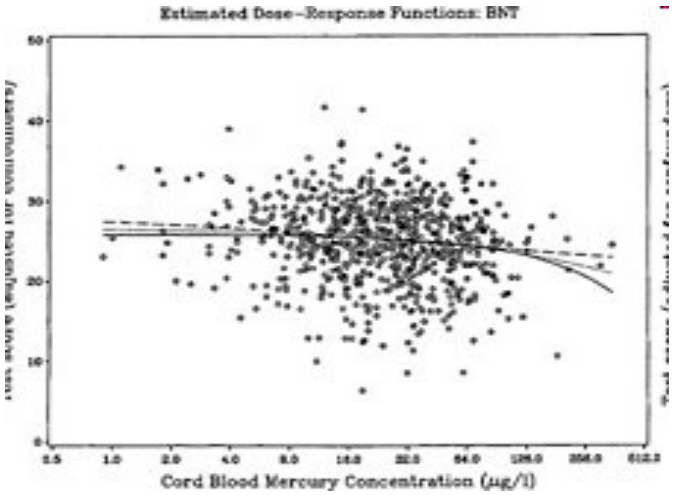
- Currenlty sampling Jersey City homes for **Cr^{+6}** in house dust and
- Sampling urine of children children in those homes
- Background of Cr^{+6} in house dust
  - including background//reference locations without crhomate production waste

Development and refinement of the MeHg RfD

Relationship among MeHg biomarkers and receptors

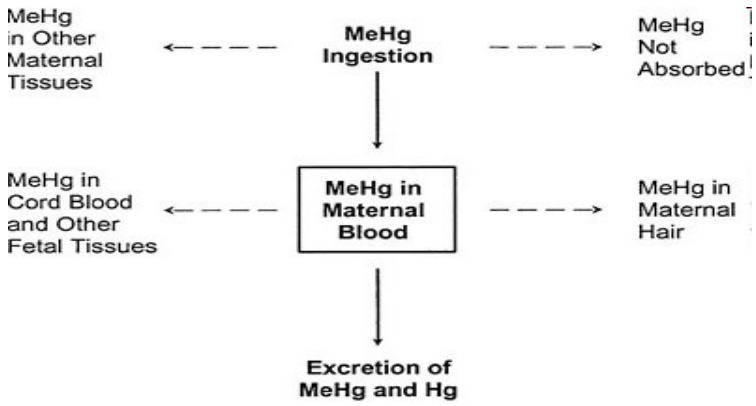


Key epidemiological studies included MeHg exposure biomarkers



- A critical dose (or point-of-departure - POD) was derived based on benchmark dose modeling
  - this gives a biomarker concentration (cord blood Hg)
  - but a dose is needed to derive an RfD

Dose conversion using a (one compartment) pharmacokinetic mode



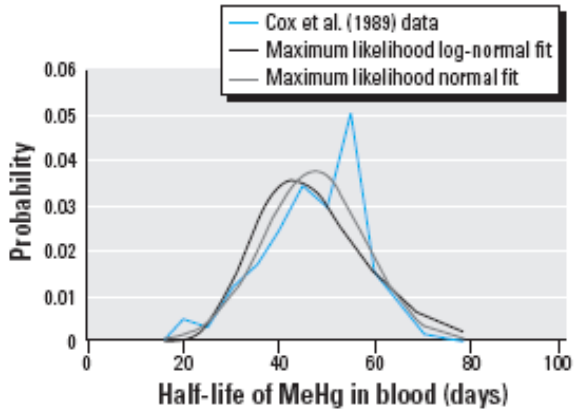
$$D = \frac{C \times (1/R) \times b \times V}{W \times A \times F}$$

Variability

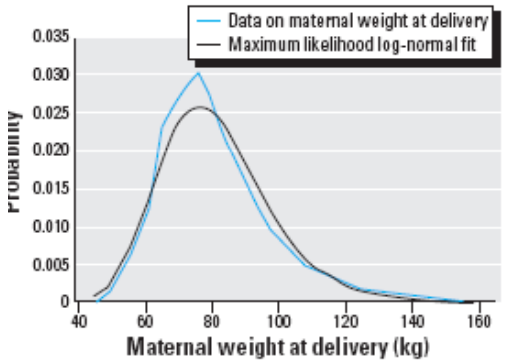
- If we use mean values to solve the dose-biomarker relationship, we only predict the relationship for the mean individual
- There is significant variability in each of the variables in the model

Stern AH.
Environ Health Perspect. 2005 Feb;113(2):155-63

For example - half life in maternal blood during pregnancy



Maternal body weight at delivery



Overall variability can be estimated using probabilistic (Monte Carlo) analysis

Table 4. Model output of selected percentiles of the maternal intake dose of MeHg corresponding to 58 µg Hg/L cord blood.

Distribution of maternal MeHg intake dose (percentile)	Maternal intake dose (µg/kg/day)
Mean ± SD	0.993 ± 0.702
1st	0.202
5th	0.301
10th	0.373
50th	0.812
50th/5th	2.700
50th/1st	4.020

Questions

Q. Gary Ginsberg: Do you have any sense of how variable the chromium background exposure in the diet is? What are the major sources of trivalent chromium in the diet? Is there any background biomonitoring data for trivalent chromium in urine that would represent the noise in background populations?

A. Alan Stern: One of the things we did when we did this work—and the New Jersey DOH did it on an even larger scale—is that they tried to construct a regression model for chromium levels in urine. We and they asked the study participants whether they drank beer in the last 48 hours, ate cereal, ate bread, exercised, smoked, and so forth. Although the literature suggests that grains are a significant source of dietary chromium, in fact nothing came out as a good predictor of chromium except for age and sex. So, the conclusion is that dietary chromium comes from lots of different diffuse sources, and there's no major source of background chromium in the diet.

A Pilot Study of the Endocrine Disruption and Inflammatory Effects of Environmental Toxicants on Fetuses

David Rich
University of Medicine and Dentistry of New Jersey
School of Public Health
(732) 235-4664
richda@umdnj.edu

Visuals follow. Please contact the speaker for more information.

Phthalates are used in many products that are ubiquitous in the urban environment, including lubricants, cosmetics, construction materials, wood finishers, adhesives, floorings, and paints. Di(2-ethyl-hexyl) phthalate (DEHP) is commonly used as a plasticizer in medical devices and building materials, increasing flexibility. CDC researchers found elevated levels of mono-(2-ethylhexyl) phthalate (MEHP), the primary monoester metabolite of DEHP in humans, in urine samples from a randomly selected US cohort, as reported in their 3rd National Report on Human Exposure to Environmental Chemicals. Recently, we reported that levels of several phthalates were elevated in amniotic fluid, maternal urine, and maternal blood collected at birth. Our group has also found that hospitalized infants excrete much higher concentrations of phthalates (MEHP, mono-(2-ethyl-5-hydroxyhexyl) phthalate [MEHHP], and mono-(2-ethyl-5-oxohexyl) phthalate [MEOHP]) in their urine than in a US population sample. Phthalates have been reported as developmental and reproductive toxicants in experimental animals, with observed anomalies including reduction in androgen-dependent tissue weights, and malformations of the external genitalia such as hypospadias. Males exposed prenatally to phthalates may have decreased anogenital distance (AGD), penile volume, and scrotal size, as well as increased incidence of incomplete testicular descent. Exposure to phthalates has also been associated with spontaneous abortion and preterm delivery in animal studies. Given that the complications of prematurity are associated with substantial morbidity, mortality, and health care costs, it is important to identify environmental exposures that may increase the risk of such outcomes. The primary mechanism triggering the onset of preterm labor is increased inflammation and the production of cytokines. In this regard, phthalates are known to induce inflammatory activity in maternal neutrophils and lymphocytes. DEHP and MEHP bind to the transcription factor PPAR-γ, potentially blocking important anti-inflammatory pathways and resulting in prolonged inflammation and cytotoxicity.

Adverse reproductive effects have been observed following exposure to other common environmental toxicants as well. Bisphenol A has been associated with endocrine effects in the fetus. Its metabolite, bisphenol A diglycidyl ether, blocks PPAR-γ, suggesting that it might interfere with the resolution of inflammation in the fetus and newborn. Previously, our research group also found high levels of perchlorate in several maternal/fetal compartments including maternal urine. It is plausible that adverse outcomes, including prematurity, represent non-specific vulnerabilities in the fetus, and that diverse environmental toxicants may disrupt normal pregnancy and development by similar mechanisms.

The ongoing pilot study described herein is designed to validate the methods and endpoints required to implement fully-powered analyses on the reproductive effects of these toxicants. We are quantifying maternal and fetal exposures to phthalates and other common environmental toxicants in a high-risk obstetrical population (i.e. with high rates of preterm delivery). We will assess whether these exposures are associated with increased risk for preterm delivery in this population or with higher incidence of alterations in genital development, such as increased

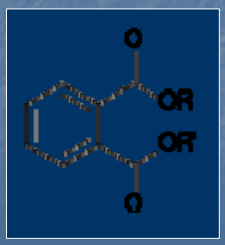
AGD, in the neonates. We also will determine whether prenatal exposure to these toxicants is associated with altered inflammatory function.

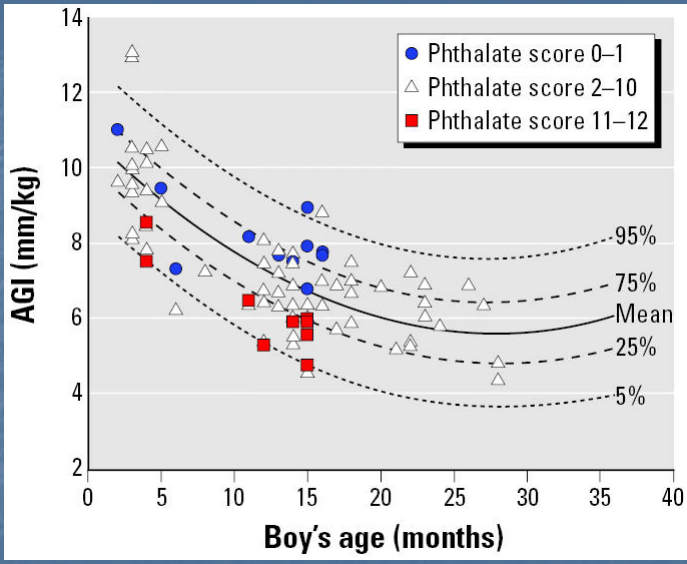
Pilot Study of the Endocrine Disruption and Inflammatory Effects of Environmental Toxicants on Fetuses

David Q. Rich, Sc.D.

Phthalates

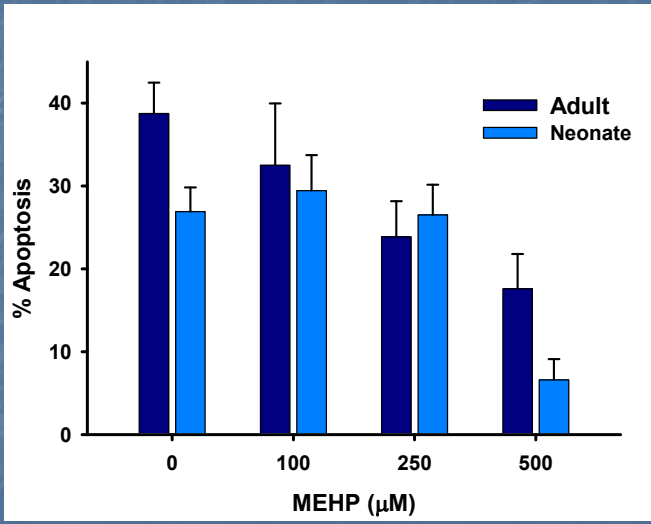
- Di (2-ethyl hexyl) phthalate (DEHP) is the only FDA-approved plasticizer for medical use.
- Flexibility, durability,broad range temperature stability and optical clarity to polyvinyl chloride (PVC) medical devices.
  - IV catheters, tubing, bags and bottles.
- Phthalates are be easily released from medical devices
- In humans DEHP is rapidly metabolized to its derivatives, including mono(2-ethyl hexyl) phthalate (MEHP)



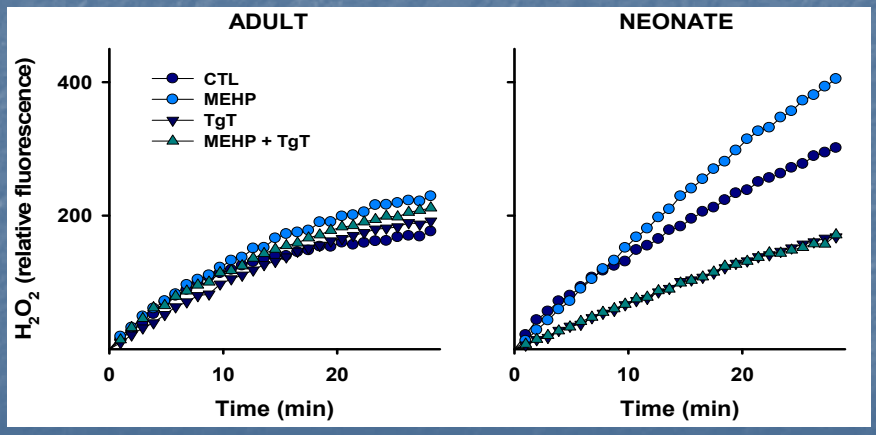


Swan et al., *Environ Health Perspect.* 2005; 113:1056–1061

MEHP inhibits neutrophil apoptosis.



MEHP stimulates H_2O_2 production in neonatal neutrophils



Perinatal Exposure to Perchlorate, Thiocyanate, and Nitrate in New Jersey Mothers and Newborns

BENJAMIN C. BLOUNT,[*,†] DAVID Q. RICH,[‡,§] LIZA VALENTIN-BLASINI,[†] SUSAN LASHLEY,[‡] CANDE V. ANANTH,[∥] EILEEN MURPHY,[⊥] JOHN C. SMULIAN,[‡,#] BETTY J. SPAIN,[†] DANA B. BARR,[†] THOMAS LEDOUX,[⊥] PAROMITA HORE,[§,▽] AND MARK ROBSON[‡,§]

Division of Laboratory Sciences, Centers for Disease Control and Prevention, Atlanta, Georgia, Department of Epidemiology, UMDNJ-School of Public Health, Piscataway, New Jersey, Environmental and Occupational Health Sciences Institute, UMDNJ-Robert Wood Johnson Medical School and Rutgers University, Piscataway, New Jersey, Division of Epidemiology and Biostatistics, Department of Obstetrics, Gynecology, and Reproductive Sciences, UMDNJ-Robert Wood Johnson Medical School, New Brunswick, New Jersey, New Jersey Department of Environmental Protection, Trenton, New Jersey, and Division of Maternal-Fetal Medicine, Department of Obstetrics and Gynecology, Lehigh Valley Health Network, Allentown, Pennsylvania, Department of Entomology, School of Environmental and Biological Sciences, Rutgers, The State University of New Jersey, New Jersey

Perchlorate is a commonly occurring environmental toxicant that may be transported across the placental barrier by the sodium-iodide symporter (NIS), possibly resulting in both increased perchlorate exposure and decreased iodide uptake by the fetus. Therefore, we measured levels of three physiologically relevant NIS-inhibitors (perchlorate, nitrate, and thiocyanate) and iodide in maternal and fetal fluids collected during cesarean-section surgeries on 150 U.S. women. Geometric means of perchlorate, thiocyanate, and nitrate levels in maternal urine (2.90, 947, and 47900 μg/L, respectively) were similar to previously published results, while urinary iodide levels (1420 μg/L) were significantly higher ($p < 0.0001$), likely because of prevalent prenatal vitamin use in the study population (74%). Thiocyanate levels were higher in the maternal serum, cord serum, and amniotic fluid of smokers compared to women with environmental perchlorate levels were positively correlated with perchlorate levels in amniotic fluid ($r = 0.57$), indicating that maternal urine perchlorate is an effective biomarker of fetal perchlorate exposure. Maternal serum perchlorate was generally higher than cord serum perchlorate (median ratio 2.4:1 for paired samples), and maternal urine perchlorate was always higher than fetal amniotic fluid perchlorate levels (mean ratio 22:1); conversely, iodide levels were typically higher in fetal fluids compared to maternal fluids. We found no evidence of either disproportionate perchlorate accumulation or lack of iodide in the fetal compartment. In this panel of healthy infants, we found no association between cord blood levels of these anions and newborn weight, length, and head circumference.

Environ. Sci. Technol. **2009**, *43*, 7543–7549

Study Design
PREGNANCY CLINIC VISITS

- Women followed clinically at RWJ High Risk Obstetrics Clinic (Target n=200)
  - >18 years of age
  - Singleton pregnancy
  - Informed Consent
- Urine collected at each visit
  - EOHSI Analyses
    - Phthalate DEHP Metabolites (11)
    - Bisphenol A + 2 metabolites
  - CDC
    - Perchlorate
    - Nitrate
    - Thiocyanate

Study Design
BABY DELIVERY

- PHYSICAL EXAM (WITHIN FIRST DAY OF LIFE):
  - Anogenital distance
  - Testicular size
  - Hypospadias
  - Penile length
  - Testicular descent
  - Malformations of genitalia
- MEDICAL RECORD REVIEW
  - Body size measurements
  - Gestational Age
- UMBILICAL CORD BLOOD COLLECTED AT BIRTH
  - Respiratory burst activity
  - Cytokine production

Progress to Date

- N=71 mothers recruited/consented
  - 2 later declined participation
  - 2 fetal deaths
  - 1-10 urines per mother (Mean=3.5)
- N=47 deliveries
  - n=31 with cord bloods collected
    - n=17 with Amplex Red analyses done
    - n=14 delivered at night when laboratory not open to process samples
  - N=16 not collected because:
    - HIV positive
    - Cord blood donated/stored
    - Emergency C-section, Premature rupture of membranes, rupture during delivery = loss of blood
  - n=47 with physical measurements made and medical records reviewed
  - n=39 <37 weeks gestational age at recruitment
    - n=17 preterm delivery (44%)

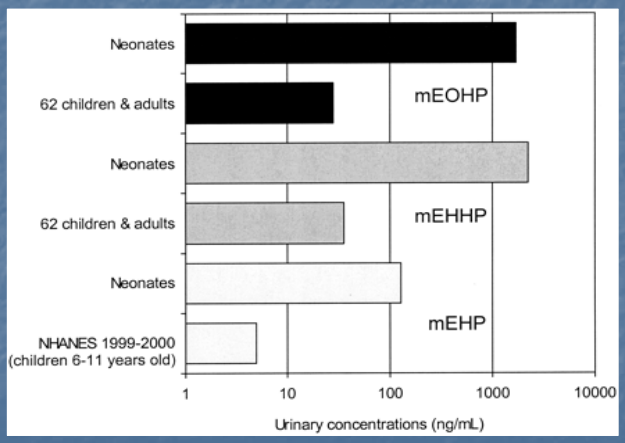
Lessons Learned

- Improved mechanisms of delivery coverage
  - Cell phone
  - Nurse approval
  - Logistics in delivery room space
  - At least daily review of NICU and delivery status logs
- Change in laboratory doing analyses of phthalates, bisphenol A
  - Urine collection and storage
- Reasons for non-consent
  - Spanish speaking mothers (perhaps cultural reasons)
  - Fear of being part of research
  - Want individual results

Where are we going?

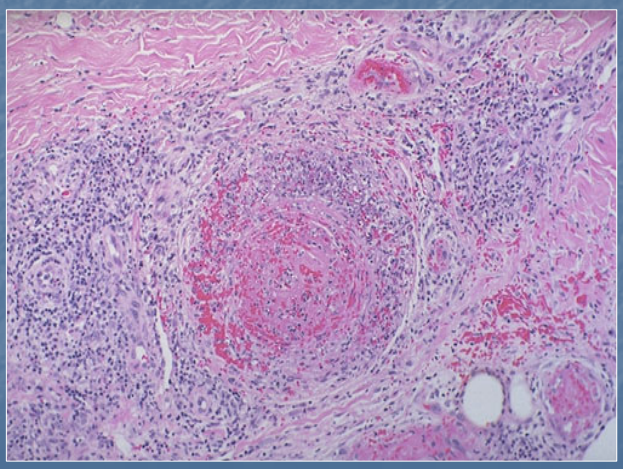
Neonatal Exposure to Phthalates

Exposure to Phthalate in NICU

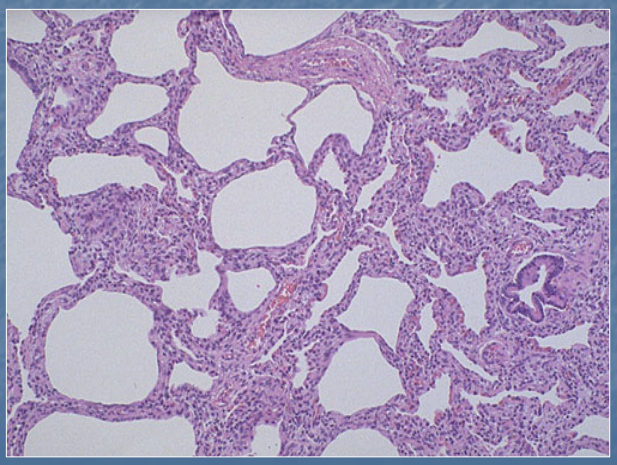


Calafat et al., Pediatrics 113: e429 - e434, 2004.

Inflammation



Bronchopulmonary Dysplasia



Acknowledgements
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- Sana Azhar
- Faith Archer
- Alan Stern
- Ben Blount
- Marlene Schwebel

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Questions

C. Virginia Thompson: I just wanted to let you know in case you didn't, that there is some good news. The major producers of plastic tubing for neonatal intensive care units (NICUs), in particular, are not using di (2-ethyl hexyl) phthalate (DEHP) anymore, generally speaking. So, it is working its way through. The group purchasing organizations aren't really purchasing it anymore.

C. David Rich: Right, but I think there's still existing systems there and that's kind of been the problem there at Bristol-Myers Squibb too in Barry Weinberger's division. There's such a backlog there.

Q. Gloria Post: For the newborns, most of the things you were looking at applied to males, so is there anything for females? Are you going to be studying anything for the girl babies?

A. David Rich: First the inflammatory effects that we are talking about in terms of body size measurements are obviously for both boys and girls. The data I've shown on anogenital index was in boys. It has also been done in girls. I don't know if it is as quite as validated there. I'm not the expert on that nor would I want to comment on that. Barry Weinberger was somewhat convinced that you could do both in boys and girls, certainly not hypospadias and testicular descent though.

Q. Gary Ginsberg: Are you doing any survey information of these women on the use of their products? Shanna Swan's data suggest that it is coming from personal care products.

A. David Rich: I actually met with Shanna Swan last week, and we talked a long time about this. She is now talking more about food. I always learn more every time I talk to her. We have a series of questionnaires based on some of what Marija Borjan had presented. Marija was involved with that first study. It was based on some of that where you are collecting all kinds of information, not only about the moms and their habits but also as you think about pathways and such. Again the study isn't necessarily designed to evaluate and differentiate between different pathways. It's just a pilot study in a sense, but in a larger study, what you are suggesting is probably very important and that would certainly want to be developed further. I agree that is certainly an important piece.

C. Perry Cohn: Any questions for the previous speakers from the phone participants? Hearing none, I have a couple of questions or actually comments. Maybe people can just comment briefly. Certainly one of the things that's important with some items and maybe more or less important is noting time of day and season for some of these measurements. Certainly, once it gets into reproductive outcome stuff, hormone stuff, a number of things can certainly change. I don't know whether all the various things that people are looking at are variable that way but certainly NHANES, for instance, does include time of the day of the blood draw, sample collection, and so on.

The other question is about nonparticipants. I noticed for instance in the perfluoroalkyl work that was done in Minnesota, that they did have a winnowing of the number of people who were involved. There was random sampling, then eligibility, then nonresponses, and so forth. I think it's important for people to be able to try to come up with some sort of answer if only age and gender or something like that to the extent that they can about what the likely characteristics of

the nonresponders are. Because of course, selection bias can potentially play a big role in some things. Maybe it plays a role and maybe it doesn't, but it's important to try to address that, that people who respond might have very special characteristics. This is one of the important early lessons one gets when studying epidemiology.

Application of Biomonitoring Results to Risk Assessment
Round Table Discussion

Q. Gary Ginsberg: Are we jettisoning the panel discussion?

A. Perry Cohn: Yes, just because we are running late, but if you have a specific question or comment.

Q. Gary Ginsberg: I have a general question. In Connecticut we would love to get involved in biomonitoring and what we've seen this morning is an array of studies that range from status and trends, general population, NHANES-type at the state level versus very specific projects. I'm just wondering in terms of funding mechanisms, what are you more likely to get funded for? Would it be an NHANES-type of project or a specific, small, pilot project? What's the money responding to these days? Where's the money?

C. Perry Cohn: I'm not sure I have the answer. If anybody on the phone or in the room cares to comment on that, that's a good question.

C. Alan Stern: You're probably aware that about 4 years ago now, NIEHS had a proposal for states to do large-scale biomonitoring projects. We put in what we thought was a really good proposal but they didn't seem to think so.

C. Gary Ginsberg: I think 3 states got funded out of 35 that applied.

C. Alan Stern: So, if it hasn't happened with the stimulus money now, I don't see anything on that scale happening again in the foreseeable future. As for the smaller-scale focused projects, we've funded our own project for that. Maybe if you have any extra money in Connecticut…

C. Gary Ginsberg: That's why I'm asking.

C. Jim Blando: I have a quick comment about the background concentrations of hexavalent chromium. We've dealt with some of the manufacturers in the commercial staining processes that use chromic acid. One of the other sources where we've seen it is in pigments and tiles, and especially in the mortar that goes between the tiles, especially the green color is often a chromic oxide.

C. Alan Stern: That is something we hadn't come across. That's really interesting. What we found was that when we saw high levels, high in this case being over 20 ppm in the household dust of hexavalent chromium, it was without exception on wood surfaces. What we found was when there was construction or renovation in the house, it didn't seem to affect the hexavalent chromium levels, which was also a bit of surprise because we know that there is hexavalent chromium in cement and in drywall. But, that is a good thing to keep in mind. Thanks.

Overview Talk: High Throughput Testing/Genomics in Toxicology and Risk Assessment

Helmut Zarbl
Robert Wood Johnson Medical School
University of Medicine and Dentistry of New Jersey
(732) 445-2354
zarbl@eohsi.rutgers.edu

Please contact the speaker for more information.

Questions

C. Bob Howd: I was confused as to why you were talking about thresholds and uncertainty factors for carcinogens because that's not the way we treat carcinogens.

A. Helmut Zarbl: That shows my naïveté. I'm not a risk assessor. I know that you do the slope of the curve and then you determine the one-in-a-million cancer risk, so maybe that slide isn't appropriate. But I think that the point is still taken that it gives us data in that region where we are modeling now.

