Analytical Methods (and Their Challenges) for Pharmaceuticals and Personal Care Products in Water

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Outline

- Introduction
- Analytical methods at MWD
  - List of analytes
  - Quality assurance/quality control
- Method comparison
- Upcoming project on analytical methods
- Summary

Analytical Methods for PPCPs in Water

- **Sample Concentration**
  - **Solid Phase Extraction (SPE)**
- **Compound Separation**
  - **Gas Chromatography (GC)**
  - **Liquid Chromatography (LC)**
- **Compound Detection and Quantitation**
  - **Mass Spectrometry (MS)**
  - **Tandem Mass Spectrometry (MS/MS)**

PPCPs: Analytical Challenges

- What do you look for?
  - Universe of chemicals of potential health concern numbers in the tens of thousands
- Standard analytical procedures not available
  - Diverse structural and physiochemical properties
  - Extensive sample preparation
  - Sophisticated instrumental procedures
- Extremely low detection levels are needed.
  - Nanogram per liter levels (ng/L) - ppt
  - QA/QC protocols critical

Analytical Methods at MWD

Sample Collection

- 3 liters per sampling site
- Pre-cleaned, 1-liter amber glass bottles
- Sodium azide as the biocide
- Ascorbic acid as the quenching agent
  - Degradation of some analytes was observed in the samples with residuals not quenched
  - The majority of the analytes were stable in the presence of ascorbic acid and sodium azide for a period of 28 days
- Field blanks to assess potential contamination

Sample Preparation: Solid Phase Extraction (SPE)

- 500 mL sample volume
- Concentrates contaminants onto a solid sorbent
- Desorbs contaminants prior to instrument analysis
  - Same technology used in other standardized drinking water methods (e.g., nitrosamines, pesticides)

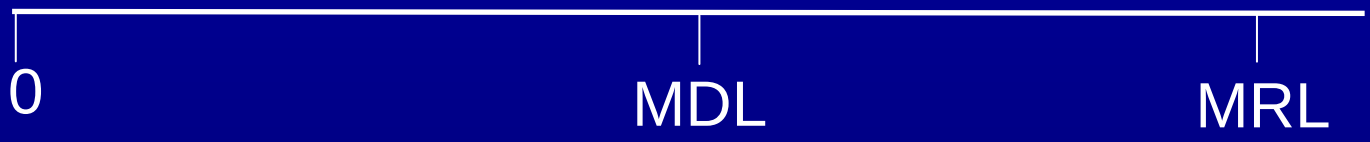
Gas Chromatography/Mass Spectrometry (GC/MS)

- Technique used to qualitatively and quantitatively identify compounds
- Used for many regulated contaminants in water
  - Volatiles (e.g., TCE, toluene)
  - Semi-volatile compounds (hydrocarbons, pesticides)
- PPCPs
  - May require compound derivatization
  - Doesn't work for some of the more water soluble and higher molecular weight compounds

Liquid Chromatography/Tandem Mass Spectrometry (LC/MS/MS)

- Used to qualitatively and quantitatively identify compounds
  - Applicable to highly water soluble and higher molecular weight compounds not amenable to GC/MS
  - May experience matrix effects (suppression or enhancement)
- PPCPs
  - MS/MS improves analysis
  - Isotopic standards
- Technology not currently used for any regulated compounds in water

Method Detection/Reporting Levels



- **MDL**
  - **Statistical determination**
  - **Produces a signal >0 with 99% probability**
- **MRL**
  - **3 to 5 times the MDL**
  - **Practical and routinely achievable quantitation level**

List of Analytes: GC/MS

Class	Compound	Use	MRL (ng/L)
Industrial By-Product	Anthracene	PAH	10
	Benzo[a]pyrene	PAH	25
Pesticide	Triazines: Atrazine, Cyanazine, Cyprazine, Propazine, Simazine	Pesticides	20
	Atrazine-Desethyl	Atrazine Degradate	20
	Atrazine-Desisopropyl	Atrazine Degradate	20
	g-BHC (Lindane)	Pesticide	10
	DDD	”	20
	Methoxychlor	”	20
Personal Care Product	Bisphenol A	Material used to make plastics	30
	DEET	Insect Repellent	20
	Nonylphenol	Surfactant	50
	Octylphenol	”	20
	Parabens (butyl, ethyl, methyl, propyl)	Antibacterial	20

List of Analytes: LC/MS/MS

Class	Compound	Use	MRL (ng/L)
Pharmaceutical	Carbamazepine	Anti-seizure	1
	Diclofenac	Anti-inflammatory	5
	Dilantin	Anti-epileptic	5
	Primidone	Anti-seizure	2
	Gemfibrozil	Anti-cholesterol	5
	Ibuprofen	Pain killer	10
	Sulfamethoxazole	Antibiotic	1
Personal Care Product	Triclosan	Antibacterial	5
	Caffeine	Stimulant	5
	TCEP	Flame retardant	5
Hormone	Ethynylestradiol	Birth control	10
Pesticide	Atrazine	Herbicide	1
	Diuron	”	5
	Linuron	”	5