C. Bob Howd: That's used for noncarcinogens.

Q. Alan Stern: My apologies in advance because this is I guess more of a rhetorical question than an information question. From a very basic biological standpoint, why would we necessarily assume that a toxic endpoint, given the potential for interacting systems at a higher biological level, why would we necessarily expect that a toxic response would be underlain by a transcriptional action or, for that matter, that a transcriptional effect would necessarily lead to a toxic response? Even if one could draw a line between a transcriptional event and ultimately a toxic response, my sense is that there would be many, many forks in the road between those. And how do you know which fork in the road that the response is actually following?

A. Helmut Zarbl: At the beginning of my talk, I said that one of the problems was distinguishing between the adaptive response and the toxic response. We know from the work of Swenberg, for example, that you could measure DNA adducts well below a no observable transcriptional effect level (NOTEL). So the cells are still being damaged. So another argument is that you could use DNA adducts, and certainly if you believe that all DNA adducts are mutagenic and carcinogenic, you could do that. My assumption is that if we do enough of these, and we don't know how to interpret adaptive from toxic yet, but if you can say that at this dose I started seeing apoptosis, DNA repair, that means that the cell knows that it has been damaged and that it is responding. So, it's just a biological point where there's enough damage to the cell that it's responding to it. That can be very far below the point where you get liver cell death or whatever. Maybe I'm completely off base but, as a microbiologist, I see that as real biological data in an area where we currently don't collect data. You could take the safest route and just say at the point where there is any change in DNA expression, that's where you start your point-of-departure modeling, for example. That's my naive assumption about risk assessment.

Q. Gloria Post: So, the studies in the animals avoid this problem but—maybe you said this quickly—but the studies in cell lines really don't take into account metabolism and kinetics. And those are some of the issues. Is that right?

A. Helmut Zarbl: That's one of my big problems with the Toxicology in the 21st Century vision is that it says that we are going to move completely to human cell lines, which I think there are so many problems with that, that I don't believe it is going to work, at least not in the near term. There are all kinds of problems with toxicodynamics. There are modes of action that don't exist in the cell line, how many different cell lines do you need, and on and on. I could write a book on what's wrong with that vision, but if you throw enough money at it and you do it long enough, maybe it will be better than the Ames test. I don't know. The studies need to be done in vivo. We've done them, and Rusty Thomas has done some really elegant studies at the Hamner

Institute of Health Sciences using a similar thing. And I see similar data, anchoring it to different blood and liver biomarkers. So far, it doesn't appear to be an in vitro phenomenon.

Q. Gloria Post: We usually don't have this type of data with controlled exposures to people and effects or else we wouldn't be using animals. So we would still need to apply some uncertainty factors for the interspecies, even using your NOTEL approach to extrapolate to humans from animals.

A. Helmut Zarbl: This could be done in humans. Most of these studies have always been done with drugs in the pharmaceutical company. The argument is of course that drugs are borderline toxicants. You want a physiological response, so you're actually poisoning the cells, so you are seeing a big response. For environmental toxicants, it's going to be much lower. I think that's a question of how low can you actually go down and actually see it, and can you actually do measurements in humans at sort of occupational or ambient levels?

Q. Gloria Post: For the ones where we do have only animal data, which we will for some I'm sure, would we still need to apply uncertainty factors to account for interspecies variability?

A. Helmut Zarbl: In the interim, yes. But, if we can actually look at some of these exposures in populations, we might be able to get around that as well.

Q. Lynda Knobeloch: We actually did GenoArrays and PBDE blood measurements in 44 volunteers, and we can see associations between gene expression and PBDE levels. But we don't know what those genes do.

A. Helmut Zarbl: One of the arguments is that you don't really need to know them, that they are just biomarkers. So the fact that this panel of gene changes shows that there is a response. You don't really need to know that. Of course we'd like to get to the mode of action. That might be a dose phenomenon. It might be at the lower doses, you're changing things. The cell is just repairing itself, and it's not until the higher doses where you are getting adverse toxicity where you actually start seeing apoptosis and DNA repair and those types of things. So, we have a lot to learn but I think it's a promising area.

C. Lynda Knobeloch: With the GenoArrays, we were very excited that they could just see a difference.

Q. Gary Ginsberg: I have some of the same reservations that other people on this side of the room have expressed in terms of NOTELs for transcribed genes for genotoxic carcinogens and how one would use that for quantitative low dose risk assessment. You were mixing uncertainty factors in with low-dose approaches, which we don't really do. My question is more on the estrogen side. You mentioned a few slides about that. There's all this George Daston et al. work on this with EPA, and their transcriptosome dose responses and their claims that the effect goes away and that we don't have to worry so much about nonmonotonic dose-response on the transcriptosome level. What is your response to that, relative to the other data that you've seen on estrogens?

Q. Helmut Zarbl: You mean with endocrine disruptor-type?

Q. Gary Ginsberg: Yes, the endocrine disruptor, the estrogen dose-response, is it monotonic, nonmonotonic? Do you see a threshold? What is your take on their data with EPA versus other things that you've seen?

A. Helmut Zarbl: I haven't thought about that very carefully. I think the data are interesting, but I'm not sure what they mean. The data are monotonic for estrogen, I think. For the endocrine disruptors, you start getting interactions because they compete with one another and they bind to different estrogen receptors. So, it gets pretty complicated. I think it will take some more work to tease that out.

Q. Bob Howd: For the changes that you were talking about in the individual genes on the chips, you're measuring that as a dichotomous variable, aren't you? How does that work with regard to how much on-off?

A. Helmut Zarbl: We're not measuring on-off.

Q. Bob Howd: What amount of lighting up is the threshold for being able to notice the change in the gene?

A. Helmut Zarbl: Basically, the amount of the DNA that hybridizes to a tile on the chip is dependant on how much is in the solution that you're adding. Actually, for the new generation of chips, that's linear over 5 or 6 orders of magnitude. So, you are not actually getting an on-off, you're getting actually a value. So, it's a quantitative output. That's the beauty of it in terms of analysis. You can actually see a dose-response.

Q. Irene Dooley: I was wondering about individual variation. Wouldn't it take a lot of data from many individuals and many different genomes to be able to correlate for sensitive subpopulations and keep that data public?

A. Helmut Zarbl: Bingo. And that's why I said this stuff is not ready for primetime. As we start doing these things, we start seeing the variability, and that impinges on how you interpret the data. Unless you have, for each person or each sample, a transcriptional response, you also need to have their genotype to say that this is due to genotype and now also probably some epigenetic phenotype for the cell type that you're looking at. So the idea that this is going to completely replace toxicity testing using human cell lines, I'm very skeptical of that. I know EPA has kind of adopted it as their baby, but I think that they are going to run into a lot of problems. I could make a list as long as from here to the end of the room of reasons why it won't work, but it might work, who knows.

Q. Irene Dooley: How much does one of those chips cost? Are they over a $1,000?

A. Helmut Zarbl: For example, for an AlphaMetrix expression array, when they first came out, one chip was $12,000. Now we can get them for a reduced price of about $200. It's actually the processing and the analysis of the data that's more expensive now than the actual chips are. The chips are produced by photolithography so once they get going, it's like making computer chips, the costs just go down exponentially.

Q. Ed Ohanian: On one of your slides, you had a statement saying that the actual regulators are slow to accept change. You also had another statement about the model still needing to be

validated. You know what happens with regulators when you say that the model hasn't been validated, they will never accept it. Is this something that we can go ahead and say this is the prime time that we need to start thinking seriously risk assessment?

A. Helmut Zarbl: There are two camps in that arena. There are those who say that this is so different from classical toxicity testing that we shouldn't bother with International Conference on Formal Engineering Methods (ICFEM) validation. We should just go around it and use it as it is. For validation of this, we'd need huge databases. I did a lot of consulting for the pharmaceutical industries, and I know that they have these big databases. And they've done tens of thousands of microarrays with lots of chemicals, and they could begin to start to do prediction in a serious way. So, if you're going to validate, you're going to need even more than that. That's one of the problems. The argument has been made by some groups that we should just use it without the classical ICFEM validation. The technologies are validated. When we do these things, we reproduce the data, we control for variability, we know how to do that very well now. But that is different from validation, and that is a serious issue. How do you validate something that is so complex where you have to do a lot of data processing, a lot of statistical analysis? And when you get to the end of it, how do you validate it, and what do you compare it to? That's a really challenging issue.

C. Ed Ohanian: If I may give you some historical perspective, it took them about 8 years to accept the fact that we can use kinetics and dynamics to replace default uncertainty factors.

C. Helmut Zarbl: In our report we actually address that issue a little bit. There's no simple answer.

Q. Perry Cohn: Are you thinking of maybe combining this with biomonitoring, so that you can measure the actual levels on the chips for individuals?

A. Helmut Zarbl: In the field, that is what we call phenotypic anchoring, where we actually look at other biological endpoints and try to map those back. So, in the studies that I talked about here, we actually—in the same samples—extracted DNA at same time and we looked at DNA adduct levels. In those studies, we know what the external dose is. We haven't looked at internal dose but yes, the more of that you do, the more valid your result becomes. All of this is sort of the biological response indicators. We're at the point where the stuff has already been processed, and it's been metabolized. Now we're looking at biological endpoints. All those are good, but it's always a question of money and time.

C. Perry Cohn: Will you be around if people have further questions?

C. Helmut Zarbl: I apologize for not getting my slides in on-time. If anybody wants them, I'd be happy to send them. Just drop me an e-mail.

Pharmaceuticals, Personal Care Products, and Unregulated Contaminants

Introduction: Scott Stoner
New York State Department of Environmental Conservation
Division of Water
Bureau of Water Assessment and Management
Standards and Analytical Support Section
(518) 402-8193
sxstoner@gw.dec.state.ny.us

Presented by Octavia Conerly
U.S. Environmental Protection Agency
Health and Ecological Criteria Division
(202) 566-1094
conerly.octavia@epa.gov

Visuals follow. Please contact the speaker for more information.

Pharmaceuticals, Personal Care Products, and Unregulated Contaminants

Coordinator/Moderator:

Scott J. Stoner, NYSDEC

FSTRAC October 22, 2009

Contaminants of Emerging Concern

- Continue to be a hot issue
- Newly *present or* newly *found*
- Not commonly monitored
- Unregulated in water
- Poorly studied/poorly understood
- Concern for effects on human health or aquatic life or both

Ms. Octavia Conerly welcomed everyone to the session on pharmaceuticals, personal care products, and unregulated contaminants on behalf of Mr. Scott Stoner:

Mr. Scott Stoner was unable to coordinate this session because he came down with H1N1. I wanted to give a little bit more of a background on why this is an issue and why it continues to be an issue.

It continues to be a hot issue because there are several congressional legislative efforts that are going on right now. Lately, it hasn't been in the news as much as it was, but there's still work going on behind the scenes. Everybody tries to define what a contaminant of emerging concern is. Some people have defined it, but I think nobody really wants to stick to a real definition. Most of us say that contaminants of emerging concern are newly present or newly found contaminants and they're not commonly monitored for. Some of them could be regulated but they are poorly studied or poorly understood. Some might present a concern for effects on human health or aquatic life or both.

So, I'm going to introduce Ed. Everyone knows Dr. Edward Ohanian and for those of you don't, he will tell you some things about himself.

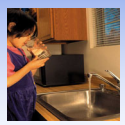
WHO/PHE PPCPs in Drinking Water Project

Edward Ohanian
U.S. Environmental Protection Agency
Office of Science & Technology
Health & Ecological Criteria Division
(202) 566-1117
ohanian.edward@epa.gov

Visuals follow. Please contact the speaker for more information.

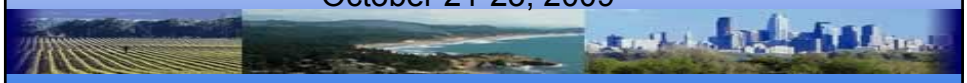
The U.S. Environmental Protection Agency is responding to the issues of pharmaceuticals and personal care products (PPCPs) in water with a four-pronged strategy aimed at: strengthening scientific knowledge; improving public understanding; identifying partnership and stewardship opportunities; and taking regulatory action when appropriate. The Agency has a number of activities underway in each of these areas. To strengthen its scientific understanding of the behavior of PPCPs in water, the Agency is conducting or funding a number of studies to better understand the potential sources and occurrence of pharmaceuticals in wastewater, biosolids and fish tissue. To understand risks to human health, EPA has research underway to help understand whether very low levels of pharmaceuticals in water might present a risk to human health. In addition, recently, the Agency consulted the National Academy of Sciences (NAS) which convened a panel of experts to provide their ideas and opinions for understanding risks to human health. The panel had numerous suggestions for how the Agency could screen contaminants and then perform human health risk assessments for priority pharmaceuticals. The panel also discussed the importance of communicating risks (early on in the process) to the public and other stakeholders. To improve public understanding of risks, EPA developed two Web sites, one focusing specifically on PPCPs in water and the other on PPCP research. However, in order to effectively address this issue, collaboration and building partnerships for stewardship are essential components. For this reason, EPA is participating, along with ten other Federal agencies, on the Federal Interagency Pharmaceuticals in the Environment workgroup to better coordinate Federal research efforts. To establish international partnerships, EPA is participating in the World Health Organization (WHO) Task Force on PPCPs in drinking water. Agency decisions are based on the foundation of sound science and reliable information. Once this foundation is established, the Agency's strategy is to rely on existing regulatory tools, when appropriate, to minimize the amount of pharmaceuticals entering the environment from wastewater sources.

WHO/PHE PPCPs in Drinking Water Project



Edward V. Ohanian, Ph.D., Director
Health and Ecological Criteria Division
Office of Water
U.S. Environmental Protection Agency
Washington, DC

2009 FSTRAC Meeting
Princeton, New Jersey
October 21-23, 2009



…to protect human health and the environment

WHO/PHE Expert Consultation for Guidelines for Drinking-Water Quality Singapore June 19-22, 2008

- Australia
- Canada
- Denmark
- Germany
- Italy
- Japan
- Netherlands
- Singapore
- United Kingdom
- United States

Overview

- PPCPs in water - Reasons for Concern
- Scope of Work
- Draft conclusions and recommendations
- Timetable

…to protect human health and the environment

Reasons for International Concern

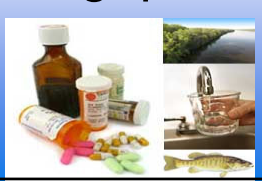
- Detection of PPCPs in environmental samples
- Persistence and long-term health and environmental effects
- Increase use of prescription drugs by aging world population
- Increase use of veterinary and agricultural drugs worldwide
- Recent USA reports on environmental effects of pharmaceuticals

Scope of Work

- Review advances in analytical and removal techniques
- Review screening and prioritization schemes
- Review human health risk assessment methods
- Review of availability of data to conduct RA
- Review take-back/safe disposal programs
- Consider feasibility/need to develop WHO drinking-water guidelines for these substances

Summary of Draft Conclusions and Recommendations of WHO Preliminary Expert Committee's Meeting on PPCPs in Drinking Water

June 19-22, 2009
Singapore



Occurrence

- A number of pharmaceuticals have been identified in surface and ground water primarily impacted by human, industrial and animal wastewater discharges, largely at trace concentrations mostly in the low μg/L range. There are few comprehensive systematic studies of occurrence in drinking water. Available studies show traces of few pharmaceuticals in the low ng/L range, typically more than 1000 fold less than the lowest therapeutic dose.
- From a treatment perspective, pharmaceuticals are not unusual organic chemicals. Treatment effectiveness is reasonably predictable based upon physical and chemical properties of the compounds.

Human Health Risk

- Several studies reported ecological effects of PPCPs in water; however, this review's focus was on "human health risk".
- Based on current evidence on margins of exposure to individual compounds, the development of global drinking water quality guideline values for pharmaceuticals is not warranted.
- When local circumstances, for example based on catchment surveys, indicate a potential for elevated concentrations, screening values can be developed. Various methodologies have been developed for screening levels risk assessments and are typically based on human data and modelled exposure data.

Human Health Risk (Cont'd)

- Current risk assessment methods do not explicitly address human health effects at low level chronic exposure to chemical mixtures, including pharmaceuticals.
- Appreciable adverse impacts on human health are unlikely at current levels of exposure associated with drinking water.

Recommendations

- Concerns over pharmaceuticals should not divert water suppliers and regulators from pathogenic microbial water quality issues.
- Routine monitoring is not recommended, but targeted well designed and quality controlled investigative studies could provide more information on potential human exposure from drinking water.
- Chemical risk assessment methodologies for low level chronic exposure to mixtures would benefit from further research for all life stages.

Recommendations (Cont'd)

- Current evidence does not support a general requirement for additional or specialised drinking water treatment to reduce concentrations of pharmaceuticals from water sources.
- Methods for prioritising pharmaceuticals should be refined.
- Enhanced preventive measures including education for prescribers and the public can reduce disposal and discharges to the environment and will reduce human exposure.

2008 NRC's Key Observations

- Levels vary from ppt-ppb based on detection limits
- Potency, presence, and persistence identified as key criteria for prioritization
- EPA's risk assessment paradigm adequate w/ "tweaking"
  - Chemical Safety Adjustment Factors for kinetic/dynamic differences
  - Departure from chemical by chemical assessment of risk
  - Identify therapeutic classes of drugs posing greatest risk
  - Explore efficient and effective screening tools
- Lack of data on sensitive populations
- Risk communication essential to build public trust

Timetable for Planned Work

- Issues scoping, followed by establishment and approval of draft plan of work by WHO Drinking-Water Quality Committee; formation of Expert Committee and Advisors – Summer 2008
- Expert Committee prepares draft background paper on "The State-of-Science on PPCPs" – Spring 2009
- Meeting of Expert Committee to review paper and identify topics for fact sheets in Singapore – Summer 2009
- Drinking-Water Quality Committee review of paper content, conclusions, recommendations, and fact sheets – Fall 2009
- Peer review and finalize paper and fact sheets - 2010

Questions

Q. Alan Stern: Among the issues that the World Health Organization (WHO) considered in coming up with its conclusions and draft recommendations, did they consider human health risk indirectly from promotion of environmental bacterial resistance from antibiotics?

A. Ed Ohanian: I don't think so. Michele, did it?

C. Michele Giddings: It came up for discussion, but it didn't become a major point. It was discussed in the overall aspect of it because we did talk about animal husbandry a bit and how that has potentially created antibacterial resistance.

Q. Gloria Post: What does it exactly mean or did they clarify further, departure from chemical by chemical assessment of risk? Do they mean structure activity relationships?

A. Ed Ohanian: Not departure from chemical by chemical assessments, departure from risk assessments for individual chemicals, individual pharmaceuticals.

Q. Gloria Post: What else would you do?

A. Ed Ohanian: Well, because that would take us forever. If you look at how many pharmaceuticals we have, there are about 80,000. That's going to be incredibly large. We thought maybe we need to bring in the clusters, the groups. That's what they were talking about.

Q. Helmut Zarbl: Did they consider any effects of animal pharmaceuticals? Because there are studies showing that downstream of feedlots, fish are feminized for miles.

A. Ed Ohanian: Michele, I think we did.

A. Michele Giddings: Yes, secondarily. Because the focus was on human health we recognized the fish and the implications of veterinary drugs but we stuck to the human health aspect.

Q. Bob Howd: In California, one of the concerns is accumulation of chemicals in general in the water supply because of increasing water reuse. So, that is of significance for downstream water reuse but also for ground water recharge. Was the propensity for accumulation of chemicals in that context part of the discussion?

A. Ed Ohanian: No. I hesitated to mention California at that meeting.

C. Bob Howd: They like us in Europe.

C. Ed Ohanian: No, seriously Bob, we have not.

C. Michele Giddings: There was a concurrent meeting going on with the International Network of Drinking-water Regulators and we met with them afterward. It was very evident that some of the developing countries were so glad to see the recommendations that come out of this. I can give you an example of a regulator from South Africa who was being pushed to put in granular activated carbon (GAC)-powdered activated carbon (PAC) on their treatment plants when they hadn't even looked to see if there was a problem just because it had been reported in other

places. They were glad to see these recommendations basically saying work on your microbes, don’t worry about this, we’ll get back to you with more as we get more information.

Strategy for Addressing Contaminants of Emerging Concern in Water: An Update

Octavia Conerly
U.S. Environmental Protection Agency
Health and Ecological Criteria Division
(202) 566-1094
conerly.octavia@epa.gov

Visuals follow. Please contact the speaker for more information.

The U.S. Environmental Protection Agency is responding to the issue of contaminants of emerging concern such as pharmaceuticals and personal care products (PPCPs) and endocrine disruptors in water with a four-pronged strategy (published August 2008) aimed at: strengthening scientific knowledge; improving public understanding; identifying partnership and stewardship opportunities; and taking regulatory action when appropriate. Since the announcement of the strategy, the Agency has made significant progress in each of these areas. To strengthen its scientific understanding of the behavior of PPCPs in water, the Agency conducted or funded a number of studies to better understand the potential sources and occurrence of pharmaceuticals in wastewater, biosolids and fish tissue. To understand risks to human health, the Agency consulted the National Academy of Sciences (NAS) which convened a panel of experts to provide their ideas and opinions for understanding risks to human health. The panel had numerous suggestions for how the Agency could screen contaminants and then perform human health risk assessments for priority pharmaceuticals. The panel also discussed the importance of communicating risks (early on in the process) to the public and other stakeholders. To improve public understanding of risks, EPA has developed two websites, one focusing specifically on PPCPs in water and the other on PPCP research. However, in order to effectively address this issue, collaboration and building partnerships for stewardship are essential components. For this reason, EPA participated, along with ten other Federal agencies, in the Federal Interagency Pharmaceuticals in the Environment workgroup to better coordinate Federal research efforts. To establish international partnerships, EPA continues to participate in the World Health Organization (WHO) Task Force on PPCPs in drinking water. Agency decisions are based on the foundation of sound science and reliable information. Once this foundation is established, the Agency's strategy is to rely on existing regulatory tools such as the Contaminant Candidate Listing process to minimize the amount of pharmaceuticals entering the environment from wastewater sources.

Strategy for Addressing Contaminants of Emerging Concern in Water: An Update

Federal **S**tate **T**oxicology & **R**isk **A**ssessment **C**ommittee Annual Meeting

Princeton, NJ
October 2009

EPA's Strategy

EPA is pursuing a four-pronged strategy:

- Strengthening Science
- Improving Public Understanding
- Identifying Partnerships and Promoting Stewardship Opportunities
- Taking Regulatory Action When Appropriate

Strengthening Science

Since strategy's announcement in August 2008, significant progress has been made.

- **POTW Wastewater Sampling Study**
  - Final report issued August 2009
    - www.epa.gov/waterscience/ppcp/studies/potw
- **Targeted National Sewage Sludge Survey**
  - Final Report issued January 2009
    - www.epa.gov/waterscience/biosolids/tnsss-fs
- **Fish Tissue Pilot Study**
  - Results published August 2008
    - www.epa.gov/waterscience/studies/fish-tissue
  - Expanded through National Rivers & Streams Assessment Program
- **University Grants**
  - University of Florida; Duke University

Strengthening Science

- Ambient Water Quality Criteria
  - SAB comments received December 2008
- NAS workshop: *"Characterizing the Potential Human Toxicity of Low Doses of Pharmaceuticals in Drinking Water: Are New Risk Assessment Methods or Approaches Required?"*

  - http://dels.nas.edu/best/risk_analysis/Documents/newsletter3.pdf

Key Observations from Workshop

- Levels vary from ppt-ppb based on detection limits
- Potency, presence, and persistence identified as key criteria for prioritization
- EPA's risk assessment paradigm adequate w/ "tweaking"
  - Chemical Safety Adjustment Factors for kinetic/dynamic differences
  - Departure from chemical by chemical assessment of risk
  - Identify therapeutic classes of drugs posing greatest risk
  - Explore efficient and effective screening tools
- Lack of data on sensitive populations
- Risk communication essential to build public trust

Improving Public Understanding

- Working to broaden EPA PPCP websites to cover other contaminants of emerging concern
- Coordinated with ONDCP, FDA to revise the Federal Guidelines for Proper Disposal of Drugs for consumers - October 2009
  - http://www.whitehousedrugpolicy.gov/publications/pdf/prescrip_disposal.pdf

Identifying Partnerships and Opportunities for Stewardship

- World Health Organization (WHO) Task Force on PPCPs in Drinking Water
  - Held meeting July 2009
- Pharmaceuticals in the Environment (PiE) Workgroup to coordinate federal research efforts
  - Draft report presented to T&R February 2009
- Other efforts supported by EPA:
  - Take-back programs
    - University of Maine (expanded as state-wide program)
    - Area Resources for Community and Human Services
      - http://www.epa.gov/aging/grants/winners/rx-meds-technical-report508.pdf

Taking Regulatory Actions

- If sufficient information exists, we take action
  - Health Care Industry Study
    - Plans to publish a preliminary effluent guideline plan
  - Ambient Water Quality Criteria for Aquatic Life
    - Plans to develop criteria for triclosan
  - Universal Waste Rule
    - Currently reviewing public comments

Taking Regulatory Actions

Third Contaminant Candidate List (CCL3)

- Pharmaceuticals were evaluated to identify those that had the potential to occur in PWSs at a level of frequency that may cause adverse health effects. One included on Draft CCL3 (nitroglycerin).

- EPA sought additional information on the concentrations of pharmaceuticals in finished or ambient water during the public comment period.

Taking Regulatory Actions

Third Contaminant Candidate List (CCL3) published September 2009

- Added 1 antibiotic and 9 hormones based on additional health effects and occurrence data in water;
  - Erythromycin
  - 17-alpha estradiol
  - 17-beta estradiol
  - Equilenin
  - Equilin
  - Estriol
  - Estrone
  - Ethinyl estradiol (EE2)
  - Mestranol, and
  - Norethindrone

Taking Regulatory Actions

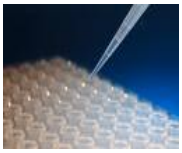
Endocrine Disruptor Screening Program

- **Federal Food, Drug, and Cosmetic Act (FFDCA)**
  - Requires EPA to:
    - Develop a screening program
    - Test all pesticide chemicals (both active and inert ingredients)
- **Safe Drinking Water Act (SDWA) Amendment**
  - Allows EPA to require testing of chemical substances in sources of drinking water

Taking Regulatory Actions

Endocrine Disruptor Screening Program

- Two-Tiered Approach
  - Tier 1 (screening)
    - In vitro and in vivo screens
    - Detect potential to interact with endocrine system



  - Tier 2 (testing)
    - Tier 2 data called in only after review of Tier 1 data
    - Multi-generation studies covering a broad range of taxa
    - Provide data for hazard assessment

Taking Regulatory Actions

Endocrine Disruptor Screening Program

- Issued the Final List of Chemicals for Initial Screening April 2009
  - 58 Pesticide actives
  - 9 High ProductionVolume / pesticide inerts
- Selection based on potential human exposure
  - Pesticide Active Ingredients: presence in food and water, residential use, and occupational contact
  - HPV inerts in human and eco biomonitoring, water, air
- Selected chemicals found in multiple exposure pathways.
- **Not** a list of "known" or "likely" endocrine disruptors

Taking Regulatory Actions

Endocrine Disruptor Screening Program

- EPA Intends to Issue Test Orders
  - Under FFDCA §408(p)(5)
  - Under FIFRA §3(c)(2)(B)

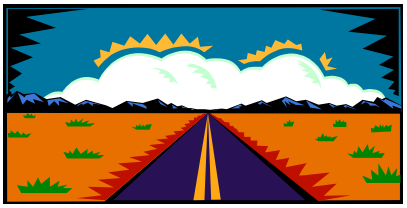
- Two Types of Orders (based on recipient)
  - Manufacturers and Importers
  - Pesticide Registrants

Taking Regulatory Actions

Endocrine Disruptor Screening Program

- Approximately 750 test orders will be issued for 67 chemicals.
- Currently, EPA anticipates issuing test orders over several months period.
- Test Orders for chemicals will require all the assays in the Tier 1 battery.
- Responses to Test Orders due 90 days from receipt
- Test data due 24 months from issuance of Test Order

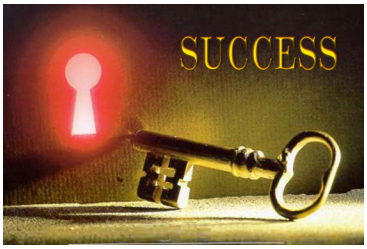
Regulatory Challenges Ahead



- Availability of analytical methods and treatment technologies
- Prioritizing groups of pharmaceuticals
- Limited publicly available data for human pharmaceuticals
  - Toxicological
  - Chronic, low-dose exposure
  - Mixtures

Collaboration is key

Work with Federal/non-Federal, and international partners in targeting timely research, monitoring, testing and risk analyses efforts to fill data gaps to support criteria development and regulatory actions



For more information

Visit our websites:

Pharmaceuticals & Personal Care Products in Water

www.epa.gov/waterscience/ppcp

EPA's Research on Pharmaceuticals

www.epa.gov/ppcp

EPA's Endocrine Disruptor Screening Program

www.epa.gov/endo/

Octavia Conerly
202-566-1094
conerly.octavia@epa.gov

New York's Continued Progress on Pharmaceuticals

Scott Stoner
Standards and Analytical Support Section
Division of Water
Bureau of Water Assessment and Management
New York State Department of Environmental Conservation
(518) 402-8193
sxstoner@gw.dec.state.ny.us

Visuals follow. Please contact the speaker for more information.

Pharmaceuticals in our waters are just one of many groups of emerging contaminants, but one that continues to garner extensive media attention. The New York State Department of Environmental Conservation (NYSDEC), continues its proactive steps to reduce the discharge of unused medications into the water. Actions are focused on controlling the sources, through the ongoing "Don't Flush Your Drugs" campaign for household drugs, facilitation of drug collection events, preparation of drug management guidance for health care institutions, and implementation of the state's Drug Management and Disposal Act. NYSDEC continues to collaborate with the NYS Department of Health, and other states, regarding pharmaceuticals, and to work closely with the U.S. Geological Survey on research on environmental levels, effects, and treatment options in New York State.

New York's Continued Progress on Pharmaceuticals

Scott J. Stoner
Chief, Standards and Analytical Support Section
Chair, Pharmaceuticals Work Group
NYSDEC
October 22, 2009

In the News

- *Frogs, fish, and pharmaceuticals a troubled brew…* [CNN 11-14-03]
- *Stay calm everyone, there's Prozac in the drinking water* [London Observor 8-8-04]
- *Study Finds Traces of Drugs in Drinking Water in 24 Major U.S. Regions* [AP/FOXnews.com; 3-10-08]
- *Human Drugs Found in Fish Near Treatment Plants* [AP/Discovery Channel; 3-25-09]
- *Companies Leak Drugs Into US Drinking Water* [AP/Newser.com; 4-19-09]
- *Intersex fish 'widespread'* [Miami Herald; 9-15-09]

Pharmaceuticals in Water:
Why DEC Remains Concerned (1)

- Designed to have biological effects
- Resistant to degradation
- Not readily treated in wastewater
- 225 Million prescriptions per year in NYS, plus over-the-counter drugs
- Many sources to our waters

Pharmaceuticals in Water:
Why DEC Remains Concerned (2)

- Effects of intended uses are well known, but…
- Concern is exposure at lower levels, especially to aquatic life:
  - Intersex fish
  - Changes in fish sex ratios
  - Changes in fish nesting behavior
- Potential concerns for human health:
  - Potential to increase drug resistant bacteria
  - Low level chronic exposure (hormones)

Pharmaceuticals in Water:
Rationale for Action

- Too often society has waited too long… (legacy pollutants)
- We must not let today's emerging contaminants become tomorrow's legacy pollutants

Sufficient evidence to warrant action:
DEC is taking proactive steps to reduce the input of pharmaceuticals to our waters

How do Drugs Get Into our Waters?
Widespread and Diverse Sources

- Households - Flushing (unused medicines)
- Health care institutions – Flushing
- Drug manufacturing facilities
- Animal feedlots
- Aquaculture
- Land application of organic materials
- *All of us* ! (drugs pass through our bodies and through wastewater treatment plants)

Reducing Pharmaceuticals in Waters:
Recap: Initial DEC Actions

- Reduce the flushing of unused drugs
- Pharmaceuticals Work Group
- Roundtable on Managing Unused Drugs
- Disposal guidance for households
- Press release: Don't Flush Your Drugs
- Website: www.dontflushyourdrugs.net

Reducing Pharmaceuticals in Waters:
Ongoing DEC Actions

- Extensive outreach: Don't Flush Your Drugs!
- Pharmaceuticals disposal in health care institutions
- Encouraging local drug collection events and nationwide system for returns
- Implementing State legislation
- Targeted source reduction
- Facilitating research into environmental levels, effects, and treatment technologies

Ongoing DEC Actions:
Extensive Outreach

- NY State Fair – 2009 – Don't Flush Your Drugs
  - Display poster by toilet
  - Flyers in restrooms
- Articles:
  - NYS Conservationist (April 2009)
- Presentations:
  - Pharmacy groups
  - Scientific conferences

Ongoing DEC Actions:
Household Collection Events

- Encouraging collection events
- Hurdles: costs, disposal, controlled substances (DEA regulations)
- Must include law enforcement and approved disposal plan
- Collections to date include:
  - Pharmacies
  - Household hazardous waste days
  - Stand-alone drug collections

Ongoing DEC Actions:
Implementation of State Legislation

- S7560A: Drug Management and Disposal Act
- Effective March 24, 2009
- Amends Environmental Conservation Law
- Notice on proper disposal posted in stores that sell drugs
- Outreach conducted
- Sample poster and guidance on DEC website

Ongoing DEC Actions:
Unused Drug Management

- DEA should revise rules to facilitate collections while still preventing diversion (comments submitted)
- Manufacturer-funded product stewardship is key to long-term solution
- Joined the Product Stewardship Institute to advance national returns system

Ongoing DEC Actions:
Targeted Source Reduction

- Working with a pharmaceutical manufacturing facility and small municipal waste water treatment plant to reduce discharges
- Interns funded through pollution prevention program

Ongoing DEC Actions:
Facilitating Research

- Working with USGS and NYS DOH
  - WWTP removal efficiency
  - presence of pharmaceuticals in surface waters
  - presence of endocrine disruptors
  - impacts to aquatic environment
  - additional WWTP technologies

Acknowledgements

- Ken Kosinski, Co-Chair, DEC Pharmaceuticals Work Group
- Resa Dimino, DEC Commissioner's Policy Office
- Lloyd Wilson, NYS Dept. of Health
- Patrick Phillips, USGS

More Information:

NYSDEC's Website:

www.dontflushyourdrugs.net

Scott Stoner:
518-402-8193
sxstoner@gw.dec.state.ny.us

Questions

C. Scott Stoner: I wish I could be there in person. I am feeling better and I appreciate all the e-mails of well wishes. Octavia, I want to personally thank you very much agreeing to fill in on very short notice to moderate this session. I've learned that the key to running a successful session is to get sick and ask Octavia to moderate it because she is doing a fabulous job. I thank you very much, Octavia.

Q. Lynda Knobeloch: I just wanted to say, great presentation, and that I love your poster. We may ask if we can modify it for use in Wisconsin.

A. Scott Stoner: It's on our Web site and we have sent it to pharmacies. If you want to just send an e-mail. I'm hoping to be back in the office on Monday of next week. I can just maybe route it officially to our Web folks, but it's out there. We have it out there as a sample poster for the pharmacies to use so I don't think there will be any problem with that. But I can just run it through the official channels if you want to just contact me after the meeting.

C. Lynda Knobeloch: Will do. Thanks.

Q. Virginia Thompson: Good presentation. I have a question about the targeted source reduction project you mentioned, working with a pharmaceutical manufacturing facility to reduce discharges. We've explored this to some extent, and we haven't had much luck in getting information from pharmaceutical manufacturers about what components go into their drugs, what's being discharged, and so forth. We know they have that information because they track it. Have you had any luck getting that kind of information?

A. Scott Stoner: We've actually been to that manufacturer several times, and Ken Kosinski has kind of spear-headed this. He's been out there probably a half-dozen times. We've gotten excellent cooperation from them. They really see us as partnering with them to try to reduce discharges. We haven't gone to the manufacturing association for this. We've talked directly and met with the management at that facility. It's been a very collaborative relationship.

Q. Jim Blando: Scott, when you do these collection programs, what happens to what is collected?

A. Scott Stoner: The drugs that are collected, I believe that the controlled and non-controlled pharmaceuticals are just lumped together. Because if you don't have to sort them, you don't need the pharmacist there as well, as I understand it. The law enforcement officer takes possession of all the drugs that are collected and maintains custody and control of it, drives to an incinerator, and witnesses the drugs going into the incinerator for destruction. So, that's the process.

Q. Ed Ohanian: I noticed on one of your slides, you mentioned that you collaborated with the wastewater treatment plant to reduce discharge. Could you tell me more about that? Is it through a memorandum of understanding (MOU) or how have you been engaged with them?

A. Scott Stoner: It's the same effort that we're working on with that large manufacturing facility. That facility forms a significant part of the influent to a small municipal treatment plant. We have been meeting with both the manufacturing representatives and the representatives from the small village. We regulate because it is a pretreatment type of situation, we don't directly

regulate the manufacturer, but we regulate the village through a State Pollution Discharge Elimination System (SPDES) permit (equivalent to a National Pollutant Discharge Elimination System [NPDES] permit), a waste water discharge permit. We regulate the village and then the village would regulate the manufacturer. We've been working with and meeting with both. We've supplied interns to both. We don't have an MOU, but the village is a permanent discharger that falls under the DEC regulations.

C. Ed Ohanian: Thank you, Scott.

C. Octavia Conerly: We'll have time for more questions during the roundtable.

Overview of PPCP Research in Pennsylvania

Rhonda Manning
Pennsylvania Department of Environmental Protection
(717) 772-4472
rmanning@state.pa.us

Visuals follow. Please contact the speaker for more information.

What's in Our Water?

Concentrations of Selected Pharmaceuticals, Antibiotics, Hormones, and Wastewater Compounds In Pennsylvania's Source Water

Rhonda Manning

PA DEP
Harrisburg, PA 17105

FSTRAC
Princeton, NJ
October 21-23, 2009

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Assessing Pennsylvania's Watersheds

- PA DEP Phase I
- PA DEP Phase II
- PADEP Phase III Temple Univ. AOP Study

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DEP Project Overview Phase I

- **Purpose:**
  - To document the occurrence and distribution of selected pharmaceuticals and antibiotics in streams and well water in South Central PA

USGS science for a changing world

pennsylvania DEPARTMENT OF ENVIRONMENTAL PROTECTION

DEP Project Overview Phase I

- Screen for pharmaceutical and antibiotic compounds in South-Central PA
  - 6 streams—effluent dominated
  - 6 streams—agricultural areas
    - Samples were collected at locations upstream and downstream of the municipal effluents or animal feeding operations
  - 6 wells

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Data Analysis

- Pharmaceuticals
  - Suite of 15 compounds
  - USGS National Water Quality Laboratory (NWQL) in Denver, CO
- Antibiotics
  - Suite of 31 compounds
  - USGS Organic Geochemistry Research Laboratory (OGRL) in Lawrence, KS

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Target Pharmaceuticals

- Acetaminophen
- Caffeine
- Carbamazepine
- Codeine
- Cotinine
- Dehydronifedipine
- Diltiazem
- Diphyenydramine
- Fluoxetine
- p-Xanthine
- Rantidine
- Salbutamol
- Sulfamethoxazole
- Thiabendazole
- Trimethoprim
- Warfarin

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Target Antibiotics

Macrolides
Azithromycin
Erythromycin
Anhydro-erythromycin
Roxithromycin
Tylosin
Virginiamycin

Quinolines
Ciprofloxacin
Lomefloxacin
Norfloxacin
Ofloxacin
Sarafloxacin
Enrofloxacin

Tetracyclines
Chlorotetracycline
Epi-chlorotetracycline
Iso-chlorotetracycline
Epi-iso-chlorotetracycline
Doxycycline
Oxytetracycline
Epi-oxytetracycline
Tetracycline
Epi-tetracycline

Sulfonamides
Sulfachloropyridazine
Sulfadiazine
Sulfadimethoxine
Sulfamethazine
Sulfamethoxazole
Sulfathiazole

Other Antibiotics
Lincomycin
Trimethoprim
Chloramphenicol
Ormetoprim

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Streams Receiving Wastewater Effluent

- Spring Creek, Berks County
- Lititz Run, Lancaster County
- Killinger Creek, Lebanon County
- Middle Spring Creek, Franklin County
- Mountain Creek, Cumberland County
- *Conoy Creek, Lancaster County

*disqualified

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Streams in Agricultural Areas Dominated by AFOs

- Muddy Run, Chester County
- Bachman Run, Lebanon County
- Snitz Creek, Lancaster County
- Trout Run, Lebanon County
- Little Chickies Creek, Lancaster County
- Three Square Hollow Run, Cumberland County

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Wells

- 6 locations in Adams, Huntington, Lancaster and Union Counties
- Primarily represent agricultural areas
- Not used for drinking water

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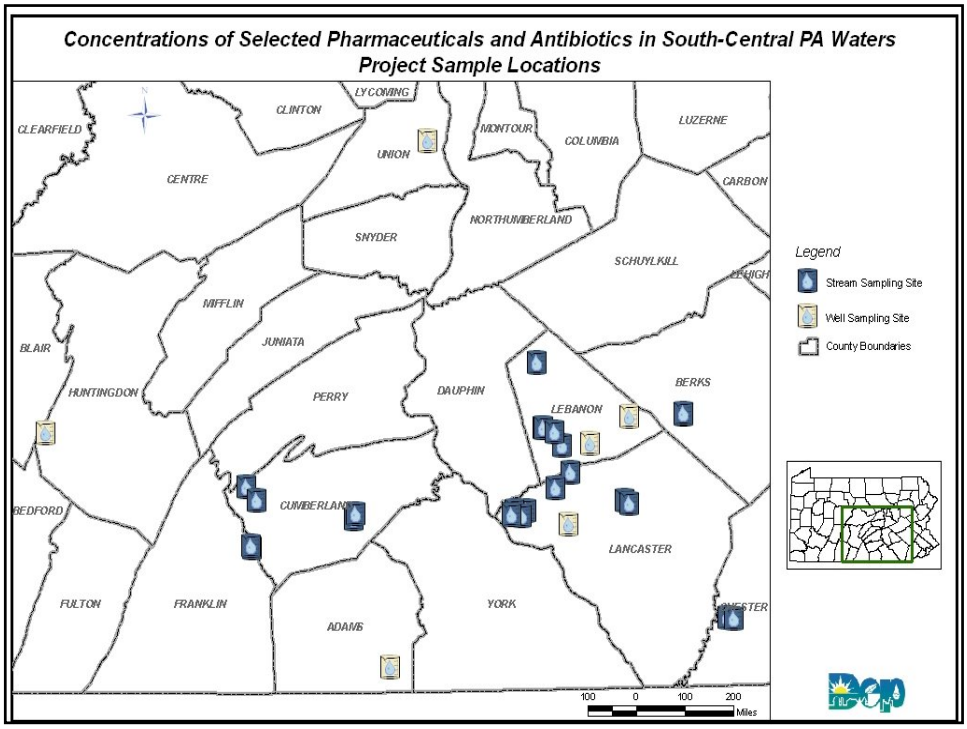

Data Analysis

- Samples collected in March/April, May, July and September 2006
- Analyses were completed on 120 environmental samples and 21 quality-control samples

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Phase I Results

- *Streams Receiving Wastewater Effluent*
  - Pharmaceuticals:
    - Caffeine (4.75 µg/L) (micrograms per liter)
    - Para-xanthine (0.853 µg/L)
    - Carbamazepine (0.516 µg/L)
    - Ibuprofen (0.227 µg/L)
  - Antibiotics:
    - Azithromycin (1.65 µg/L)
    - Sulfamethoxazole (1.34 µg/L)
    - Ofloxacin (0.329 µg/L)
    - Trimethoprim (0.256 µg/L)

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Phase I Results

- *Streams Receiving Runoff from AFOs*
  - Pharmaceuticals: (max. conc. of 0.053 µg/L)
    - Acetaminophen
    - Caffeine
    - Cotinine
    - Diphenhydramine
    - Carbamazepine
  - Antibiotics: (max. conc. of 0.157 µg/L)
    - Oxoxytetracycline
    - Sulfadimethoxine
    - Sulfamethoxazole
    - Tylosin

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Phase I Results
Livestock Wells

- 5 detections total in 24 samples
  - Four compounds were detected
    - 2 pharmaceuticals
      cotinine and diphenhydramine
    - 2 antibiotics
      tylosin (2) and sulfamethoxazole
  - Tylosin is the only compound detected that is used in agriculture. Others related to human uses.

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Phase I Results
Stream Sampling

- 12 of 16 (81%) pharmaceuticals were detected at least once.
- 12 of 32 (38%) antibiotics were detected at least once.
- 78% of all detections were downstream from wastewater discharges.
- Few detections above discharges and concentrations were lower than the downstream samples.

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Phase I Results
Stream Sampling

- The average number of compounds detected downstream of:
  - Animal feeding operation = 3
  - Municipal-wastewater discharges = 13
- Carbamazepine (Mood stabilizing, epileptic drug) was the most frequently detected compound below both AFO and WWT discharges.
- All concentrations are low – PPT

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Concentrations of Selected Pharmaceuticals and Antibiotics in South-Central Pennsylvania Waters, March through September 2006

http://pubs.usgs.gov/ds/300/

U.S. Geological Survey Data Series 300

By Connie A. Loper, J.Kent Crawford, Kim L. Otto, Rhonda L. Manning, Michael T. Meyer, and Edward T. Furlong

USGS
science for a changing world

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DEP Project Overview
Phase II: 2007-2010

- **PART 1: Continuation of Phase I**
  - Continue to characterize surface water downstream of wastewater treatment plants
    - 5 locations from Phase I plus 3 new sites and 1 reference stream
    - 6 sites in the Susquehanna watershed, 2 sites in the Potomac watershed, and one site in the Delaware watershed
  - Added hormones and wastewater compounds in water and streambed sediment
  - Sampling will occur one time per year for 3 years beginning May 2007

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DEP Project Overview Phase II

- **PART 2: Evaluate Sourcewater for EC's**
  - 27 Water Quality Network (WQN) Stations
  - Stations were chosen based on their proximity to Public Water Supply surface water intakes (within 3 miles)
  - Samples will be analyzed quarterly for pharmaceuticals, antibiotics, and hormones as well as pathogens and bacteria
  - 11 sites in the Susquehanna watershed, 11 in the Ohio watershed, 4 in the Delaware watershed and 1 in the Potomac watershed.

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Preliminary Results

- Indicate all 27 sites had at least 1 compound detected
- 12 of the 15 (80%) pharmaceutical compounds analyzed were detected at least once
- 16 of 32 (50%) antibiotic compounds were detected at least once
- 9 of 19 (47%) hormone compounds were detected at least once

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Commonly Detected Pharmaceuticals

- Caffeine – Stimulant
- Carbamazepine - Mood stabilizing (epileptic)
- Acetaminophen- Analgesic
- Diphenhydramine - Antihistamine (Benadryl)
- Cotinine - Metabolite of nicotine

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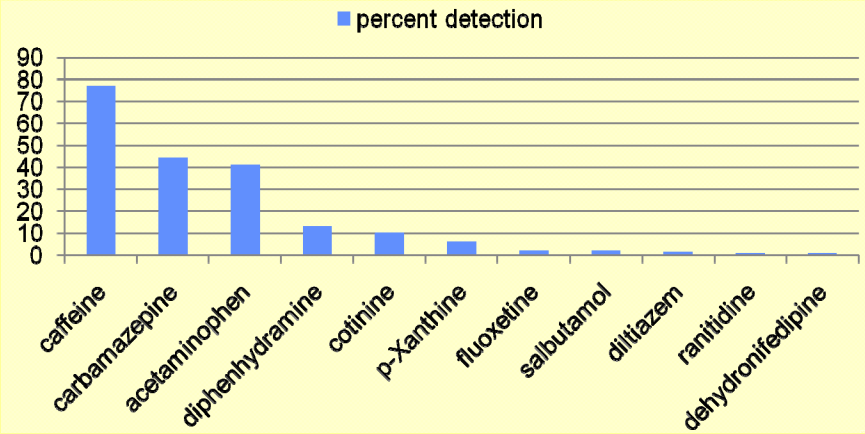
Pharmaceuticals Detected



Commonly Detected Antibiotics

- Sulfamethoxazole - Human use
- Trimethoprim - Human use
- Azithromycin - Human use
- Ofloxacin - Human use
- Tylosin - Used for cattle, swine, and poultry

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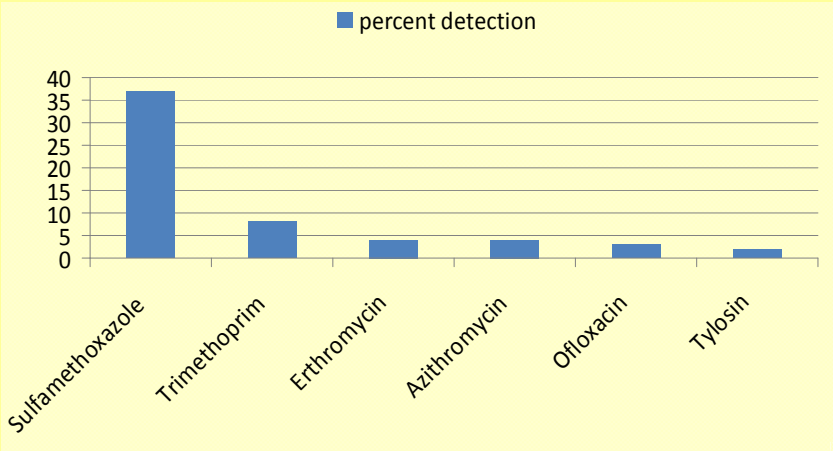
Antibiotics Detected



Commonly Detected Hormones

- Estrone - Female – Estrogen
- 4-androstene 3,17 dione Male – testosterone precursor)
- 17 beta estradiol - Female – Estrogen
- Cis-androsterone Male – Testosterone metabolite

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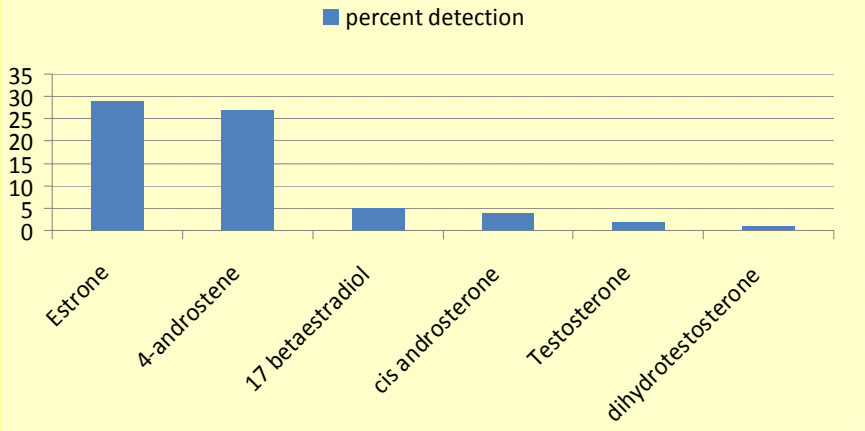
Hormones Detected



Preliminary Findings

- Detections and concentrations are flow related
- Seasonal component to some compounds – use related
- Some compounds are related to specific sites
- Many compounds attach to sediment and may bio accumulate

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Our ability to measure contaminants currently exceeds our understanding of their environmental effects

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DEP Project Overview
Phase II

- **PART 3: Fish Health Assessment**
  - 16 sites statewide
  - Target species include white suckers and smallmouth bass
  - Water and bed sediment will also be analyzed for pharmaceuticals, antibiotics, hormones, and waste water compounds
  - A final report is anticipated early 2010

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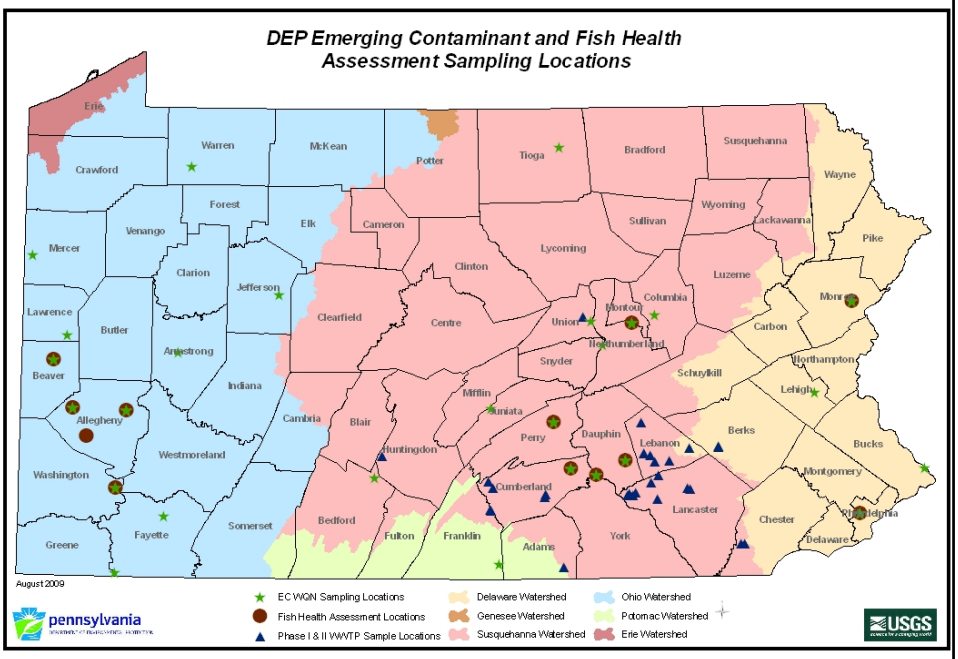
PADEP Environmental Forum on
Emerging Contaminants
Friday, October 16, 2009
10am, RCSOB Auditorium
Hear All About It!!