Fate and Transport

- Some EDCs and PPCPs are persistent in the environment – can be used as markers
  - Carbamazepine
  - Primidone
- Some are biodegradable
  - Caffeine
- Some can undergo photolysis
  - Gemfibrozil
  - Ibuprofen
  - Ethynylestradiol

Quality Assurance/Quality Control

- **QA/QC protocols at MWD**
  - **Calibration curve based on extracted standards (min. 5 points)**
  - **Duplicates and matrix spikes to assess precision and accuracy, respectively**
    - ✓ **20% for relative percent difference**
    - ✓ **70-130% spike recovery (except for TCEP)**
  - **Field blanks and method blanks to assess potential contamination from the field and the laboratory procedures, respectively**
    - ✓ **Only report levels at least twice that in the blanks**
  - **13 isotopically labeled standards are used to correct for matrix effects in LC/MS/MS analysis, with the exception of TCEP**

QA/QC Continued

- **Inter-laboratory QA/QC**
  - **Selected samples and selected analytes are analyzed by MWD, OCWD, and SNWA in parallel for method validation**
- **Round Robin Test in April 2008**
  - ✓ **5 samples prepared at MWD**
  - ✓ **Different concentrations of PPCPs**
  - ✓ **MWD, OCWD, and SNWA participated**
  - ✓ **7 of 10 common analytes had an RSD less than 30%**

Round Robin Test Results (ng/L)

Surface Water, fortified with different levels of PPCPs

Analyte	Lab A	Lab B	Lab C
Bisphenol A	475	509	410
Caffeine	131	113	150
Carbamazepine	107	110	110
DEET	517	429	600
Gemfibrozil	282	123	210
Ibuprofen	258	201	200
Octylphenol	497	299	<25
Primidone	105	104	98
Sulfamethoxazole	113	104	92
Triclosan	242	156	210

Available Analytical Methods

- **USGS**
  - **5 methods used in the study published in 2002 ES&T**
    - ✓ **SPE followed by LC/MS**
    - ✓ **Continuous liquid-liquid extraction followed by GC/MS**
  - **Method published in 2008**
- **EPA 1694**
- **Shane Snyder et al**
  - **Used for several AwwaRF studies**
  - **SPE followed by LC/MS/MS**
- **MWD/OCWD/NWRI study**
  - **Adapted methodology of S. Snyder**
- **Others**

Method Comparison

Summary	MWD	EPA 1694	USGS
Number of Analytes	33	74	14
Type of Analytes	PPCPs, including one flame retardant, Bisphenol A, etc.	PPCPs; not including flame retardants, Bisphenol A, etc.	PPCPs; not including flame retardants, Bisphenol A, etc.
Method Description	SPE followed by GC/MS; SPE followed by LC/MS/MS	SPE, followed by LC/MS/MS	SPE, followed by LC/MS
Matrix Applicable	Water	Water, Soil, Sediment, Biosolids	Water
MRLs (ng/L)	1-50	2-500	15-100
Preservatives	Ascorbic acid, sodium azide	80 mg/L sodium thiosulfate	None; filtered
Isotope Dilution	Used for 13 of 14 LC analytes	Used for 18 Analytes	No
Holding Studies	Yes	No	Yes
Inter-laboratory Comparison	Yes	No	No
Potential Issues	---	Accuracy due to matrix effects; Range of precision and accuracy 5-200 %	Accuracy due to matrix effects (range of recovery 2-138%); MS/MS not used

USEPA Method Approval

- New methods are approved and published in CFR only when required to analyze regulated constituents
  - CDPH typically adopts EPA approved methods
- Constituents are regulated if:
  - There is significant occurrence
  - Occurrence is at concentrations considered to be adverse to human health
  - Regulation would result in risk abatement
- Certified methods are not likely until PPCPs are regulated or required to be monitored (e.g., UCMR)

Cost Considerations

- Methods require significant capital investment
  - Instrumentation
  - Automated sample prep stations
  - Reference standards
- Methods require advanced analytical expertise
- Most water utilities do not have sufficient resources to conduct these methods
  - Only a few can, e.g. MWD, SNWA, and OCWD
- Commercial labs charge $400- $2,000 per sample depending on analytes and matrices

Upcoming Research Project on PPCP Methods: AwwaRF RFP 4167

- **Objectives**
  - Evaluate existing methods
  - Low levels (ng/L) of EDCs and PPCPs
  - Inter-laboratory comparison
  - Part of the Strategic Initiative
- **Anticipated Timeline**
  - Application deadline June 6, 2008
  - Award in Aug/Sept 2008
  - 18 months

PPCP Analytical Method Summary

- Analytical methods for PPCPs are an emerging technology
  - Require specialized instrumentation and techniques (isotope dilution)
  - Require specialized expertise
  - Not currently used for routine compliance monitoring
- Expert laboratories have developed reliable methods
- Method approvals are unlikely in near future
  - EPA method approval only happens when compounds are regulated or monitoring is required
  - Requires extensive QA/QC and inter-laboratory verification
- Expensive

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