DEP Project Overview Phase II

- **Part 4: Identification of Pathogenic Bacteria**
  - **USGS Michigan Water Science Center has developed assays for actual bacterial pathogens such as *E. coli* O157, a broad class of pathogenic *E. coli* called Shiga-toxin producing *E. coli* (STEC) and Enterococci that carry the *esp* gene**
  - **These DNA-based methods may be used to identify the source of fecal pollution**
  - **The USGS MI WCS and the DEP BOL will analyze for pathogenic and fecal source markers from *E. coli* and enterococci in a side by side PCR method comparison**

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Advanced Treatment of Drinking Water to Remove Trace Emerging Contaminants DEP –Temple University

- **Steroid hormones**
  - 17α estradiol
  - 17β estradiol
  - 17α dihydroequilin
  - 17α ethinylestradiol
  - Estriol
  - Estrone
  - Equilin
  - Equilinen
  - Norethindrone acetate
  - 19-norethisterone
  - Mestranol
  - Bisphenol A

- **Technologies**
  - UV
  - UV/Peroxide
  - Ozone/Peroxide
  - Ozone/UV

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What Have We Learned?

- **Present at *sub-ppb concentrations* in water.- Streams and Groundwater**
- **Present as complex *mixtures*.**
- **Reflect wide range of *human activities*.**
- **Some cpds *mobile and persistent*.**
- **Detectable conc. related to fate and transport not just the amount used.**

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Summary of Results

- Several compounds are commonly detected but most are rarely found
  - Acetaminophen, caffeine, carbamazepine, sulfamethyloxozale
- Found at large and small sites in various settings.
- Distance from point discharges related to detections
  - Higher concentrations near wastewater treatment discharges.

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Summary of Results

- Groundwater less affected than surface water
- Look for patterns in seasonality – land use – flow conditions in data.
- Other sources – Landfills – pharmaceutical manufacturing

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Closing Thoughts

- Drinking water is only one route of exposure
- Humans are exposed to some compounds at far greater concentrations through other contact:
  - food, food preparation, the intended purpose of the product, dermal absorption, inhalation (overspray), etc.

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"I can tell you with absolute certainty that, if we regulate contaminants based upon detection rather than health effects, we are embarking on a futile journey without end"

- Dr. Shane Snyder

In his statement before the Senate Subcommittee on Transportation Safety, Infrastructure Security, and Water Quality

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Acknowledgements

- US EPA
- PA DEP Safe Drinking Water Fund
- USGS Water Science Center

Questions??

Thank You

Rhonda Manning

rmanning@state.pa.us

(717) 772-4472

Program Analysis and Support

Bureau of Water Standards and Facility Regulation

PA Department of Environmental Protection

Questions

Q. Julius Nwosu: You did mention that you had some sediment samples that had high concentrations away from the mixing zone. Did you look into that to see what the reasons were for that?

A. Rhonda Manning: We just found out about that last Friday from Vicki Blazer. She had teased through the data. We don't have all the data back. We have some preliminary data, but that's one area that we are going to look into.

Q. Irene Dooley: Thank you for your presentation. I was wondering why triclosan was not selected.

A. Rhonda Manning: There's a wide variety. I left it up to my chemist to decide what he wanted to include. He collaborated with a lot of different people, and this is what it is.

Q. Fred McGarry: The wells that were sampled in Phase I, were those bedrock wells or overburden wells?

A. Rhonda Manning: They were private wells, but they weren't used for drinking water. I don't know. I'll have my GIS well geologist look into that.

Pharmaceuticals and Endocrine Disrupting Compounds in Minnesota Lakes

Mark Ferrey
Minnesota Pollution Control Agency
(651)-757-2355
mark.ferrey@state.mn.us

Richard Keisling, Larry Barber, and Jeffrey Writer
U.S. Geological Survey
Heiko Schoenfuss, St. Cloud State University

Visuals follow. Please contact the speaker for more information.

Several studies have shown that endocrine disrupting chemicals (EDCs), pharmaceuticals, and other unregulated contaminants are commonly found in surface waters that receive waste water effluent. Although there is no evidence that these contaminants actually pose a risk to human health at the part per trillion concentrations at which they are usually detected in the aquatic environment, there is growing evidence that these chemicals do have effects on fish and wildlife at very low concentrations.

Previous studies on these compounds in Minnesota have focused on the Mississippi River and its tributaries, mostly in close proximity to waste water treatment plants. Those studies revealed that many compounds including bisphenol A, the alkylphenols nonylphenol and octylphenol, several alkylphenol ethoxylates, and a variety of pharmaceuticals are commonly associated with surface waters receiving waste water treatment plant effluent. Little is known, however, about the presence or the concentrations of these compounds in lakes.

In 2008, we sampled twelve lakes and four rivers in Minnesota, analyzing the surface water and sediment for contaminants typically associated with waste water, including several pharmaceuticals, hormones, and suspected EDCs. In addition, fish that were collected from the same locations were analyzed for evidence of endocrine disruption. We found that many of the chemicals that were detected in the river studies, such as bisphenol A, alkylphenols, pharmaceuticals, and hormones, were also present in the surface water and bed sediment of lakes, including lakes without any surrounding development. Male fish from several lakes contained elevated levels of vitellogenin, a protein associated with egg production in females and not normally found in males. This indicated that male fish were exposed to estrogenic compounds in their environment. The results of this study suggest that EDCs and other organic waste water compounds may be common in lakes. These chemicals may be eliciting endocrine disrupting effects in fish.

Minnesota Statewide EDC Study

2007-2008

Heiko Schoenfuss, St. Cloud State University

Richard Kiesling, Jeffrey Writer, Larry Barber, USGS

Mark Ferrey, Minnesota Pollution Control Agency

Previous studies

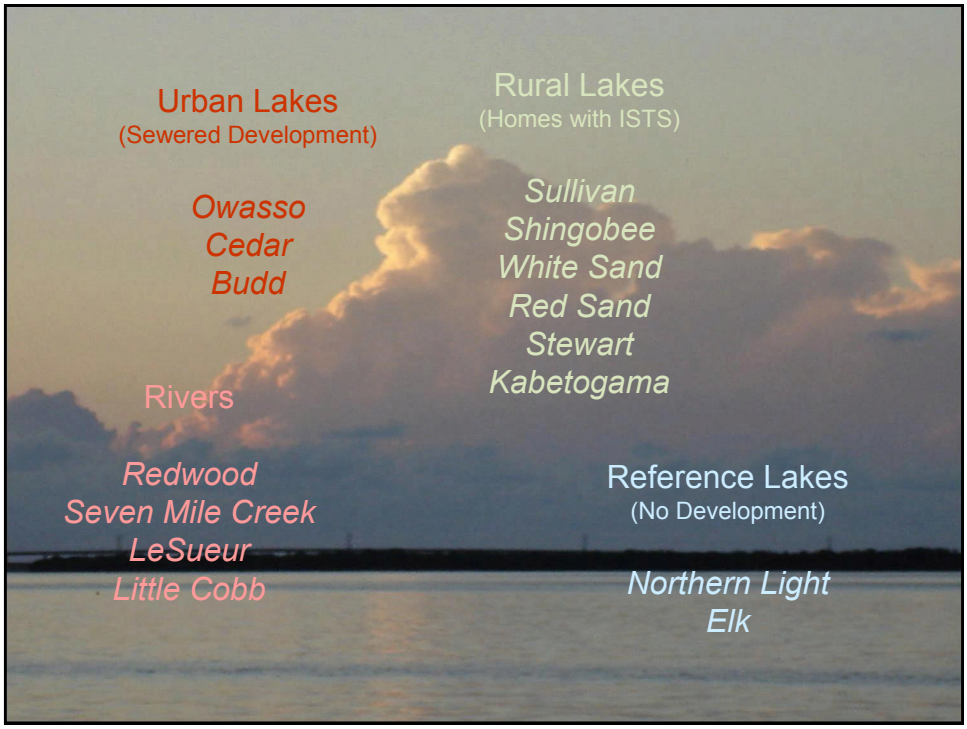
- 2000 USGS National reconnaissance study.
- 2002 USGS Minnesota reconnaissance study.
- Mississippi River longitudinal study.
- Tributary study
  - Grindstone, Redwood, Crow Rivers.

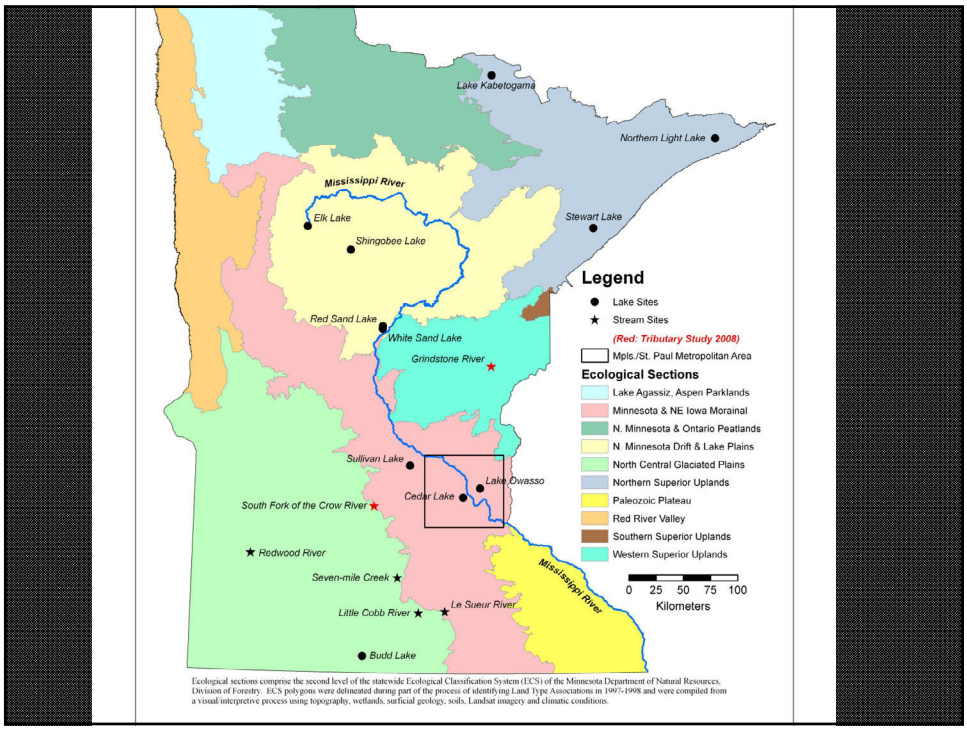
- All of these studies were on rivers.
- All of these studies had a wastewater treatment plant (WWTP) focus.

Little is known about the presence of endocrine disrupting compounds (EDCs), pharmaceuticals, and organic wastewater compounds (OWCs) in lakes.

Possible Sources of EDCs and OWCs to Lakes

- Most lakes not affected by WWTPs
- Individual Sewage Treatment Systems (ISTSs)
- Lawn runoff
- Agricultural row-crop runoff
- Feedlot runoff
- Storm water runoff


Urban Lakes
(Sewered Development)
Owasso
Cedar
Budd
Rural Lakes
(Homes with ISTS)
Sullivan
Shingobee
White Sand
Red Sand
Stewart
Kabetogama
Rivers
Redwood
Seven Mile Creek
LeSueur
Little Cobb
Reference Lakes
(No Development)
Northern Light
Elk

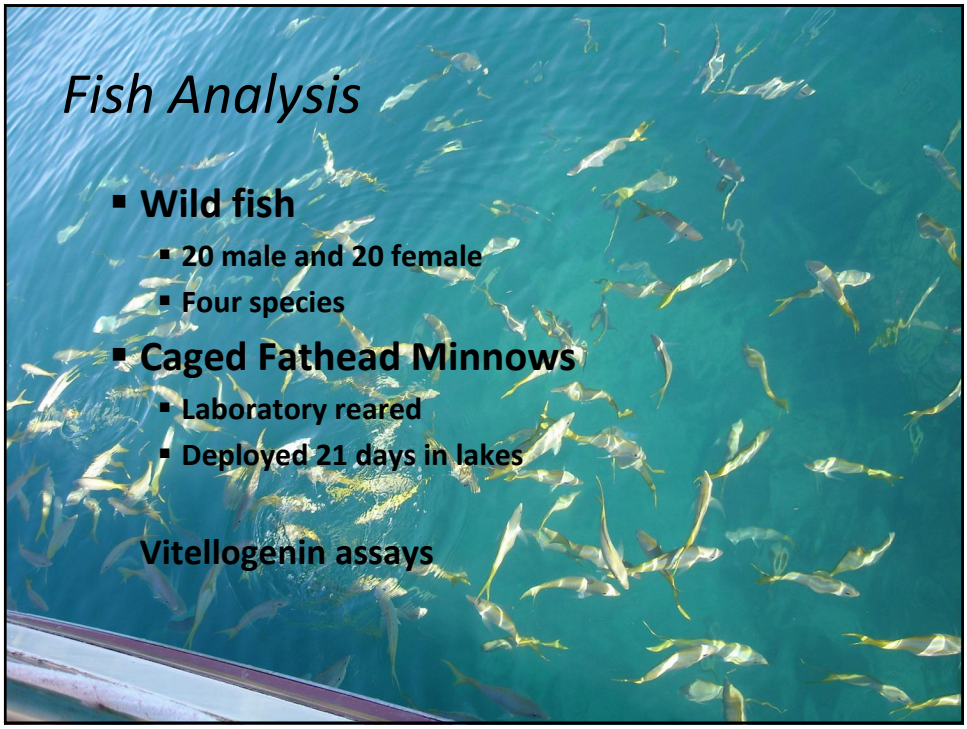

Lake Kabetogama
Northern Light Lake
Mississippi River
Elk Lake
Shingobee Lake
Stewart Lake
Red Sand Lake
White Sand Lake
Grindstone River
Sullivan Lake
Lake Owasso
Cedar Lake
South Fork of the Crow River
Redwood River
Seven-mile Creek
Little Cobb River
Le Sueur River
Budd Lake
Mississippi River
Legend
Lake Sites
Stream Sites
(Red: Tributary Study 2008)
Mpls./St. Paul Metropolitan Area
Ecological Sections
Lake Agassiz, Aspen Parklands
Minnesota & NE Iowa Morainal
N. Minnesota & Ontario Peatlands
N. Minnesota Drift & Lake Plains
North Central Glaciated Plains
Northern Superior Uplands
Paleozoic Plateau
Red River Valley
Southern Superior Uplands
Western Superior Uplands
0 25 50 75 100
Kilometers
Ecological sections comprise the second level of the statewide Ecological Classification System (ECS) of the Minnesota Department of Natural Resources, Division of Forestry. ECS polygons were delineated during part of the process of identifying Land Type Associations in 1997-1998 and were compiled from a visual/interpretive process using topography, wetlands, surficial geology, soils, Landsat imagery and climatic conditions.

Analytical

- Organic wastewater compounds
  - Bisphenol A
  - Alkylphenols
    - Nonylphenol
    - Octylphenol
    - Ethoxylates
- Pesticides

Analytical

- Pharmaceuticals
  - Antibiotics
  - SSRIs (antidepressants)
  - Triclosan
- Hormones
  - 17 β - estradiol
  - Estrone
  - Ethinylestradiol
  - Testosterone
  - Androstenedione

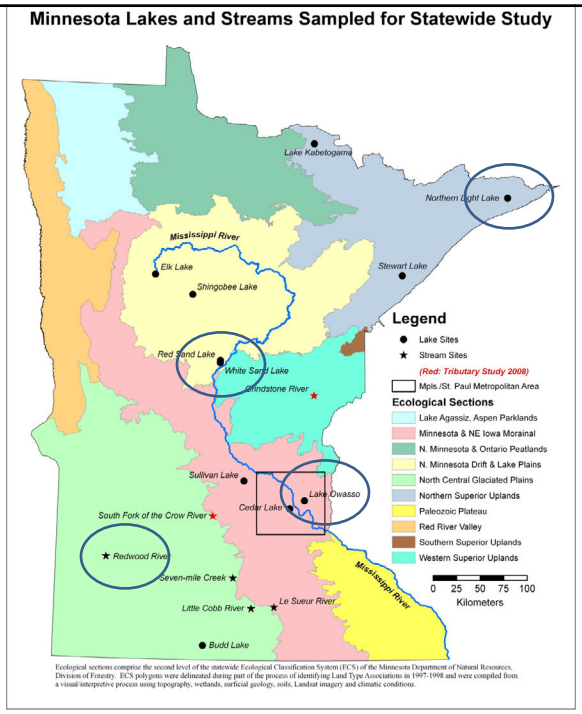

Fish Analysis
Wild fish
20 male and 20 female
Four species
Caged Fathead Minnows
Laboratory reared
Deployed 21 days in lakes
Vitellogenin assays

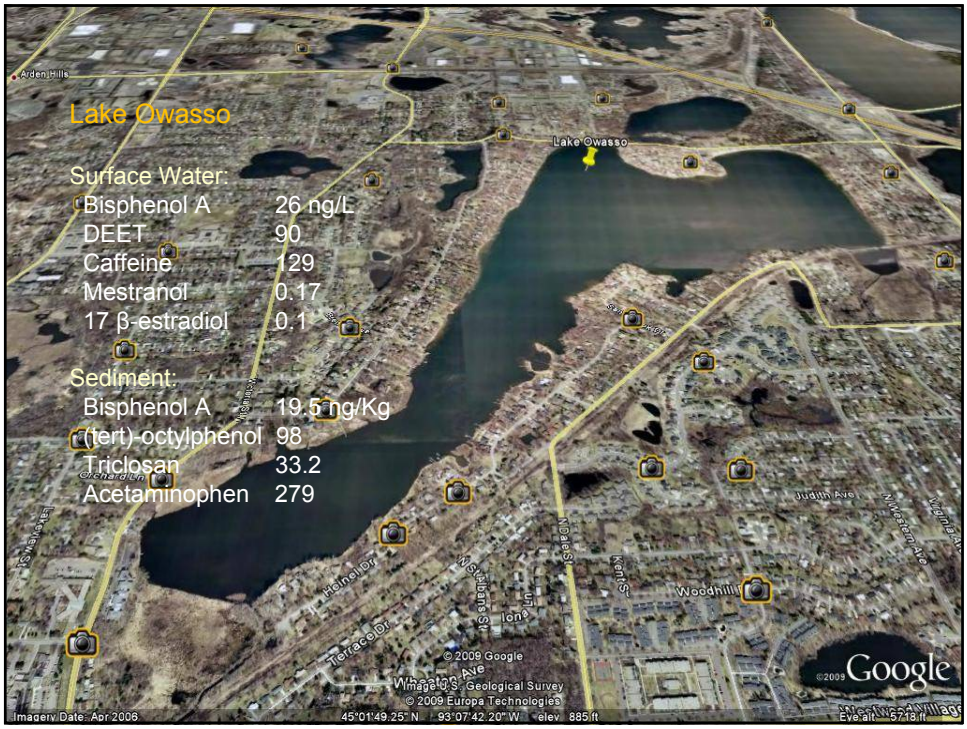
HOMER PAINT BUCKET

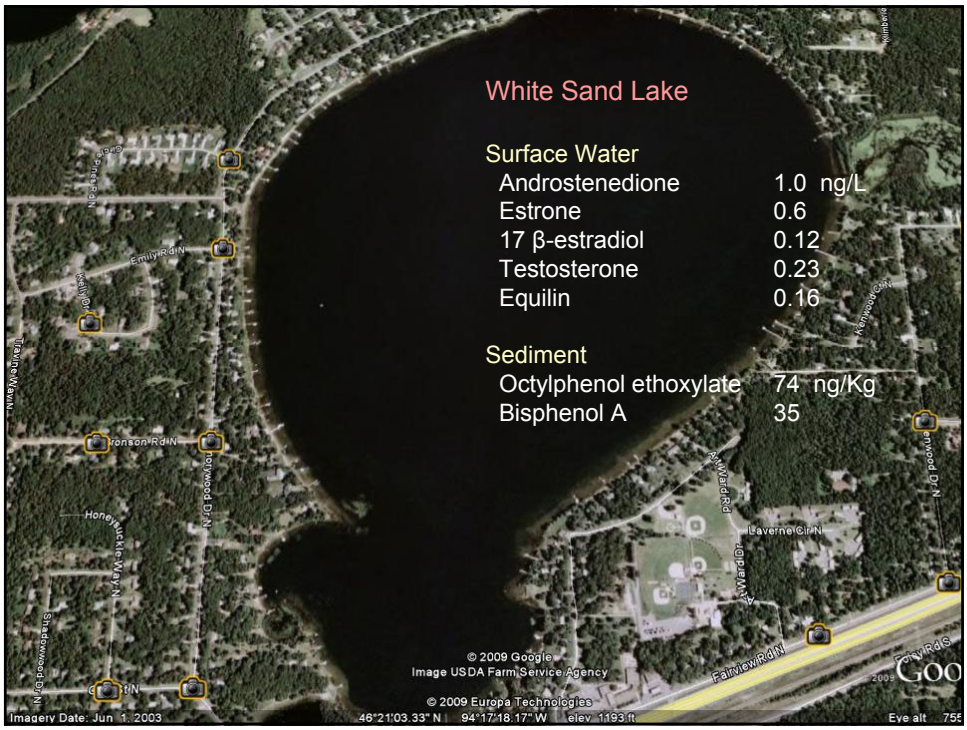
Frequently detected chemicals

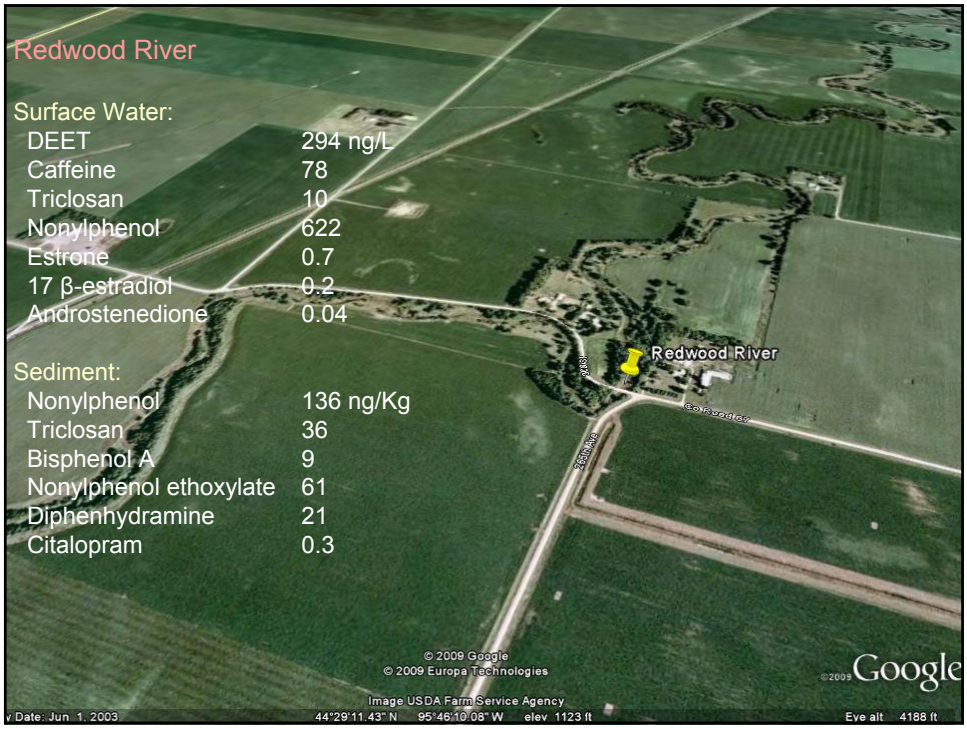
Alkylphenol ethoxylates
Alkylphenols
Androstenedione
Estrone
17 β-estradiol
Bisphenol A

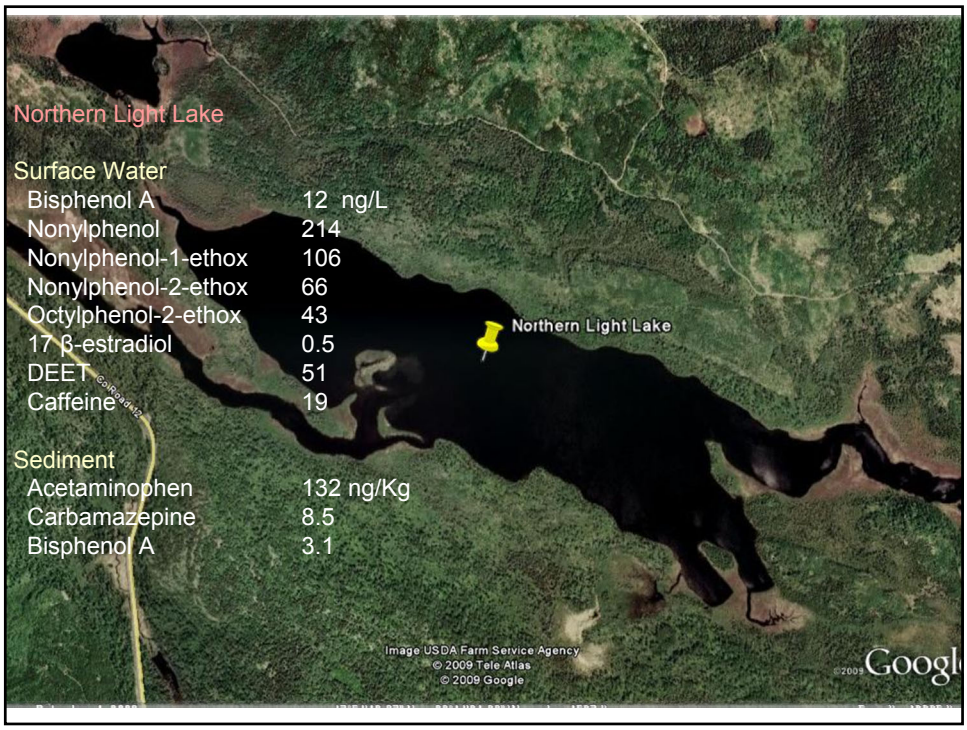
Carbamazepine
Acetominophen
Triclosan
DEET
Caffeine




Lake Owasso
Surface Water:
Bisphenol A 26 ng/L
DEET 90
Caffeine 129
Mestranol 0.17
17 β-estradiol 0.1
Sediment:
Bisphenol A 19.5 ng/Kg
(tert)-octylphenol 98
Triclosan 33.2
Acetaminophen 279
Lake Owasso
Arden Hills
Woodhill
Judith Ave
Terrace Dr
Wheaton Ave
© 2009 Google
Image U.S. Geological Survey
© 2009 Europa Technologies
Imagery Date: Apr 2006
45°01'49.25" N 93°07'42.20" W elev 885 ft
Eye alt 5718 ft
Google


White Sand Lake
Surface Water
Androstenedione 1.0 ng/L
Estrone 0.6
17 β-estradiol 0.12
Testosterone 0.23
Equilin 0.16
Sediment
Octylphenol ethoxylate 74 ng/Kg
Bisphenol A 35
Emily Rd N
Honeysuckle Way N
Fairview Rd N
Laverne Cir N
© 2009 Google
Image USDA Farm Service Agency
© 2009 Europa Technologies
Imagery Date: Jun 1, 2003
46°21'03.33" N 94°17'18.17" W elev 1193 ft
Eye alt 755


Redwood River
Surface Water:
DEET 294 ng/L
Caffeine 78
Triclosan 10
Nonylphenol 622
Estrone 0.7
17 β-estradiol 0.2
Androstenedione 0.04
Sediment:
Nonylphenol 136 ng/Kg
Triclosan 36
Bisphenol A 9
Nonylphenol ethoxylate 61
Diphenhydramine 21
Citalopram 0.3
Redwood River
© 2009 Google
© 2009 Europa Technologies
Image USDA Farm Service Agency
Date: Jun 1, 2003
44°29'11.43" N 95°46'10.08" W elev 1123 ft
Eye alt 4188 ft
Google


Northern Light Lake
Surface Water
Bisphenol A 12 ng/L
Nonylphenol 214
Nonylphenol-1-ethox 106
Nonylphenol-2-ethox 66
Octylphenol-2-ethox 43
17 β-estradiol 0.5
DEET 51
Caffeine 19
Sediment
Acetaminophen 132 ng/Kg
Carbamazepine 8.5
Bisphenol A 3.1
Northern Light Lake
Image USDA Farm Service Agency
© 2009 Tele Atlas
© 2009 Google

	Maximum concentration detected (ppb)			
	Urban	Septic	Reference	Two Harbors (WWTP effluent)
Bisphenol A	0.04	0.02	0.01	0.05
DEET	90	0.6	0.2	1.9
Caffeine	129.4	0.01	0.02	13.8
Triclosan				0.6
4-nonylphenol (NP)		0.1	0.2	1.5
NP- 4EO				0.06
NP- 3EO		0.1		0.5
NP- 2EO		0.2	0.07	1.5
NP- 1EO	0.06	0.09	0.1	0.9
4-octylphenol (OP)				
OP- 4EO				
OP- 3EO		0.01		
OP- 2EO	0.03	0.03	0.04	
OP- 1EO				
tert-Octylphenol		0.01		0.1

	Maximum concentration detected (ppb)			
	Urban	Septic	Reference	Two Harbors (effluent)
Bisphenol A	0.04	0.02	0.01	0.05
DEET	90	0.6	0.2	1.9
Caffeine	129.4	0.01	0.02	13.8
Triclosan				0.6
4-nonylphenol (NP)		0.1	0.2	1.5
NP-4EO				0.06
NP-3EO		0.1		0.5
NP-2EO		0.2	0.07	1.5
NP-1EO	0.06	0.09	0.1	0.9
4-octylphenol (OP)				
OP-4EO				
OP-3EO		0.01		
OP-2EO	0.03	0.03	0.04	
OP-1EO				
tert-Octylphenol		0.01		0.1

	Maximum concentration detected (ppb)			
	Urban	Septic	Reference	Two Harbors (effluent)
Bisphenol A	0.04	0.02	0.01	0.05
DEET	90	0.6	0.2	1.9
Caffeine	129.4	0.01	0.02	13.8
Triclosan				0.6
4-nonylphenol (NP)		0.1	0.2	1.5
NP-4EO				0.06
NP-3EO		0.1		0.5
NP-2EO		0.2	0.07	1.5
NP-1EO	0.06	0.09	0.1	0.9
4-octylphenol (OP)				
OP-4EO				
OP-3EO		0.01		
OP-2EO	0.03	0.03	0.04	
OP-1EO				
tert-Octylphenol		0.01		0.1

Lakes	Vitellogenin Male/Female Ratio (%)				
Location	Sunfish	Minnow	Perch	Shiner	Caged fathead minnow
Cedar	0.6	14			0.6
Owasso	1	47		28	1
Budd	0	1		8	1.6
White Sand	105			45	
Red Sand					
Sullivan	0.1				
Stewart	9		4		
Shingobee	31	11	40	0.8	0.4
Kabetogama		12			0.5
Northern Light			66		
Elk	59	20	2	6	0.2

Rivers	Vitellogenin Male/Female Ratio (%)				
Location	Sunfish	Minnow	Perch	Shiner	Caged fathead minnow
Little Cobb	0	560		37	0.8
Le Sueur		4		46	0.5
7 Mile Upstream		22			0
7 Mile Mid		65		118	0
7 Mile Down		226		14	0.7
Redwood Up				0.1	
Redwood Down 1				0.6	
Redwood Down 2				1.1	

- Organic wastewater compounds appear widespread in Minnesota's aquatic environment.
- Concentrations are higher in bed sediment than water.

- Lakes with ISTSs contained more alkylphenols than lakes surrounded by sewered development.
- Fish showed evidence of exposure to estrogenic chemicals

Future study

- WWTP study
- Continued lake study
- Ground water EDC Study

Green Pharmacy:
Strategies for Reducing the Pharmaceutical Footprint

Nicholas Anastas
Poseidon's Trident, LLC
(617) 698-7105
nanastas@poseidonstrident.net

Visuals follow. Please contact the speaker for more information.

The presence of Pharmaceuticals and Personal Care Products (PPCPs) in the environment has recently received increasing attention in both the popular and scientific press. Improved analytical detection techniques have led to the identification of prescription and "over-the-counter (OTC) drugs, fragrances, personal care products and compounds that can adversely impact the endocrine system. The consequences of these compounds on the environment and the potential impact on human health have not yet been fully investigated.

Each point along the lifecycle of a pharmaceutical or personal care product can be examined for the possibility of reducing the potential environmental risks. Benign-by-design is an approach for applying the principles of green chemical design build molecule from scratch that are less hazardous. Feedstock should ideally come from renewable feedstocks, materials for manufacturing and distribution must be recyclable.

Physicians must be judicious in their prescribing practices to ensure that a three month supply of medicine is not prescribed for a seven day rash. Flushing medications into the domestic sewer systems or into septic systems are no longer acceptable practices. Medicines need to be recycled efficiently through return programs or complete mineralization practices, i.e., combustion/ incineration.

Current wastewater and drinking water treatment systems are not designed to efficiently remove these inherently water-soluble environmental pollutants. Treatment practices must be altered to reflect this new challenge. This talk will present the driver and barriers to reduce the environmental load of PPCPs to the environment through the application of Green Pharmacy.

Reducing the Environmental Pharmaceutical Footprint

Opportunities for Risk Reduction of Pharmaceuticals and Personal Care Products on the Environment

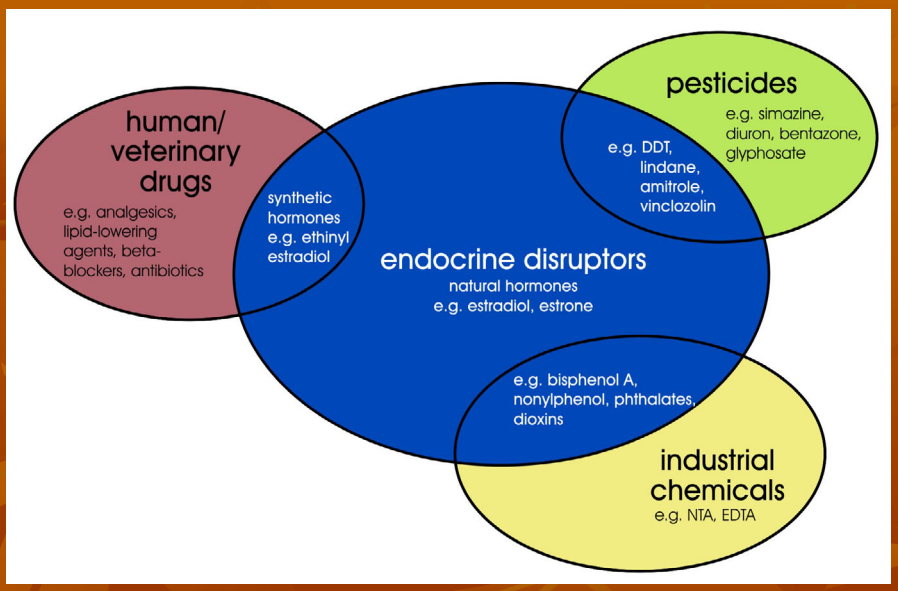
Nicholas D. Anastas, Ph.D., M.S.
Poseidon's Trident, LLC
October 22, 2009

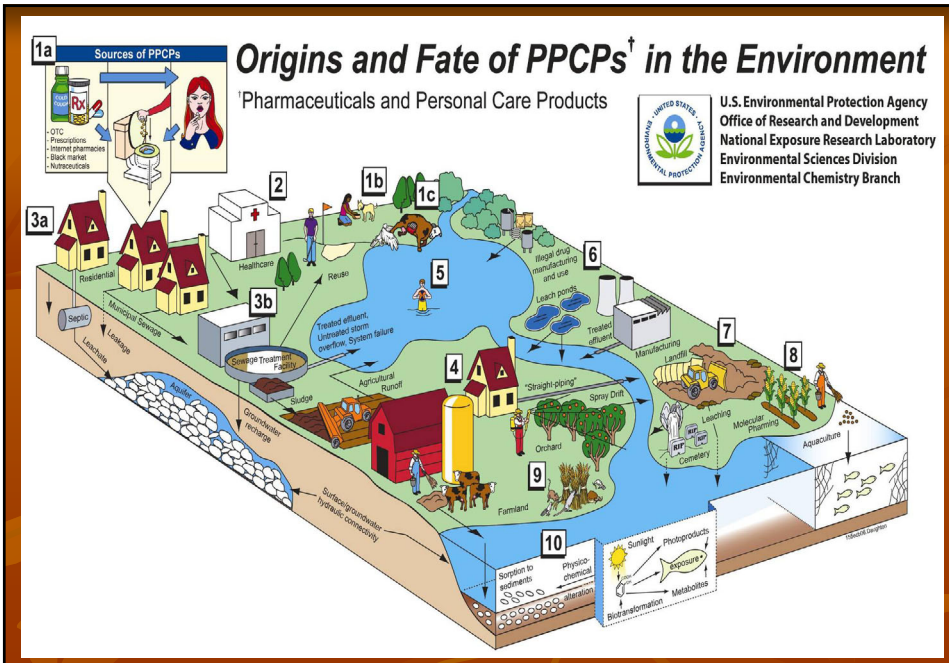
Talk Overview

- Overview of environmental PPCPs
- Lifecycle of PPCPs
- Greening Chemistry and Green Pharmacy
- Treatment of drugs in the water
- Proper disposal options
- Next steps

Ah, those chemists

Micro Constituents in Water: Where Do They Come From?

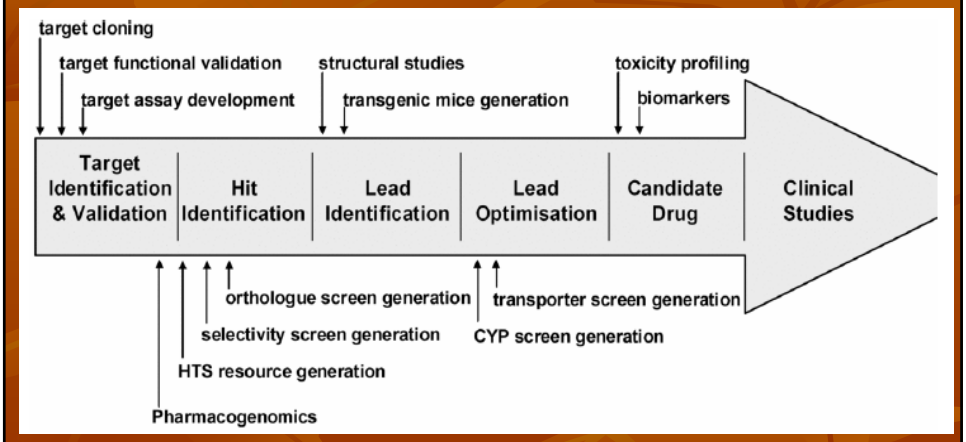

human/
veterinary
drugs
e.g. analgesics,
lipid-lowering
agents, beta-
blockers, antibiotics
synthetic
hormones
e.g. ethinyl
estradiol
pesticides
e.g. simazine,
diuron, bentazone,
glyphosate
e.g. DDT,
lindane,
amitrole,
vinclozolin
endocrine disruptors
natural hormones
e.g. estradiol, estrone
e.g. bisphenol A,
nonylphenol, phthalates,
dioxins
industrial
chemicals
e.g. NTA, EDTA


Origins and Fate of PPCPs† in the Environment
†Pharmaceuticals and Personal Care Products
U.S. Environmental Protection Agency
Office of Research and Development
National Exposure Research Laboratory
Environmental Sciences Division
Environmental Chemistry Branch
1a
Sources of PPCPs
OTC
Prescriptions
Internet pharmacies
Black market
Nutraceuticals
1b
1c
2
3a
3b
4
5
6
7
8
9
10
Residential
Healthcare
Reuse
Septic
Municipal Sewage
Leakage
Leachate
Sewage Treatment Facility
Sludge
Treated effluent, Untreated storm overflow, System failure
Agricultural Runoff
Aquifer
Groundwater recharge
Surface/groundwater hydraulic connectivity
Illegal drug manufacturing and use
Leach ponds
Treated effluent
Manufacturing
Landfill
Leaching
Cemetery
Molecular Pharming
Aquaculture
"Straight-piping"
Spray Drift
Orchard
Farmland
Sorption to sediments
Physico-chemical alteration
Sunlight
Photoproducts
exposure
Metabolites
Biotransformation

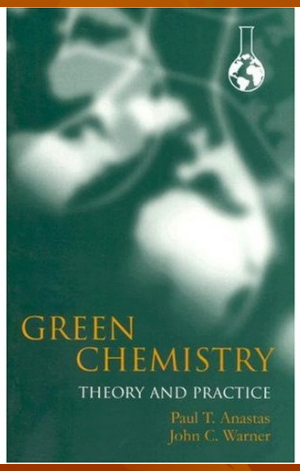
Environmental side effects of medication

- Non-target effects of medicines
- Antibiotics
- Metabolism to more active products

Drug Discovery and Development



Risk Reduction Options
Green Chemistry



"The design of chemical products and processes that reduce and eliminate the use and generation of hazardous substances".

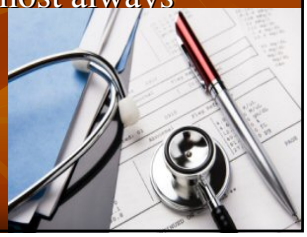
Follows a set of Twelve Principles of Green Chemistry to reduce intrinsic hazard

Risk Reduction Strategies
Manufacture and Distribution

- Emphasis on using renewable feedstocks
- Encourage biodegradable packaging

Risk Reduction Strategies
Prudent Prescribing Practices

- Educate the medical community on the potential environmental "side effects"
- Encourage the use of trial medications
- Antibiotics do not treat viral infections ("the common cold")
  - Bronchial infections in children almost always viral



Risk Reduction Strategies
Patient Education and Responsibility

Patient education:

Effective medical practice
(a pill is not always
necessary for every visit)

Environmental consequences of overprescribing

Risk Reduction Strategies Properly Disposing PPCPs

- Take-back programs
  - Incineration
- Disposal in household trash
- Flushing should be minimized because of potential environmental consequences
  - Balance between public health and environmental protection
    - Reducing diversion potential while minimizing environmental harm

Take-back/Return Programs

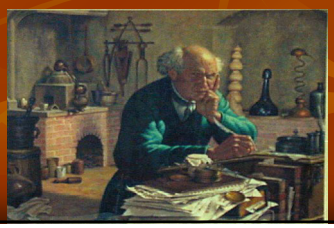
- Reverse distribution
- Hazardous waste recycling days
- Returns to pharmacy for residential customers
- Mail-back programs

Available National Options and Tools to Encourage "Green Pharmacy"

- Promote the use of green chemistry
- Change education
- PPCP stewardship programs

Conclusions

- The practice of "green pharmacy" has already begun
- Green pharmacy is a holistic, comprehensive approach to reducing the environmental footprint of PPCPs
- Paracelsus: "*Sola dosis facet venenum*"
  - **The dose makes the poison**



Pharmaceutical Disposal Issues and Actions Across the United States

Virginia Thompson
U.S. Environmental Protection Agency Region 3
(215) 814-5755
thompson.virginia@epa.gov

Visuals follow. Please contact the speaker for more information.

The many issues surrounding proper disposal of pharmaceuticals create complexity for individuals, healthcare providers, and governments. This complexity has led to a variety of stewardship approaches. This presentation will discuss the recommended disposal methods for individuals, the regulatory challenges for institutions, and the gray areas in between. The presentation will also provide a brief overview of stewardship programs and the changing statutory climate at the state and federal levels.

Pharmaceutical Disposal Issues and Actions Across the United States

Presentation to FSTRAC Meeting
October 22 2009

Virginia Thompson
EPA Region 3

Outline of Presentation

- Why there's pharm waste
- How we dispose of the waste
- Stewardship programs
- State & Federal legislation
- Source reduction

Who's Responsible for Pharms in the Environment?

- Pharm manufacturers?
- Government?
- Medical community?
- Individuals?
- Agriculture?

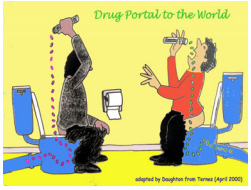
ANSWER:
(f) All of the above!

Why Is There Pharm Waste?

We don't use all of our drugs:

- Change prescriptions
- We feel better
- Doesn't work
- Death
- Bulk "economy size" OTC drugs

Disposal and Concerns



- Excretion by using drugs
  - Green Chemistry?
- Flushing leftovers
  - No longer recommended

- Trash
  - Reaches ground water thru landfill?
  - Diversion ("pharming" parties)
- Incineration—current best practice
  - Not available for individuals

Individuals

- Household hazardous waste exempt from regulation
- Federal Guidelines recommend:
  - Locating a collection site
  - Mixing with coffee grounds, kitty litter
  - Putting in nondescript container in trash

Institutions are Heavily Regulated

- RCRA P, U, & Characteristic waste
- DEA Controlled Substances (narcotics)—diversion issue
- State health & environmental depts.
- State Boards of Pharmacy
- Local sewage treatment plants

The *Blurry* Middle Ground: Both Individual & Institutional

- Hospices
  - Individual owns medications
  - Family must discard after death
- Long-Term Care Facilities
  - Chain of custody not regulated by DEA
  - State health dept. regulates
  - Facility has control over dispensing & disposing
  - Individual owns medications
- Diversion is primary concern

This All Adds Up To…..

What Communities Are Doing: Types of Stewardship Activities

- In response to public concern:
  - One-time consumer collection events
  - Short-term collection campaigns
  - Permanent collection locations
    - Pharmacies
    - Police stations
    - HHW facilities
  - Mail-back programs

Stewardship Around the Country

- Collection events:
  - New England, NY, PA, DE, VA, CA, Wisconsin, Chicago, Michigan, San Fran, many more over past year
  - R5 "1 million pills, 1 million pounds" Earth Day Challenge in 2008
  - Require police & pharmacist
- Permanent collection locations:
  - Washington State, Chicago, Los Angeles, others
- Mail-in programs:
  - Maine, Philadelphia, Wisconsin

Recent State Actions

- California "No Drugs Down the Drain" campaign Oct 2008
- New York educational campaign & website—"Don't Flush Your Drugs"
- New Jersey Guidelines on proper disposal
- Pilot Project in Potomac Watershed—Elder Expo in Frederick, MD Oct 2009

Stewardship Around the World

- European Union—"appropriate collection systems" for unwanted pharms
- Australia—program success based on clear, simple program
- Canada—program co-sponsored by pharmacies & pharmaceutical industries
- Japan—under development

Existing State Laws: Take-Back for Consumers

- Maine
  - Prepaid mailers
  - Drugs received by Maine DEA (unique in US)
  - 2007 state passed funding to match EPA grant; funds extended for 2 years in 2009
- California
  - All retail pharmacies must collect drugs for proper disposal

Proposed State Legislation

- Maine, Minnesota, Oregon, & Florida
  - Require pharm manufacturers to develop & pay for statewide collection programs
- Washington State
  - Similar bill did not move forward during 2009 session
- PA bill requires pharmacies to accept returned drugs
- California
  - Pharmacies to accept consumer drugs

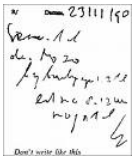
Bills in U.S. Congress—2009

- Safe Drug Disposal Act
- Secure & Responsible Drug Disposal Act
- Each has companion bill in US Senate

- HR 1262—Water Quality Investment Act
- PSI is monitoring all legislation:
  http://www.productstewardship.us/

Source Reduction Activities

- Growing recognition collections & mail-backs are labor-intensive, costly, & not sustainable
- Need sustainable, long-term solutions
- Source reduction efforts starting to blossom:
  - Maine & Medicare approved short-term initial prescriptions for 15 meds
  - EPA Region 3 working with partners to consider prescribing, dispensing, & insurance practices
  - Green chemistry to change how pharms are metabolized

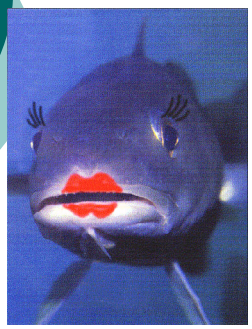


BlueCross BlueShield

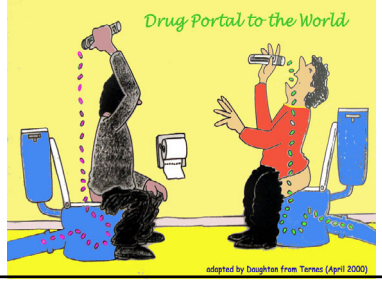
Relevant Web Sites

- www.epa.gov/ppcp
- www.epa.gov/waterscience/ppcp
- http://www.whitehousedrugpolicy.gov/publications/pdf/prescrip_disposal.pdf
- http://www.nj.gov/dep/docs/Prescription_Med_Disposal.pdf
- http://www.iisgcp.org/unwantedmeds/
- http://www.nerc.org/documents/operating_unwanted_medication_collections_final_2006.pdf
- http://www.productstewardship.us/displaycommon.cfm?an=1&subarticlenbr=540

Contact Info



Virginia Thompson
EPA Region 3
Thompson.virginia@epa.gov
215-814-5755



Questions

Q. Irene Dooley: What about the mail-back chain-of-custody? Aren't there concerns that it might not ever get back to the U.S. Drug Enforcement Administration?

A. Virginia Thompson: The Maine program is very specific. It goes to a state agency, called the Maine Drug Enforcement Administration. As I understand it, they are in pretty nondescript boxes. I forget if you call a 1-800 number. I know you do that in Wisconsin. You call a 1-800 number, and they write down what they will be expecting from you in the mail. In Maine, they have a tracking number, so there is a chain-of-custody.

C. Octavia Conerly: The envelope has a tracking number that they keep track of.

Research on Occurrence and Treatment Removal of Unregulated Contaminants from Drinking Water

Eileen Murphy
New Jersey Department of Environmental Protection
(609) 984-7944
eileen.murphy@dep.state.nj.us

Visuals follow. Please contact the speaker for more information.

National and state studies have reported the presence of hundreds of unregulated synthetic organic chemicals in surface waters, groundwater and finished drinking water. Among the contaminants found are pharmaceuticals and their degradation products, gasoline byproducts, pesticides, and consumer products. Although the levels detected are very low (approximately 1 ppb or less), researchers are unable to address the issue of cumulative risk from the consumption of mixtures of these chemicals.

Regulators traditionally have focused on developing drinking water standards on a chemical-by-chemical basis. This paradigm has served us well historically. However, the research shows that the issues facing the regulatory community today cannot be addressed using the traditional model. Today, scientists are finding numerous chemicals at low levels, rather than fewer, more common chemicals at relatively high levels. Clearly, the chemical-by-chemical, risk-based paradigm cannot address this new phenomenon.

Several new research studies being funded in total or in part by the NJDEP are investigating whether advanced water treatment methods can be used to effectively remove these organic contaminants. Two drinking water systems that rely upon ground water as their source will install carbon unit demonstration projects at their facilities. They were selected because they both contained high numbers of organic chemicals in raw water when they were sampled in previous studies. We will track the fate and breakdown of organics from the raw water to determine the optimal conditions for organics removal by the carbon over the course of several years.

A fundamental issue that these demonstration projects will address is how to measure the effectiveness of removal for the unregulated contaminants. If a treatment approach regulatory strategy is adopted, it is important to know how to monitor removal efficiency of the treatment.

Regulators and scientists are working together in NJ to determine ways to address the occurrence of unregulated chemicals in drinking water. How can the public be protected adequately while providing a reasonable approach to water systems? This talk will present some options that the state is considering and describe some of the on-going projects the state has funded to help regulators make policy decisions on drinking water contamination by unregulated contaminants.

FSTRAC 2009

Research on Occurrence and Treatment Removal of Unregulated Contaminants from Drinking Water

Eileen Murphy, Ph.D.

October 22, 2009

FSTRAC Fall 2009 Meeting

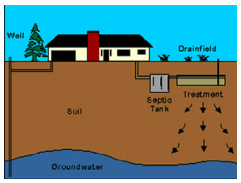
Today's talk

- **The early years… Unregulated contaminants in NJ waters and drinking waters: USGS & NJDEP**
- **What's going on now?**
  - **Demonstration Projects**
  - **Tailored Collaboration**
  - **Settlement of Environmental Penalty**
- **Treatment option?**

Unregulated contaminants in drinking water

Trace levels of organic chemicals found in finished drinking water

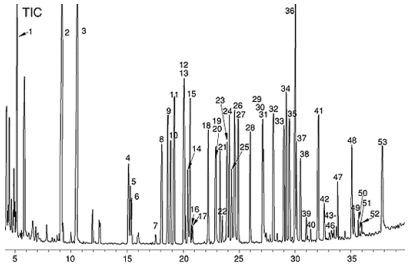
"Scanning" studies: Source: industrial, septic Groundwater



Drinking Water Studies
Source: wastewater, runoff
Surface Water

"TIC"
Tentatively Identified Contaminant

- **Certified method on "scanning" mode**
- **Required chemist review**
- **No standard**



Summary of Scanning Studies

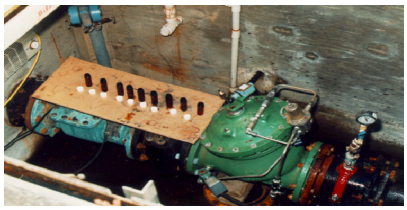
(1 of 3)

- Analytical methods capable of detecting unregulated compounds at ultra-trace levels (below one ppb)
  - 600 TICs in NJDEP-EOHSI study
  - Most in raw samples
- QA procedures vital for interpretation of results
  - Compounds in both samples and blanks
  - Compounds sometimes in blanks
  - False positives and negatives possible

Summary of Scanning Studies

(2 of 3)

- TICs occurred in systems where regulated compound concentration elevated
  - No TICs in control system
- Some compounds pass through existing water treatment
  - 51 TICs in raw and finished water

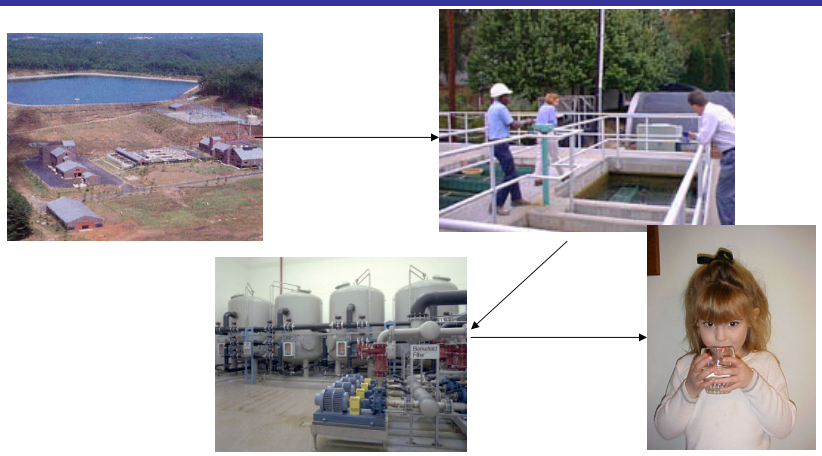


Summary Scanning Studies

(3 of 3)

- Some compounds are present in finished water but not in raw water.
- Only a fraction of detected compounds have standards, guidelines, or criteria
- Systems with carbon treatment had fewer TICs in raw & finished pairs than systems with air stripping only

Surface Water Studies



Summary of Surface Water Studies

(1 of 3)

- Advancements in analytical technology have given us the ability to detect previously unmonitored contaminants at ultra-trace levels,
- 60 of ~110 OWCs were detected in one or more stream samples,
- Most frequently detected compounds include pharmaceuticals, pesticides, fragrances, flame retardants, and plant/animal steroids,
- Stream concentrations were generally sub-ppb and did not exceed established aquatic-life criteria,

Summary of Surface Water Studies

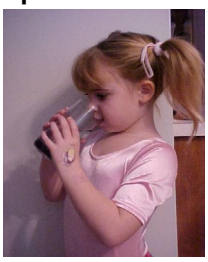
(2 of 3)

- Preliminary data indicate that some OWCs can survive conventional water-treatment processes and occur in finished water at sub-ppb levels that do not exceed drinking-water standards,
- At most locations, OWCs occur as mixtures of 2 or more compounds,
- Findings from these studies corroborate those of the USGSs National Reconnaissance Survey and other similar U.S. and European studies.

Summary of Surface Water Studies

(3 of 3)

- **Different types of advanced treatment can reduce levels of parent compounds.**
- **Parent compounds may metabolize into degradation products.**

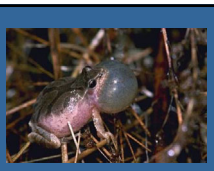


Toxicity Review

- Are these chemicals harmful?
- Follow-up to the studies
- Many compounds have little or no information
- School of Public Health toxicologists reviewed existing literature

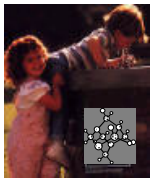
Findings of Toxicity Review

- Focused on 300 of the 600 tentatively identified compounds from the screening study.
- Reference Doses (RfD) or Minimal Risk Levels (MRL) were available for 15 of the chemicals
- Toxicology data was available for an additional 54 chemicals.
  - Of these 54 chemicals, repeated dose toxicology studies were available for 25 chemicals.
  - Acute toxicology data was available for the other 39 chemicals.
- Toxicology data could not be located for the remaining 221 chemicals.

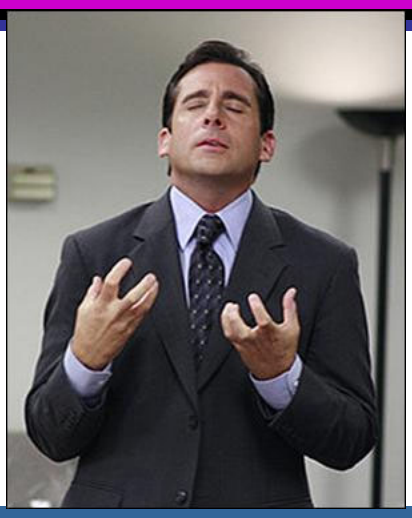


So What?

- What are the human health effects?
- What are the ecological effects?
- What are the cumulative effects when more than one compound is present?



So what do we do?

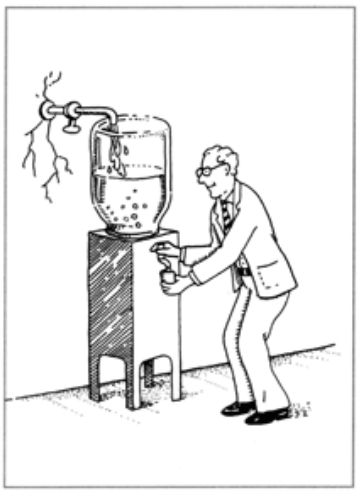


Think....

Drink dirty water?

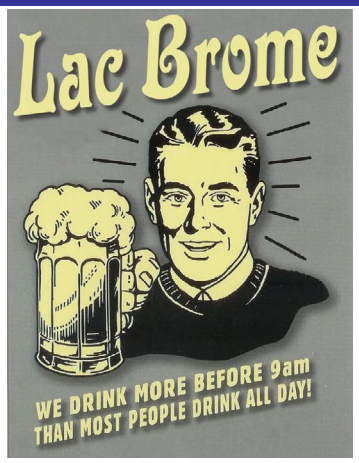
Drink Bottled Water?

Pretend to drink bottled water?

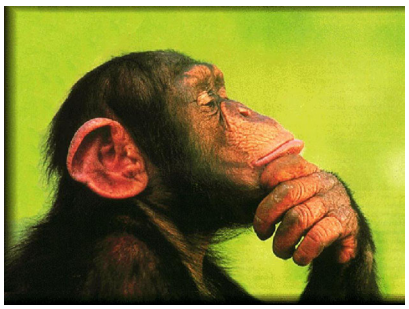


"Boy, there's nothing like spring water."

Drink more beer!



Treat the Water



- What type of treatment?
- How do we know treatment is working?
- What's the regulatory approach?

State Response

- Determine extent of exposure
- Consider options for removing exposure
- Continued fate & transport studies
- Water treatment studies

5 Options

- Chemical-specific
- Chemical class - health endpoint
- Chemical class - chemical class
- Intensive Site Remediation tracking
- Barrier treatment on selected systems (aka "treatment" approach)

Treatment Option

- **Interested Party Review**
  - **Treatment Option**
- **Literature Review: treatment options**
- **Demonstration Projects**
- **Tailored Collaboration**
- **Settlement Agreement**

Activities for Treatment Option

Literature Review: DWQI

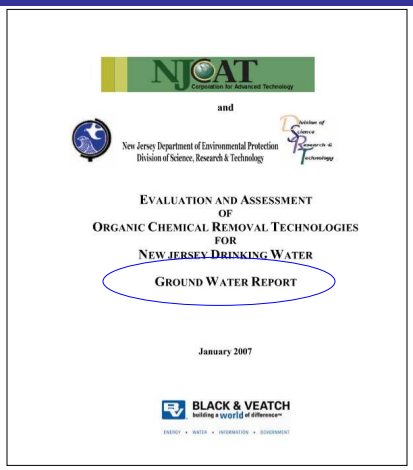
Black & Veatch

Optimal water treatment for surface water systems

Optimal water treatment for ground water systems

Private wells?

Literature Reviews



NJCAT Corporation for Advanced Technology

and

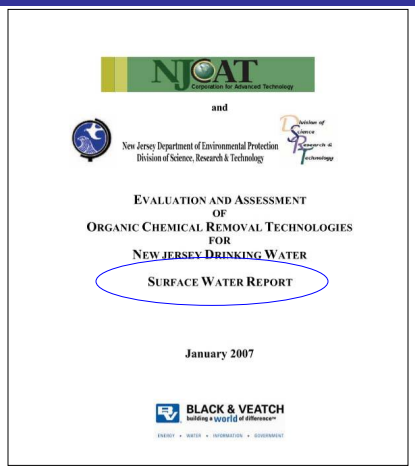
New Jersey Department of Environmental Protection
Division of Science, Research & Technology

EVALUATION AND ASSESSMENT
OF
ORGANIC CHEMICAL REMOVAL TECHNOLOGIES
FOR
NEW JERSEY DRINKING WATER

GROUND WATER REPORT

January 2007

BLACK & VEATCH
building a world of difference.



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EVALUATION AND ASSESSMENT
OF
ORGANIC CHEMICAL REMOVAL TECHNOLOGIES
FOR
NEW JERSEY DRINKING WATER

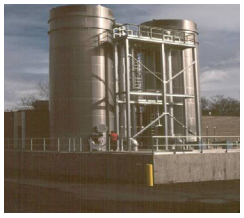
SURFACE WATER REPORT

January 2007

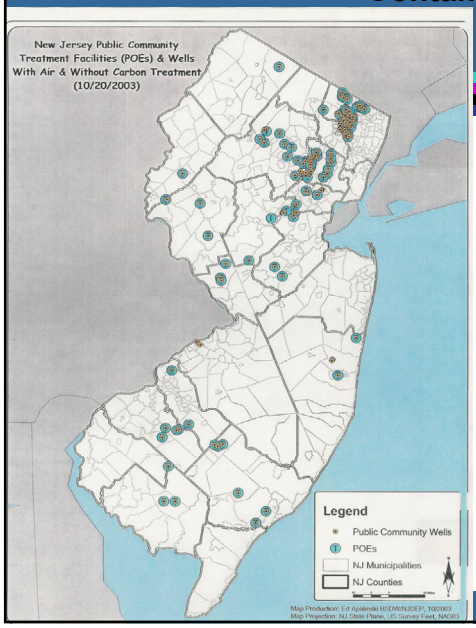
BLACK & VEATCH
building a world of difference.

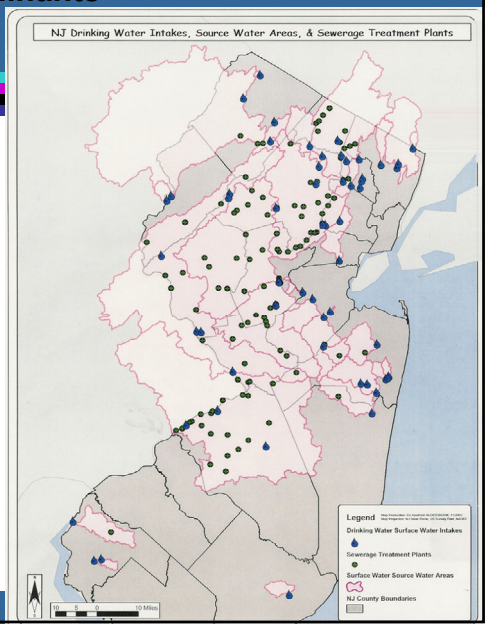
Treatment

- **Adsorption processes**
- **Oxidation processes**
- **Aeration processes**
- **Membrane processes**
- **Biological processes**



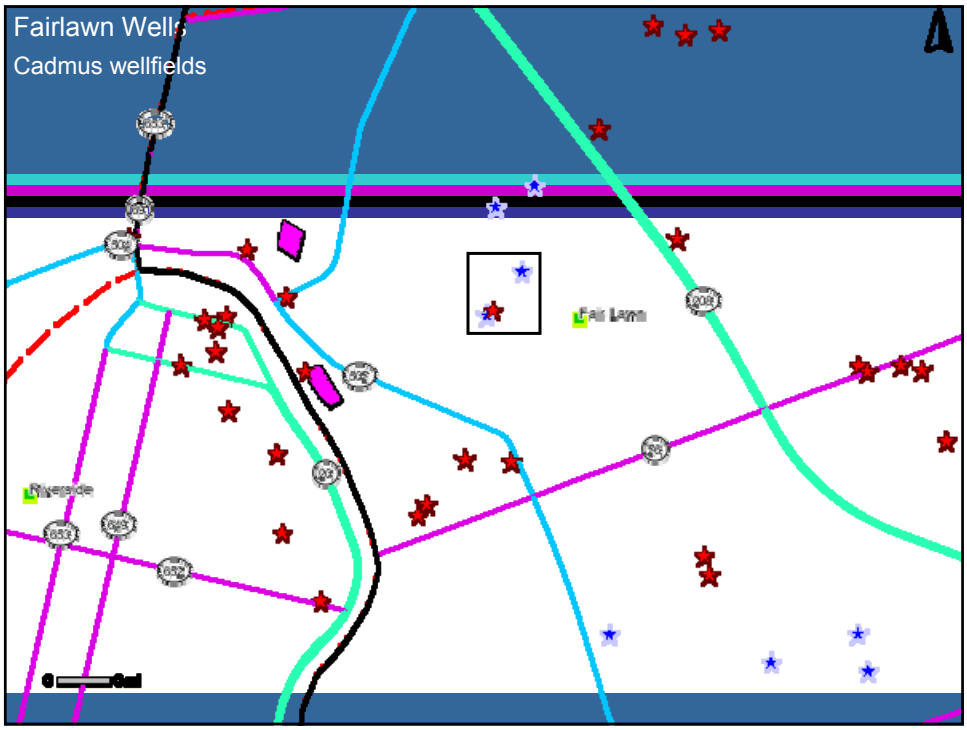
Systems Vulnerable to Contamination by Unregulated Contaminants

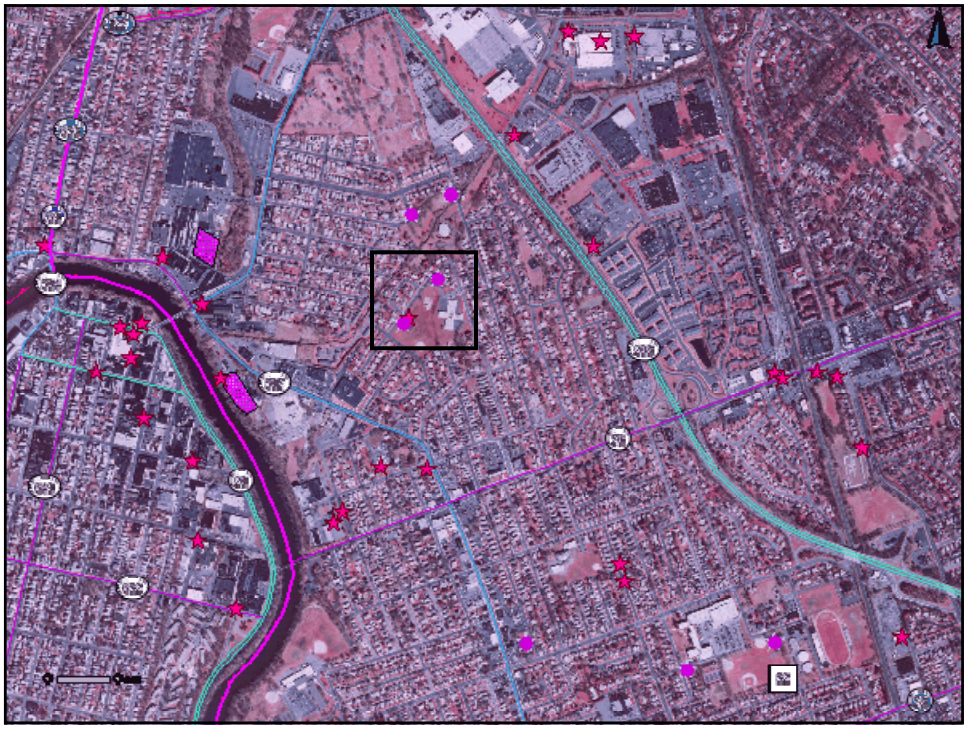


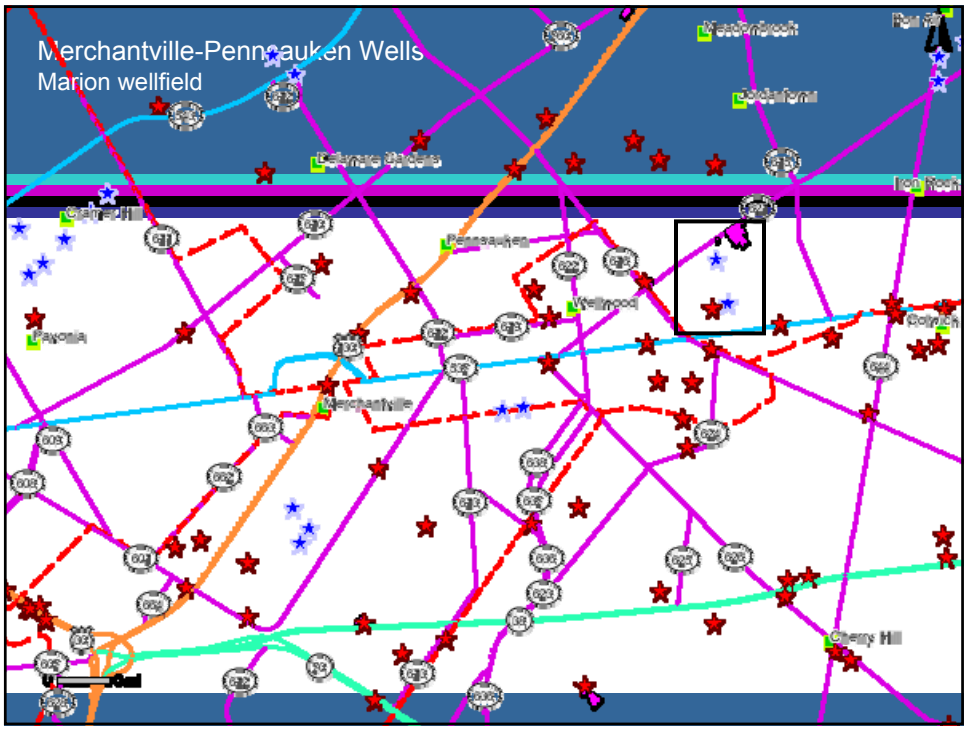


Ground water Demonstration Projects

- **Geographic:**
  - **Fairlawn (Bergen County)**
  - **Merchantville-Pennsauken (Camden County)**
- **Based on numbers of chemicals**
- **Full-scale carbon treatment units**
- **State-funded with 5 year commitment**
- **Regulated & unregulated analyses**






Merchantville-Pennsauken Wells
Marion wellfield
Pennsauken
Merchantville
Cherry Hill

Collaborative Efforts

- **Tailored Collaboration**
  - **USGS, Black & Veatch, NJDEP, various water surface water systems**
  - **Extensive monitoring of raw and throughout treatment train - advanced treatment**

Settlement Agreement
(USGS, NJDEP, NJ American Water)

- **Penalty toward project**
- **USGS methods**
- **NJ American**
  - **Raw**
  - **Treatment train**
- **Several facilities**
- **USGS methods**

Federal Treatment Studies

http://www.epa.gov/ppcp/projects/persistence.html
Last updated on Wednesday, May 9th, 2007.

Pharmaceuticals and Personal Care Products (PPCPs)

You are here: EPA Home PPCPs EPA PPCP Research Persistence of Contaminants

Persistence of Contaminants from Wastewater Discharges During Drinking Water Treatment: Identification of Compounds and Degradation/ Disinfection Byproducts, Evaluation of Removal, and Potential Exposure

Project Purpose:
To determine the effect of different drinking water treatment technologies on compound removal by examining the occurrence and fate of pharmaceuticals and other wastewater derived compounds through drinking water treatment.

Project Description(s):
Compounds in wastewater discharged from a treatment plant or septic system have the potential to end up in surface or groundwater that may ultimately be used as a source of drinking water. Two different sampling plans will be implemented to determine the presence of these chemicals in drinking water. In Phase 1, the source and finished waters of 9 - 15 drinking water treatment plants, known to be impacted by wastewater, will be sampled. The residence time of the plant will be taken into account during the sampling to give meaningful estimates of removal. The samples will be analyzed using existing USGS methods for pharmaceuticals and wastewater compounds, as well as by two new methods currently under development at the USGS. The first new method will consist of pharmaceuticals not currently included in the existing methods; the second will focus on chlorination and degradation byproducts of wastewater contaminants. Phase 2 will be a more intensive investigation of two to four drinking water treatment facilities. Residence time-weighted samples will be collected throughout the treatment train to obtain an understanding of the removal efficiency at each treatment step; the samples will be collected seasonally, to determine if there are changes in: (1) the number and concentrations of compounds present in the source water; and (2) treatment efficiency over the course of a year.

Project Outcomes:
This work will assist the USEPA's Office of Water in determining which compounds should be included in future Unregulated Contaminant Monitoring Regulation (UCMR) sampling plans. Knowledge of the occurrence and persistence of these compounds will become increasingly important in the future as the demands on potable water sources increase and communities turn to approaches such as water reuse to supplement their drinking water supply.

Contact
Susan Glassmeyer at glassmeyer.susan@epa.gov

http://www.epa.gov/ppcp/projects/evaluation.html
Last updated on Wednesday, May 9th, 2007.

Pharmaceuticals and Personal Care Products (PPCPs)

You are here: EPA Home PPCPs EPA PPCP Research Evaluation of Drinking Water Treatment Technologies

Evaluation of Drinking Water Treatment Technologies

Project Purpose:
The purpose of this project is to provide information necessary for the selection of drinking water treatment techniques that provide for optimal EDC removal and subsequently reduce human exposure to EDCs. In order to be able to evaluate the ability of conventional and advanced drinking water treatment processes to remove EDCs, appropriate analytical methods for the selected EDCs in several water matrices must be available or developed. Additionally, the applicability of bioassay(s) to evaluate the removal/presence of compounds with endocrine activity in water samples pre- and post-treatment will be evaluated.

Project Description(s):
This project investigates the efficacy of various drinking water treatment processes in removing EDCs from source waters. The project has three components. The first is the development of appropriate analytical methods for the EDCs being evaluated. Initially, a set of steroid hormones are being studied, followed by a group of alkylphenolic compounds. The second component is the application of a reporter gene assay, the MVLN assay, to evaluate the presence of estrogenic activity in water samples. The third part of the study is to conduct bench-scale experiments to evaluate the removal of EDCs by drinking water treatment processes.

The analytical method for the selected steroids has been developed and the method for the alkylphenols is currently being developed. Bench-scale studies are being conducted to evaluate the removal of steroid hormones by coagulation and granular activated carbon (GAC) adsorption. Jar tests have been conducted to evaluate the ability of coagulation, alone and in combination with powdered activated carbon (PAC) or chlorine, to remove three estrogens from Ohio River water. None of the estrogen removals following coagulation were significantly different from zero. The addition of PAC resulted in removals ranging from approximately 20 to 80 percent. Treatment of the estrogens with chlorine resulted in removals of approximately 98 percent. However, this removal is due, at least in part, to chemical transformation of the estrogens. GAC isotherm studies, using ethynylestradiol and three types of GAC, indicate that the steroids will be strongly adsorbed. However, the isotherm studies required long equilibrium times which suggest that the rate of adsorption was very slow. To further investigate the GAC adsorption kinetics, GAC column studies are currently being conducted. The results of the MVLN assay have been consistent with the analytical results for the isotherm samples, as would be expected following adsorption onto GAC.

Project Outcomes:
This ongoing research will provide information on the ability of various drinking water treatment technologies to remove EDCs that may be present in source waters. The initial phase of this work, the determination of the treatability of reproductive hormones, was conducted at the request of the Office of Ground Water and Drinking Water (OGWDW). The results of this research will be used by OGWDW, the states and municipalities, and drinking water utilities for selecting optimal EDC removal processes and subsequently reducing human exposures to EDCs.

Contact
Kathleen Schenck at schenck.kathleen@epa.gov

Future Directions

- Use results of new work to inform possible regulatory action.
- Encourage treatment at wastewater discharges (prevention)
- Encourage research on toxicology of mixtures of contaminants (EOHSI)

Research

Follow the work being done by

- USEPA
- AWWA
- USGS
- Dept. of Defense
- Dept. of Agriculture
- Academia

Questions?

I'm all ears.

Organic Waste-Water Contaminants (OWCs) in New Jersey Streams and Their Removal at Drinking-Water-Treatment Plants

Jeff Fischer
U.S. Geological Survey
New Jersey Water Science Center
(609) 771-3953
fischer@usgs.gov

Visuals follow. Please contact the speaker for more information.

Organic Waste-Water Contaminants (OWCs) in New Jersey Streams and Their Removal at Drinking-Water-Treatment Plants

Jeffrey M. Fischer[1], Paul Stackelberg[2], Kristin *Romanok[1], Jacob Gibs[1], and R. Lee Lippincott[3]*

[1]U.S. Geological Survey, 810 Bear Tavern Road, West Trenton, NJ 08628
[2]U.S. Geological Survey, 425 Jordan Road, Troy, NY 12180
[3]New Jersey Department of Environmental Protection, Trenton, NJ 08628

What OWCs Were Studied?

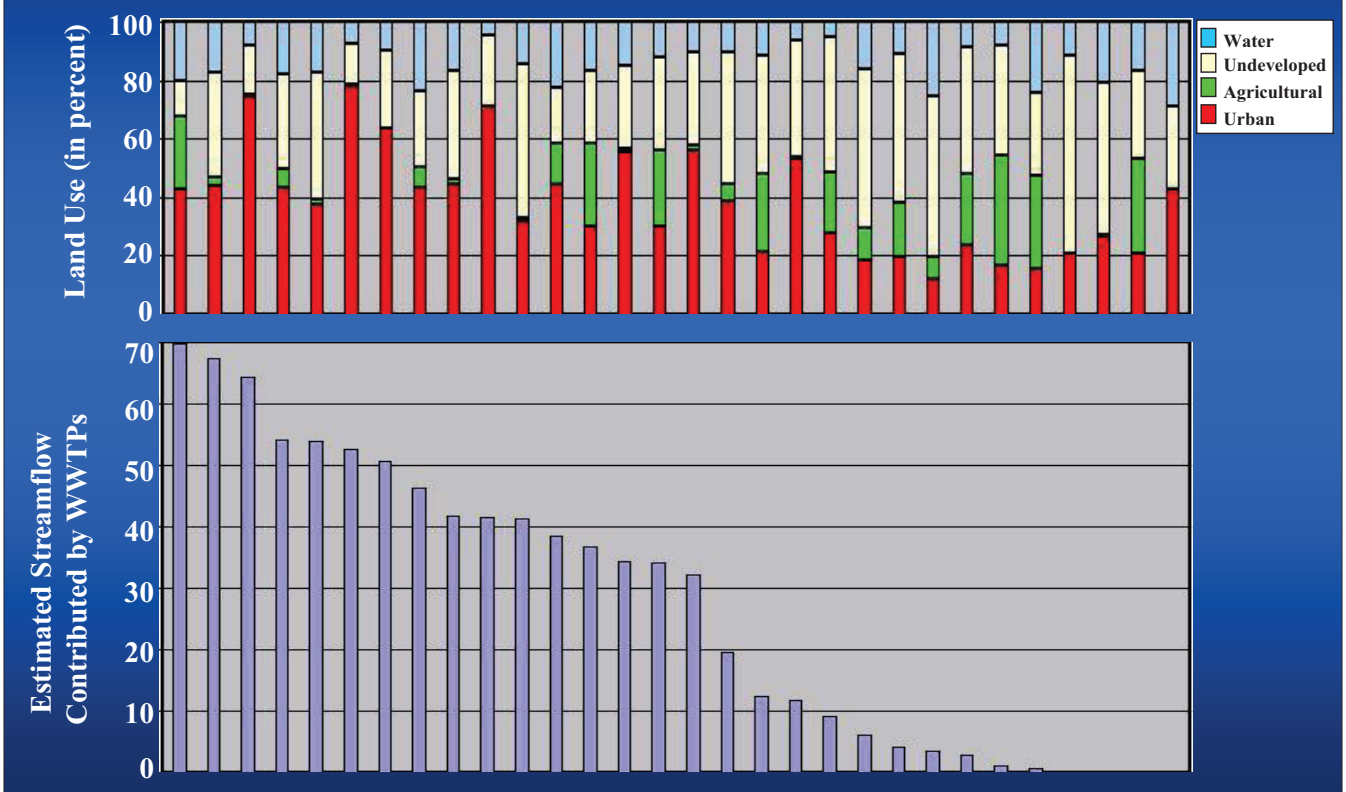
Selected ~110 widely use ones.

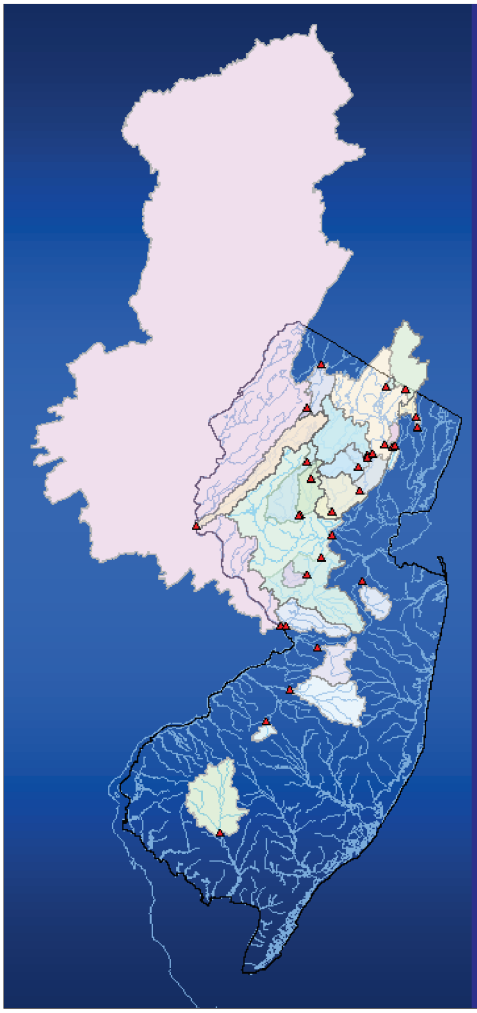
- Antibiotics
  - Tetracyclines (6)
  - Fluroquinones (4)
  - Macrolides (3)
  - Sulfonamides (6)
  - Others (6)
- Pharmaceuticals
  - Prescription (14)
  - Non-prescription (8)
- Industrial and household use chemicals
  - Fragrances and Flavorants (8)
  - Flame Retardants (3)
  - Antioxidants (2)
  - Fuel-Related Compounds (4)
  - Detergent Metabolites (7)
  - Plasticizers (3)
  - Disinfectants (2)
  - Solvents and Preservatives (4)
  - Pesticides (12)
  - Plant and Animal Steroids (4)
  - PAHs (6)
  - Other (8)

Organic Wastewater Contaminants (OWCs) in New Jersey Streams

- Determine the occurrence, distribution, and concentration of the targeted compounds in New Jersey's streams.
- Determine whether the concentration of these compounds vary spatially as a function of land use, or point or non-point sources.

Vulnerability Gradient



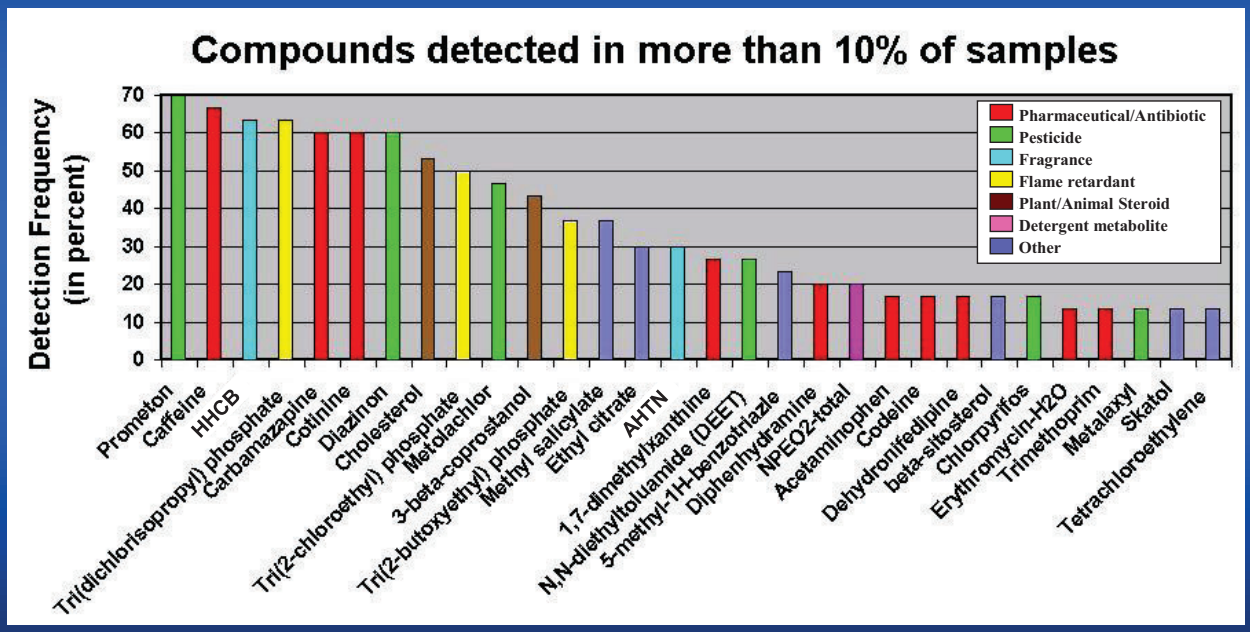


Synoptic Survey
30 Sampling Sites

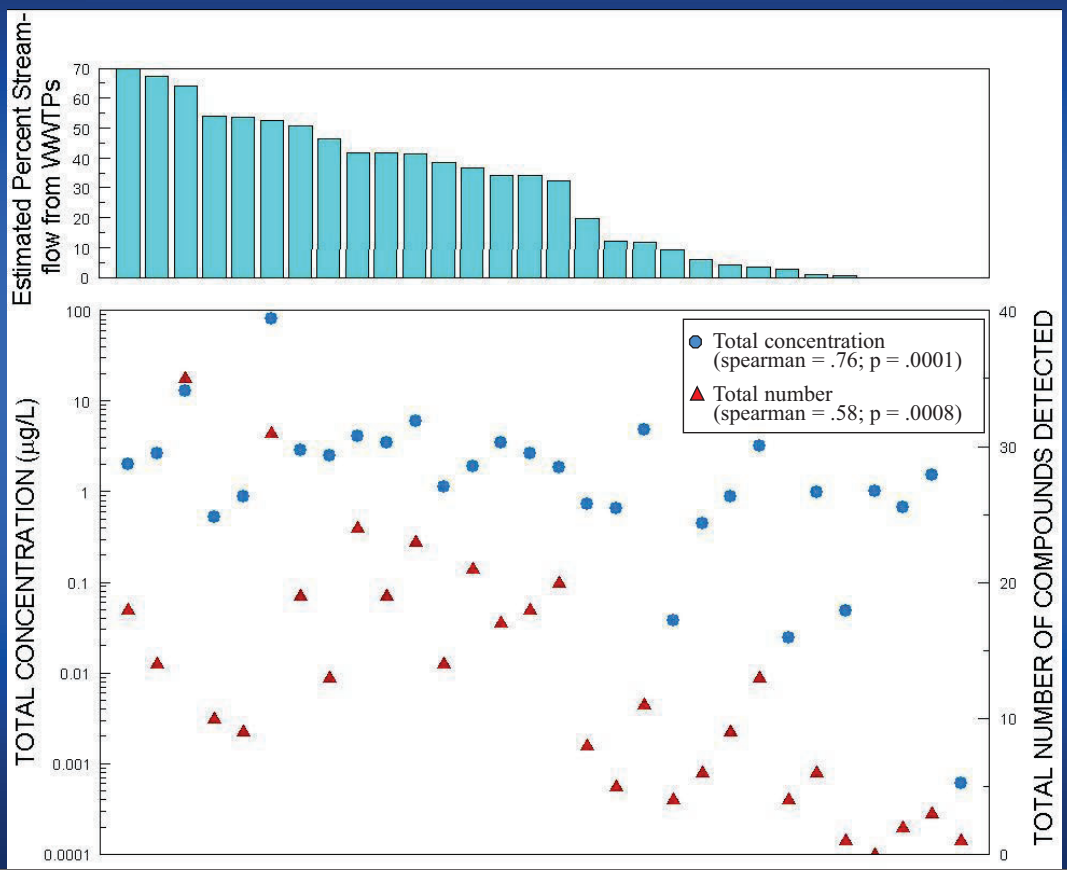
Assunpink Ck @ Trenton
Passaic R @ Pine Brook
Hohokus Bk @ Paramus
Dead R nr Millington
Passaic R @ Little Falls
Hohokus Bk @ Ho-Ho-Kus
Singac Bk @ Singac
Passaic R nr Chatham
Lamington R (Black R) nr Ironia
Peckman R @ West Paterson
Rockaway R @ Pine Brook
Matchaponix Bk @ Spottswood
Millstone R @ Blackwells Mills
Whippany R nr Whippany
Raritan R @ Queens Bridge
Whippany R nr Pine Brook
N. Branch Raritan R nr Chester
Beden Bk nr Rocky Hill
Ramapo R nr Mahway
N. Branch Raritan @ Burnt Hills
Wallkill R nr Sussex
Musconetcong R @ Riegelsville
N. Br. Rancocas Ck @ Ewanville
Lamington R @ Burnt Mills
Delaware R @ Trenton
Crosswicks Ck @ Extonville
Cupsaw Bk nr Wanaque
Maurice R nr Millville
Wallkill R @ Sparta
Haynes Ck @ Lake Pine

- 30 drainage basins sampled in the fall
- 11 sites listed in blue were sampled seasonally
- Basins ranged in size from about 6500 mi² to less than 4 mi²

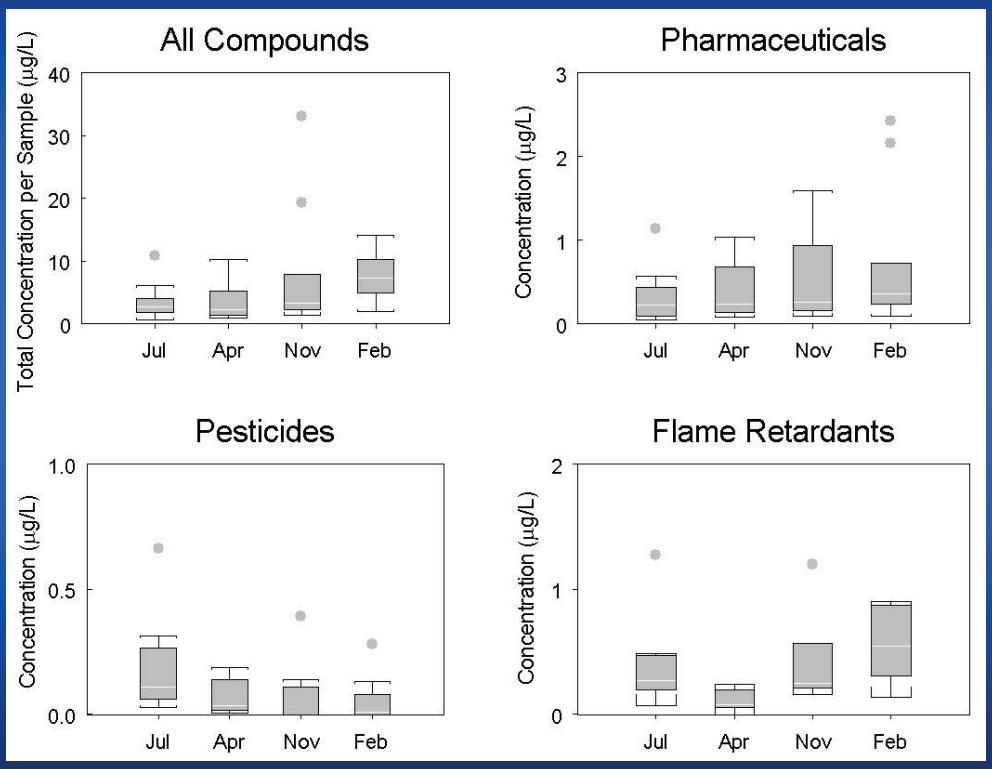
Most Frequently Detected Compounds in NJ Stream Synoptic Survey



Relationships between OWCs and Waste-Water Treatment Plant Discharges



Seasonal Variability in Concentration



New Jersey Study – Major Findings

- 1 or more OWCs detected at 97 percent (29 of 30) of sites.
- Primary classes of compounds detected include prescription and nonprescription drugs, pesticides, fragrances, and flame retardants.
- 90% of samples contained more than 1 OWC and 50% of samples contained 11 or more OWCs.
- Concentrations generally low (sub-ppb) and did not exceed established drinking-water guidelines, health-advisories, or aquatic-life criteria.
- Guidelines, advisories, and criteria not established for many of the compounds detected.

Fate of OWCs at two Drinking-Water Treatment Plants

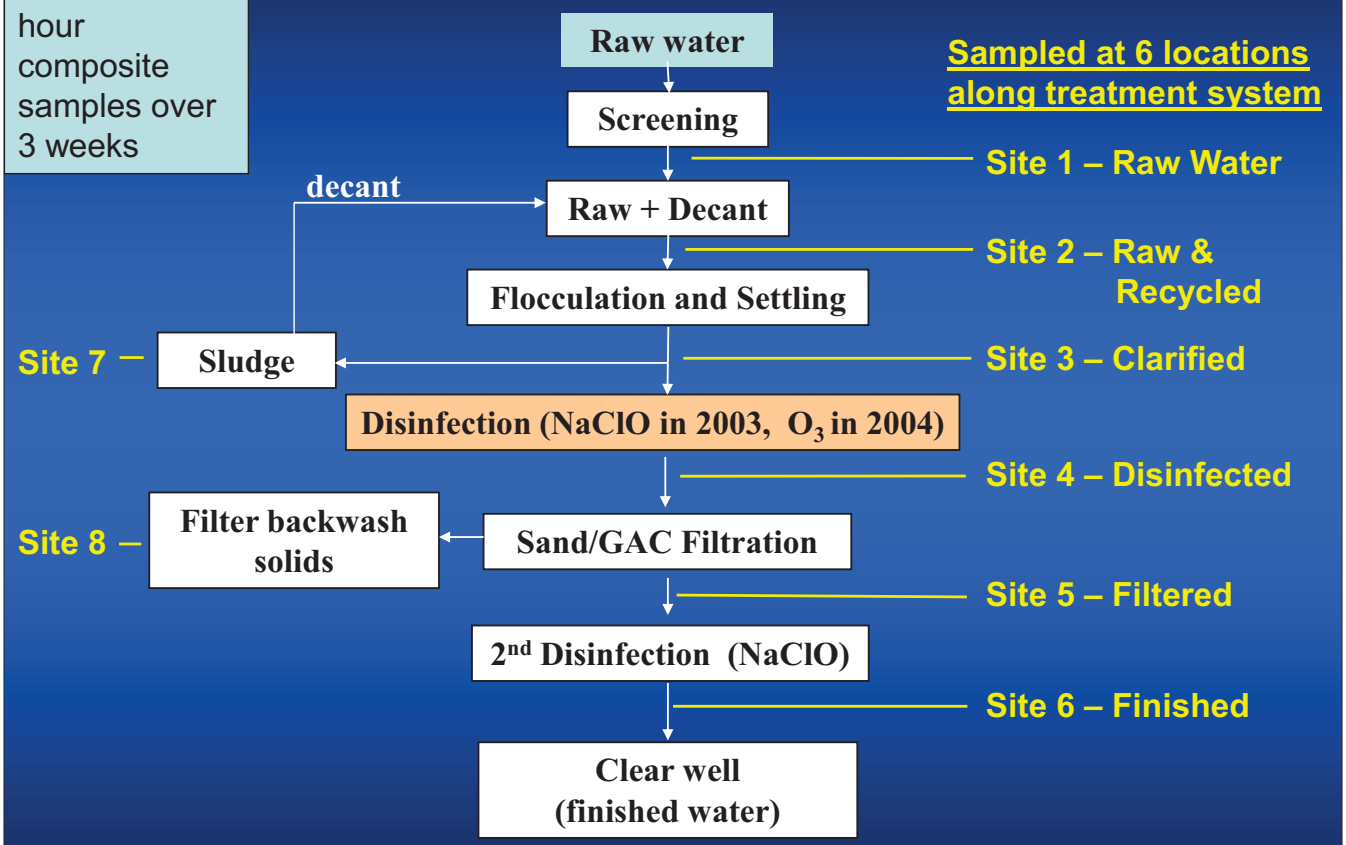
Identify the primary physical or chemical processes that govern the fate of OWCs at a drinking-water treatment plant

Are OWCs removed and, if so, are some processes more effective at removing them that others?

USGS
science for a changing world

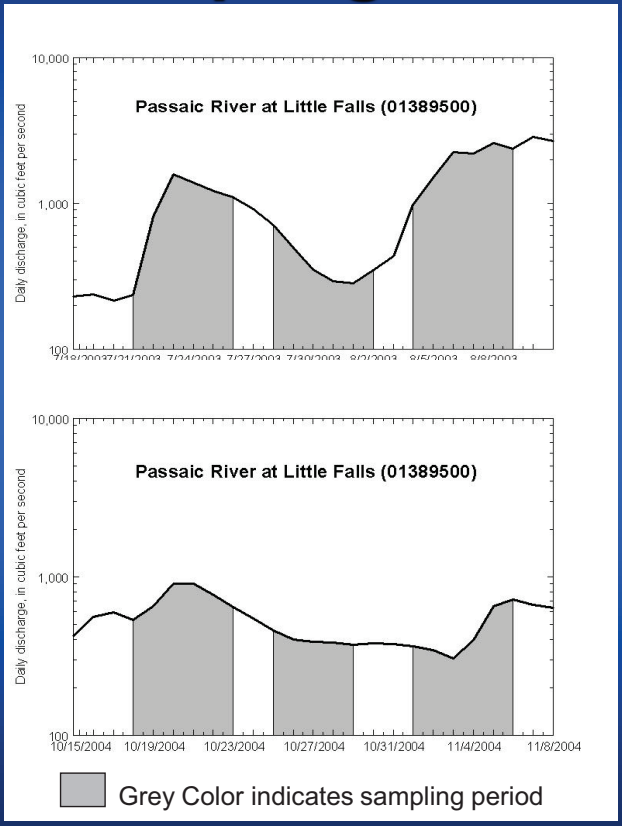
Plant and Study Design

Collected 24 hour composite samples over 3 weeks



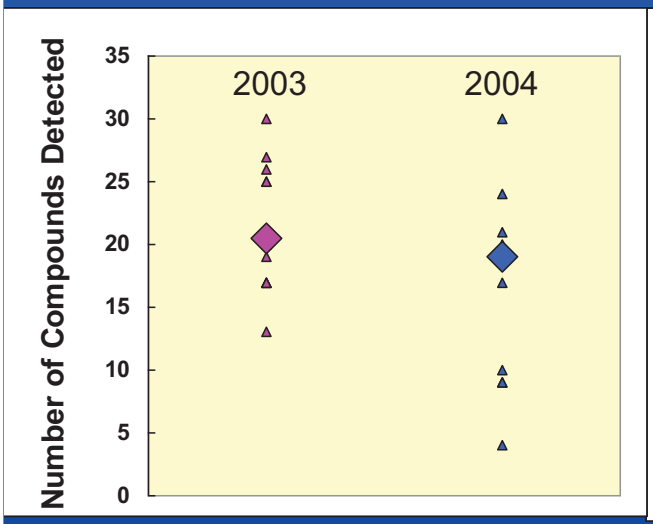
Sampled before & after switch from chlorine to ozone disinfection

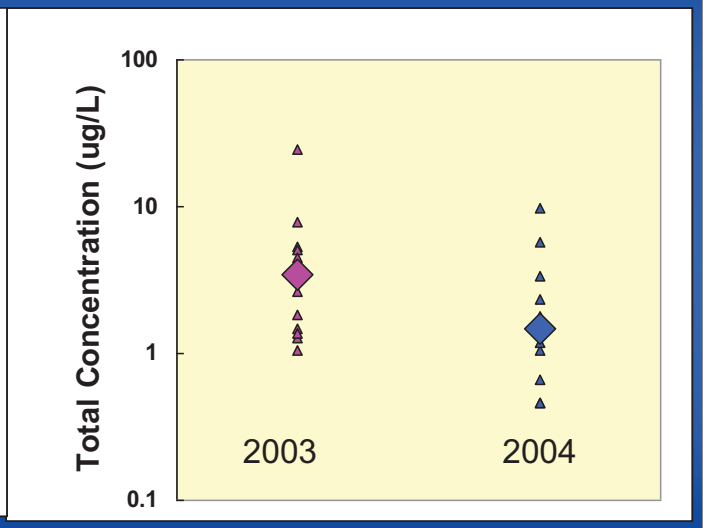
Sampling Conditions 2003 & 2004



- Time of year
  - 2003 July-Aug
  - 2004 Oct-Nov
- Stream Flow
  - 2003
  - 2004
- Analytical

Differences in Compound Detections and Concentrations in Raw Water 2003-2004

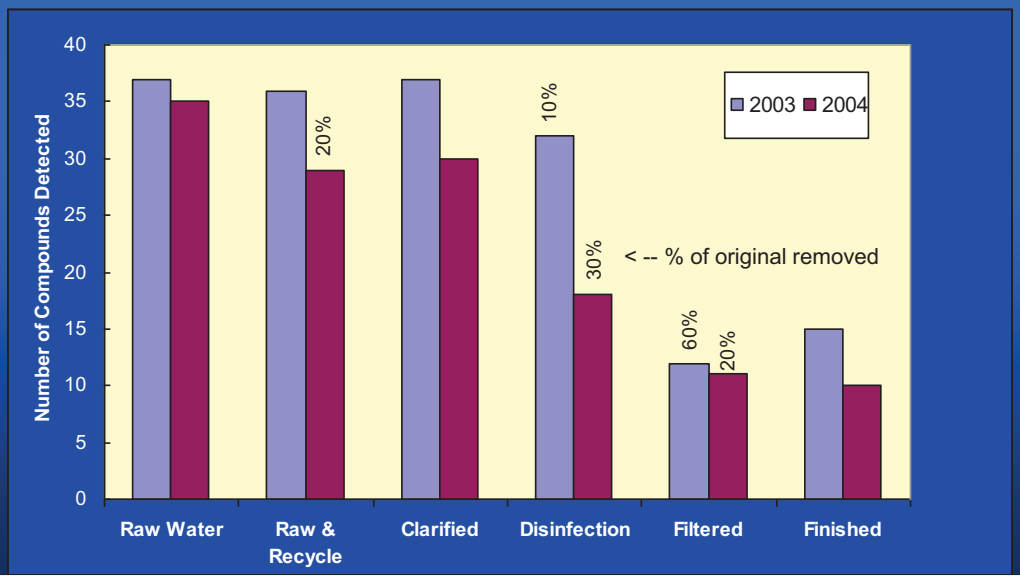




24 hour composite samples collected over 3 weeks

OWC Removal at Different Treatment Stages

- For both years approximately 75% of detected OWCs were no longer detected by final treatment stage
- Ozone was more effective at removing OWCs than chlorine
- Activated Carbon in filters removed many of remaining OWCs
- Typically 5 to 8 OWCs detected in finished water

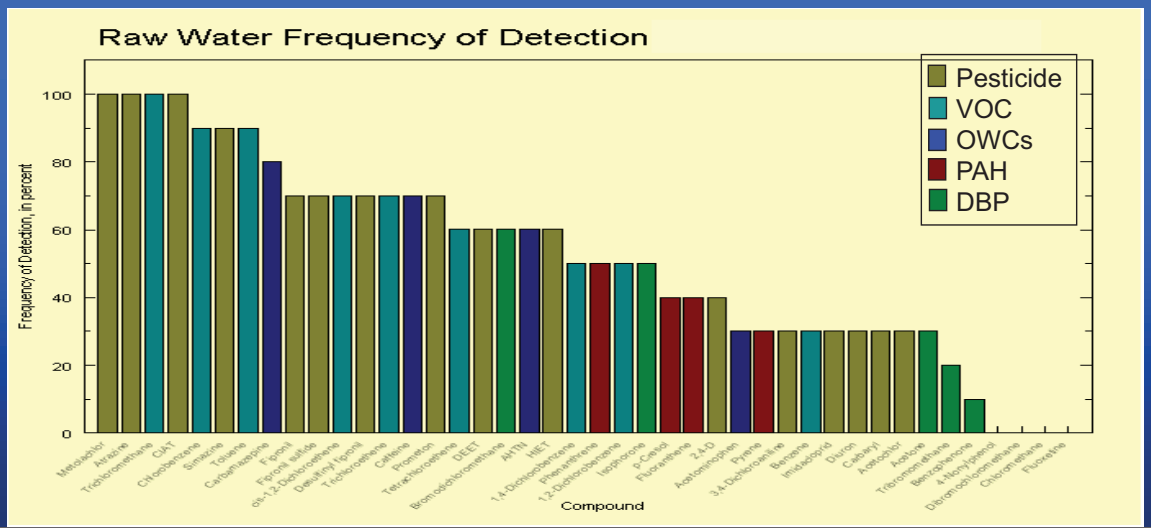


At another treatment plant ….

Sampled raw and finished water at intake for conventional and advanced treatment plants at same time

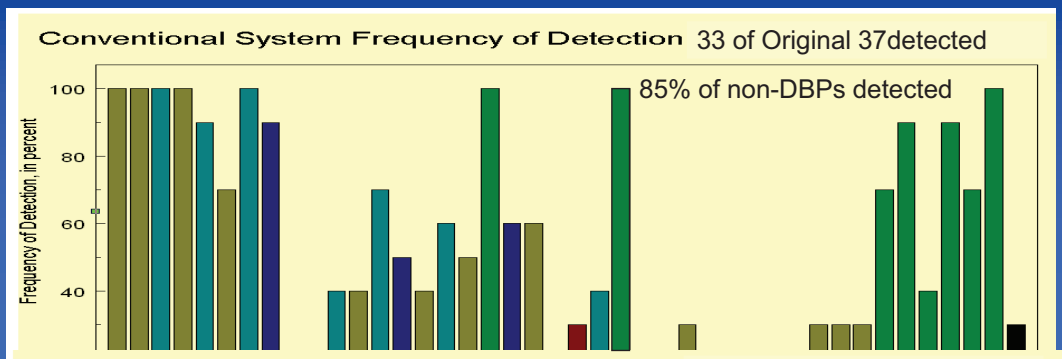
Sampled for more VOCs, DBPs, and pesticides

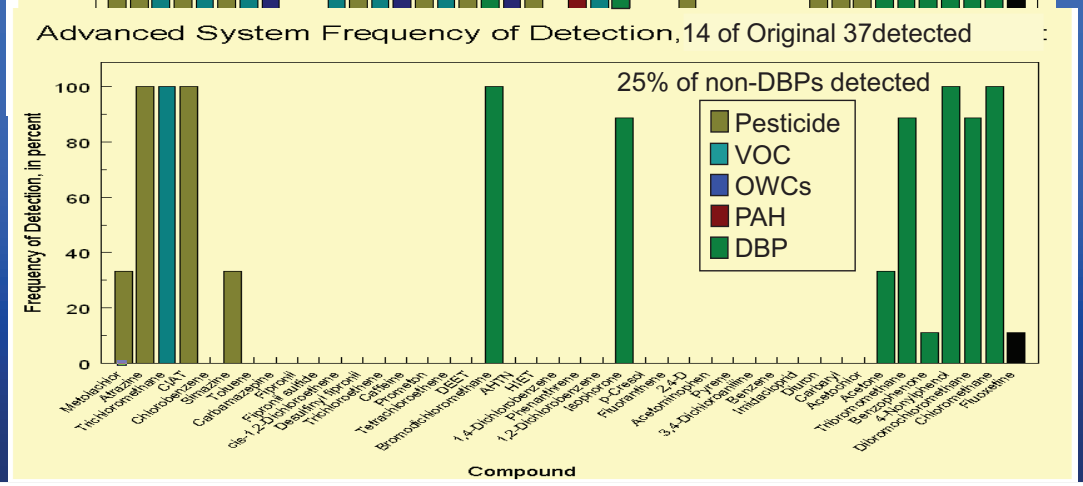
- 37 compounds detected more than 20% time
- Primarily Pesticides and VOCs
- Very few detections of OWCs



Removal in finished water

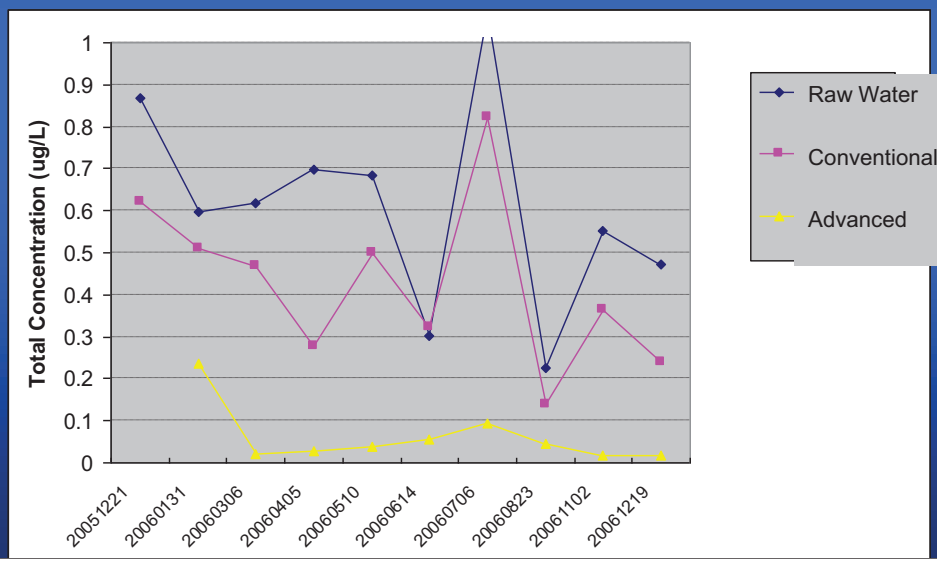
Question remains as to whether OWCs completely mineralized, or just converted to something else?

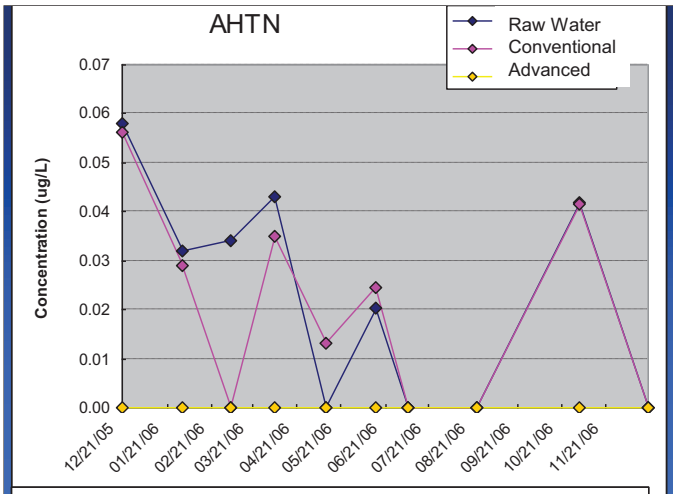


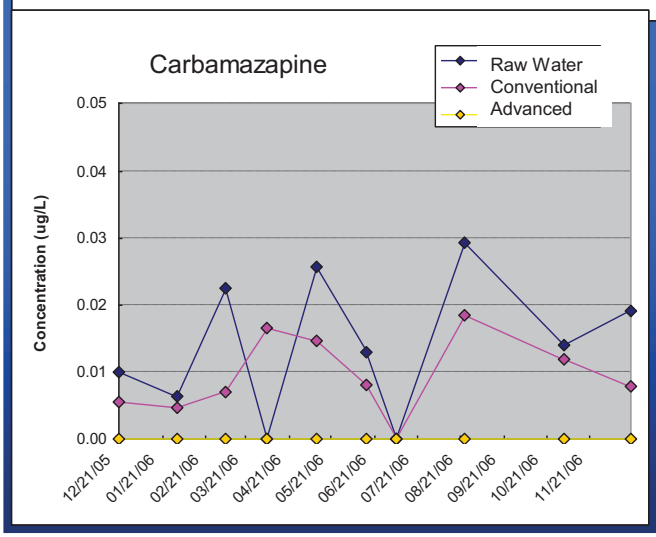


Reductions in Concentrations in Finished Water

- Advanced treatment typically reduced total concentration in raw water by 60% to 90%
- Conventional treatment typically reduced total concentration in raw water by zero to 40%

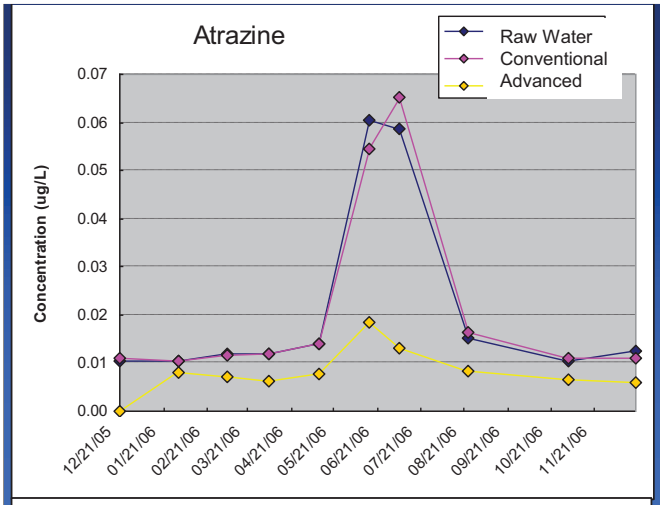


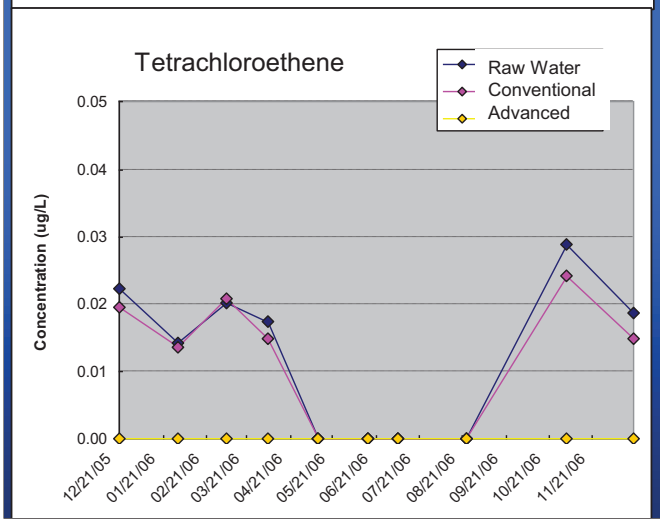




OWCs

- Little or no reduction in concentrations at Conventional Plant
- Most removed at Advanced Treatment Plant
- Other frequently detected OWCs include caffeine, and acetominophen

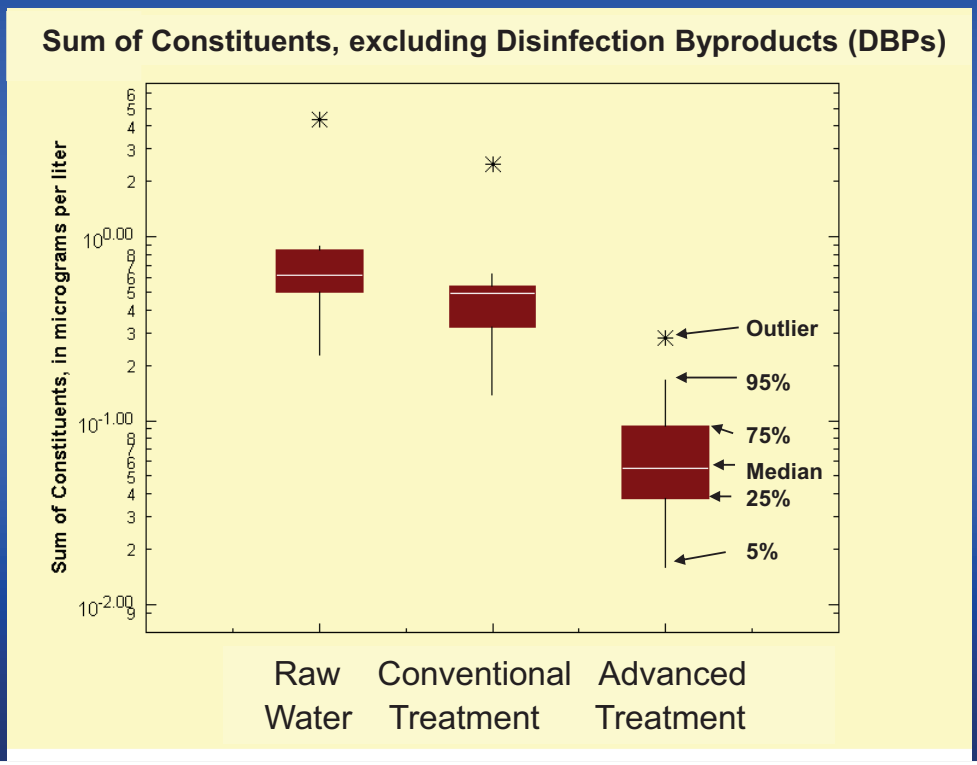


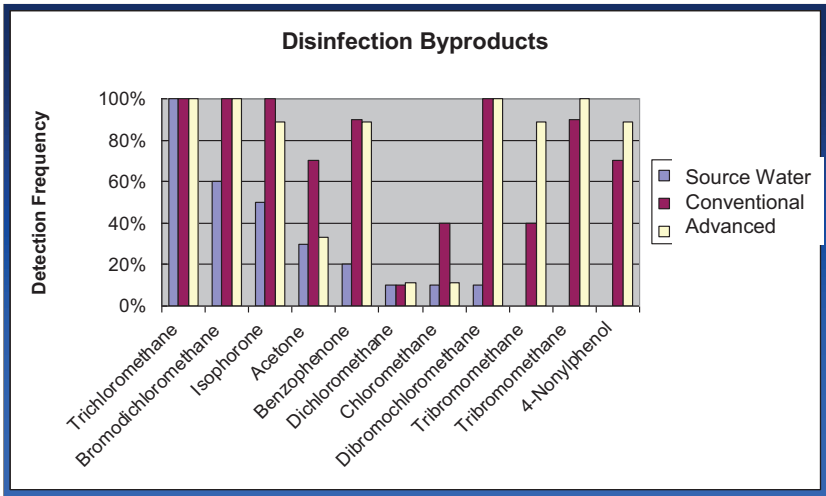


Pesticides & VOCs

- Little reduction in concentrations at Conventional Plant
- Concentrations reduced at Advanced Treatment Plant

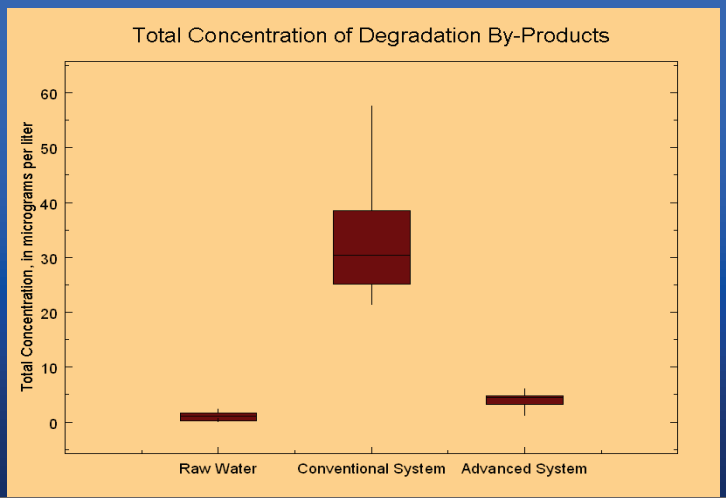
Overall reduction of concentrations in finished water of compounds originally detected





Disinfection Byproducts in Finished Water

- Increased frequency of detection and concentrations in finished water
- Advanced plant concentrations are lower than conventional plant primarily due to reduced concentrations of Trichloromethane, Bromodichloro-methane



Major Findings

- **Conventional treatment plants were least effective at removing OWCs.**
- **Ozone was more effective than chlorine at removing compounds and reducing concentrations.**
- **Activated carbon filters removed many compounds ozone and chlorine missed.**
- **5 to 17 compounds were detected in samples of finished water.**
- **Concentrations in finished water were low (usually less than 0.05ug/L), and treatment processes reduced concentrations from 30 to 100 percent.**

OWC studies in New Jersey

2001 Drinking water treatment plant (DWTP) study – determine if OWCs removed.

2002 Stream Survey – Determine how frequently OWCs detected in streams and at what concentrations.

2003/4 DWTP study –Follow-up to original study to determine if OWCs more effectively removed by chlorination or ozonation.

2006 DWTP study – Simultaneously sample two DWTPs, one using conventional treatment and the other using advanced ozonation and activated carbon filtration.

2008 Follow-up to above study to determine which specific processes responsible for removal of OWCs.

2010 AWWARF study to expand scope of above to 5 more treatment plants.

2010 Follow-up of stream survey to look at sources/removal in waste-water treatment plants.

2010 Sampling shallow aquifer near septic systems to determine if OWCs detected.

Questions?

Jeff Fischer
fischer@usgs.gov

Additional information on other USGS OWC studies across the Nation

USGS Toxics program
toxics.usgs.gov

USGS NAWQA program
water.usgs.gov/nawqa/swqa/

Pharmaceuticals, Personal Care Products, and Unregulated Contaminants
Round Table Discussion

C. Octavia Conerly: If anyone has any questions for Ed or myself, Scott, Rhonda, Mark, Nick, Virginia, Eileen or Jeff, please let us know.

Q. Bob Howd: In Mark's slides 20 and 21, under the vitellogenin male to female ratio, there are various numbers, and I have no idea what those numbers represent. Could you clarify what those numbers are?

A. Mark Ferrey: I went over that rather quickly. The numbers in those slides are basically what amounts to a ratio between the vitellogenin induction observed in the male fish to the female fish but expressed in terms of percent. So, if you look at slide 20 at White Sand Lake, and it says 105, it means that the male fish were producing 105 percent of what the female fish were producing in terms of vitellogenin.

C. Bob Howd: Okay, thanks.

Q. Scott Stoner: I have a couple of questions. One is for Virginia. One of your slides talks about a requirement in California to return drugs to pharmacies. Is that for non-controlled substances only because of the federal restriction? Or did they get some type of a waiver?

A. Virginia Thompson: There's both a law that took effect a couple of years ago and one that is pending. I believe that they are both for non-controlled only because of DEA's restrictions.

Q. Scott Stoner: We all say that incineration is the best. That's what out experts at NYS DEC tell me and what we've basically all said today. One question that I've had from an environmental group is how well has that been documented that there are not for instance transfers through other media, particularly through the air from incineration. Has anyone asked or gotten an answer to that question?

A. Octavia Conerly: Well, Scott, people are shaking their heads no. I don't know of any studies that have looked into how or what ends up in the air after drugs are incinerated. Have you, Virginia?

A. Virginia Thompson: No, and we've tried to engage the Air Program on this question and I don't know they've looked into enough to be able answer it very well. I think it is certainly an outstanding question that we don't know the answer to yet.

Q. Scott Stoner: I have a question for Nick Anastas. Nick, you had a great point about teaching, I think you called it environmental pharmacy, to nursing students, pharmacy students, and medical students. Can you flesh that out at all? Any suggestions for details? I gave a lecture to a fifth-year jurisprudence class for Pharm.D. students, and I've got an opportunity to, I think, influence curricula or to at least get something like this in there. I'd be interested to learn more about what you are thinking.

A. Nick Anastas: Scott, I actually taught a class at UMASS–Boston in the green chemistry graduate program, and it was called green chemical design. Essentially, I went over the synthetic process, toxicology, risk assessment, global warming, global climate change, and environmental chemistry. So, I put everything together for those green chemists. With a few tweaks to that, we can give it to pharmacy schools and medical schools. So there is actually a syllabus I can share with group, if they want it.

C. Scott Stoner: I would be very interested in that.

C. Nick Anastas: Okay.

Q. Gary Ginsberg: I have a question for Mark Ferrey from Minnesota. When I looked at the data comparing PPCPs in seasonally busy lakes versus the more pristine lakes and see the increase in PPCPs in these seasonally busy lakes, it just made me wonder about the ground water in those communities. Mark, do you have any sense of what the ground water detections would look like relative to your lakes in Minnesota that had fairly robust levels of bisphenol A (BPA) in the 20s of ppb? Do you think that reflects what the ground water looks like in those communities? And then a more general question, I guess for anybody is, how do we develop a sensible testing strategy for understanding ground water detections? Do we look for areas with high percentage of private septic systems, do we look for areas that have nursing homes and hospitals that are on their own sewage systems? How do we understand ground water contamination?

A. Mark Ferrey: That's a really good question and I'm not sure anyone has the real answer for you. We certainly don't here. A couple of points I'd like to make. First of all, the detections that we saw in the lakes that I showed you and I should have pointed this out as well is that, that is not statistically reliable data. In other words, any differences that we would try to draw between lakes, or between uses, or anything like that, we would not be able to support statistically, because there is a very small samples size. We just sampled one time. Really, what we are talking about is a snapshot in time, and we might go back a month later and find very different concentrations. That is the very first thing that I think is important to point out. But, you raise a really good point in that we don't know what is existent in surrounding ground water around these lakes or really for that matter, much of anywhere. Kathy Lee did a study in Minnesota in 2002 that I alluded to a little bit where she and her group looked at ground water from a few different sites around the state and in proximity to landfills and did come up with some of these compounds. I can't recite them offhand. There is some work that's been done there, just not a lot. We're going to be pursing that further down the road.

Q. Gary Ginsberg: Are you going to be looking at ground water in these lake communities?

A. Mark Ferrey: It's not necessarily lake communities although just about wherever you go in Minnesota is a lake community. We're going to be selecting a number of wells from different, primarily shallow, aquifers and doing similar analysis on the ground water from those wells but not necessarily just focusing on lake communities. These are going to be fairly randomized wells that we have in monitoring networks, primarily around the Twin Cities, but a little bit in other parts of the state as well.

C. Gary Ginsberg: I guess we saw the potential to sample lakes as an indicator of regional ground water quality, as integrators of what is in the neighborhood and also as a way of not saying to somebody, "you've got X concentration in your well, and we don't know what that

means." If you sampled a lake, there is less onus on a public health official to say what that necessarily means on an individual basis. So, we actually are thinking about sampling lakes, and we are wondering what the correlation would be or how much that indicates what is in the local ground water. I just wanted to put that out there.

C. Mark Ferrey: Just very briefly, I would be very hesitant to draw any kind of conclusion on what is in ground water from what is in lake water. The reason is that you are really talking about two different environments. Many of these compounds will sorb very highly to organic carbon, I would imagine, or to different iron minerals and so forth, in aquifers. If they do make it to ground water, you really don't know what the fate is going to be in the ground water system. You don't know how mobile they are going to be. Whereas, they are going to behave much differently in a surface water system. I would think that without some sort of a study to show that "if you have these kind of compounds in surface water, you can find X percent of that in ground water," I'd be pretty hesitant to make that kind of a leap.

Q. Irene Dooley: I have two questions for Mark and a couple of questions for Octavia. Mark, on slides 20 and 21 of your presentation, it looks like there are different indicator fish for different lakes. Did you find any reason why shiners were better than minnows sometimes?

A. Mark Ferrey: No, the blanks on those vitellogenin concentration tables really mean that we didn't collect enough fish of that species to analyze. It really doesn't mean anything more. So, in some lakes, we didn't have any perch or any shiners, but we did have, say, sunfish or something like that.

Q. Irene Dooley: Mark, you mentioned the difference between the oligotrophic lakes in the north and south. Did you find any geological differences in the lakes? Did you find any correlation between type of lake and what you found?

A. Mark Ferrey: No, that was one of the things that we really didn't seem to find. The oligotrophic lakes seemed to show the same presence of these kinds of compounds as the mesotrophic lakes. They really didn't seem to sort out on the basis of location or trophic level. That actually was a surprise to me and I think to my colleagues as well. From my point of view, probably the greatest number of these compounds are in urban lakes, but we really didn't see that. We also saw a lot of these compounds in the oligotrophic lake in northern Minnesota. It didn't seem to break down according to type or location, other than what I showed you.

Q. Irene Dooley: Thank you, Mark. Octavia, I had wondered about the endocrine disruptor screening program. How were those compounds identified? Did the public have any notice? Also, what kind of data availability will there be from them?

A. Octavia Conerly: The list of 67 chemicals were chosen based on four different exposure pathways. All 67 chemicals either had three or four exposure pathways. The exposure pathways were food, water, occupational, and one other one that they considered. That is how they chose the first 67 chemicals. The EDSP is required to test all pesticides, so eventually they are going to test all pesticides no matter what they are. Regarding the Notice of Data Availability, I believe that was all published in the *Federal Register*.

Q. Irene Dooley: What about the data from test results? Also, did the public have an input on the selection of chemicals that were not pesticides?

A. Octavia Conerly: They all are pesticides, but the public did have input on the approach and on the draft list. I'm not sure whether the results from the testing will be made public. I would assume that it will be, but I really don't know.

C. Robert Lippincott: I attended an EPA Region 2 green chemistry meeting where they had pharmaceutical representatives from the region up in New York City. I really came away with it with the impression, being a synthetic organic chemist myself (I've taught that at a college in New Jersey), that the classically trained organic chemists were being bashed because we didn't consider green chemistry. When I walked away from the meeting, I started to think about the new jump to green chemistry. It wasn't really clear in my mind when we talk about green chemistry, what are we actually saying. Are we saying that we want to synthesize environmentally benign therapeutic agents or are we saying that we want to develop synthetic reaction mechanisms that are benign? Because when I hear about enzymatic processes, being a chemist, I wonder how efficient they are and how much yield you get from the process. Typically, when you use something nasty to synthesize something, you are talking about a very minute quantity. It might be a chiral synthetic reagent that you've used. Now, you translate that into some biochemical production phenomenon and now you are starting to talk about a volume increase. So, this is emerging and I understand it, and I applaud it because it hasn't been considered in the past. But I think we need something more than green chemistry to use as a definition of what we are talking about.

C. Nick Anastas: I think that green chemistry is only one aspect of this whole life cycle analysis. Green chemistry is getting at and offering additional opportunity for synthetic chemists. Did you have a toxicology course in your training as a synthetic chemist?

C. Robert Lippincott: No.

C. Nick Anastas: The person that I worked with used to brag about sticking his hands in trichloroethylene up to his elbows and using arsenic and cyanide and everything else. I think that is what we are trying to get away from in green chemistry. You have to maintain efficacy and reduce hazard. So, it's a very delicate balance. For example, the low hanging fruit is substituting an organic solvent with water, so you are using an aqueous solution. That's an easy one. Another one would be using ionic liquids as opposed to volatile organic solvents. Also, looking at using atom economy as opposed to looking at the yield of a synthetic reaction. But this is only one piece. One of the more difficult aspects of green chemistry is designing pharmaceuticals that are functional and break down in the environment into innocuous compounds. That is one of the most difficult aspects of the green chemistry challenges. It is young, but there have been successes. Green chemistry is not the be all and end all, but it is a good start, and it is slowly making its way into the curriculum. So, we won't slam you brown chemists, as we call them behind closed doors. A good example is R.B. Woodward who was one of the more prolific synthetic chemists of the 20th Century. He had a 29-step synthesis for strychnine. Why would you want to synthesize strychnine? It's already available. It's a poisonous compound. He just wanted to show that he could do it. That's what we want to get away from. If you look at the end product and it's toxic, if it contributes to global warming, if it explodes, or if it's a developmental or reproductive toxin, you don't even want to synthesize that compound. But synthetic chemists, I don't believe adopt that before they synthesize a compound. So, this is kind of retraining and offering other opportunities that toxicologists have.

Q. Patrick Levallois: I was interested in most of the talks. Particularly, I would like to know, following the workshop that you presented, organized by EPA with the National Research Council (NRC), there were some recommendations regarding the need to try to look more efficiently to identify for instance classes of drugs posing greatest risk, departure from chemical by chemical assessment of risk, explore efficient and effective screening tools, and so on. This workshop was held one year ago. So, what has been done since then? Is this progressing?

A. Octavia Conerly: We have several work assignments in place right now to look at prioritizing pharmaceuticals and ways to group them, whether it be by classes, categories, mode of action, therapeutic classes, or other reasons. We have work assignments in place to do that right now. We don't have any results yet, but we are moving forward to look at those things.

C. Ed Ohanian: I know you are very much surprised, but we started on it the next day. Not only that, also FDA and EPA got together actually to look into this effort regarding the clustering and screening. That's another thing that happened. I hope that by the middle of next year, we will have some sort of results. Because FDA collected all the data, instead of us creating new information, it was much better to have that kind of collaboration.

C. Octavia Conerly: If there are no further questions, that ends our session. Tomorrow the meeting starts at 8:15 a.m. Thank you for your attention. Thanks to all our presenters. We're adjourned.