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Water Analysis: Emerging Contaminants and Current Issues

Susan D. Richardson

National Exposure Research Laboratory, U.S. Environmental Protection Agency, Athens, Georgia 30605

Review Contents

This review covers developments in water analysis over the period of 2001−2002. A few significant references that appeared between January and February 2003 are also included. Previous Water Analysis reviews have been very comprehensive; however, in 2001, *Analytical Chemistry* changed its approach to include only 100−200 significant references and to mainly focus on new trends. As a result, this year the review will limit its focus to new, emerging contaminants and environmental issues that are driving most of the current research. Even with this more narrow focus, only a small fraction of the quality research publications could be discussed. Thus, this review will not be comprehensive, but will highlight new areas and only discuss representative papers in the areas of focus. I would welcome any comments you have, in particular regarding this more narrow focus—whether you find it more (or less) useful than a broader approach (richardson.susan@epa.gov).

Numerous abstracts were consulted before choosing the best ones to present here. Abstract searches were carried out using the Web of Science, and in many cases, full articles were obtained. A table of acronyms is provided (Table 1) as a quick reference to the acronyms of analytical techniques and other terms used in this review. A table of useful websites is also provided (Table 2).

The overall trends in analytical methods for water analysis include a greater use of solid-phase microextraction (SPME), increased use of fast gas chromatography/mass spectrometry (GC/MS), increased use of chiral separations (usually with chiral GC columns or using capillary electrophoresis, CE), increased use of enzyme-linked immunosorbent assay (ELISA) methods, and more on-line coupling of extraction and separation with detection, such as solid-phase extraction (SPE) coupled to liquid chromatography/mass spectrometry (LC/MS) or GC/MS and ion chromatography (IC) coupled to inductively coupled plasma mass spectrometry (IC/ICPMS). As new methods are developed, detection limits are being pushed lower—several examples in-

Table 1. List of Acronyms

AAS	atomic absorption spectrometry
AED	atomic emission detection
APCI	atmospheric pressure chemical ionization
AWWARF	American Water Works Association Research Foundation
BMX	brominated forms of MX
CCL	Contaminant Candidate List
CE	capillary electrophoresis
CI	chemical ionization
DBPs	disinfection byproducts
DNPH	2,4-dinitrophenylhydrazine
DOP	dissolved organic phosphorus
ECD	electron capture detection
EDCs	endocrine disrupting chemicals
EI	electron ionization
ELISA	enzyme-linked immunosorbent assay
EPA	Environmental Protection Agency
ESI	electrospray ionization
FAIMS	high-field asymmetric waveform ion mobility spectrometry
FID	flame ionization detection
FT	Fourier transform
GAC	granular activated carbon
GC	gas chromatography
HAAs	haloacetic acids
HAA5	five HAAs regulated by the U.S. EPA: chloro-, bromo-, dichloro-, dibromo-, and trichloroacetic acid
HG	hydride generation
IC	ion chromatography
ICP	inductively coupled plasma
ICR	ion cyclotron resonance
LC	liquid chromatography
LT1ESWTR	Long Term 1 Enhanced Surface Water Treatment Rule
MALDI	matrix-assisted laser desorption/ ionization
MCL	maximum contaminant level
MIMS	membrane introduction mass spectrometry
MS	mass spectrometry
MTBE	methyl *tert*-butyl ether
MX	3-chloro(4-dichloromethyl)−5-hydroxy-2(5*H*)-furanone
NCI	negative chemical ionization
NDMA	nitrosodimethylamine
NMR	nuclear magnetic resonance
NOM	natural organic matter
PBBs	polybrominated biphenyls
PCBs	polychlorinated biphenyls
PCR	polymerase chain reaction
PFBHA	pentafluorobenzylhydroxylamine
SPE	solid-phase extraction
SPME	solid-phase microextraction
THMs	trihalomethanes
TOC	total organic carbon
TOF	time of flight
UCMR	Unregulated Contaminants Monitoring Rule

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Table 2. Useful Websites

website	comments
www.epa.gov	U.S. EPA's website; provides a searchable link to U.S. EPA regulations and methods
www.epa.gov/ogwdw/methods/methods.html	link to EPA's Office of Groundwater and Office of Research and Development drinking water methods
www.epa.gov/ogwdw/methods/sourcalt.html	methods developed by EPA's Office of Groundwater and Drinking Water
http://www.epa.gov/safewater/mdbp/mdbp.html	EPA's microbial and DBP rules
www.gpo.gov/su_docs/aces/aces140.html	direct link to the Federal Register
www.chbr.noaa.gov/CoastalResearch	NOAA's website for algal toxin information
www.dhs.ca.gov/ps/ddwem/chemicals/NDMA/NDMAindex.htm	California Department of Health Services site for NDMA information
ehp.niehs.nih.gov/roc/toc10.html	link to NTP report on NDMA and other known/anticipated carcinogens
www.epa.gov/OGWDW/mtbe.html	U.S. EPA monitoring requirement for MTBE
http://wwwsd.cr.usgs.gov/nawqa/vocns/nat_survey.html	U.S. MTBE occurrence study
http://www.awwarf.org/exsums/256.htm	AWWARF U.S. and Canadian microcystin occurrence study
www.epa.gov/safewater/arsenic.html	EPA's website for arsenic
www.epa.gov/ncerqa/grants	EPA's STAR Grants solicitations
www.epa.gov/scipoly/oscpendo/overview.htm	EPA's EDC screening program

cluded in this review give detection limits of nanogram per liter and some even picogram per liter. The use of matrix-assisted laser desorption/ionization (MALDI)-MS and electrospray ionization (ESI)-MS has also increased for the analysis of microorganisms. In the last two years, further advances have been made, moving beyond simple fingerprinting and empirical matching to modeling and algorithm development, microorganism−protein database development, and complete sequencing of protein biomarkers. MALDI- and ESI-MS are also being used to probe the structures of high molecular weight natural organic matter (i.e., humic materials). Previously, mass spectral analysis of humic material was only possible through the use of chemical and thermal degradative techniques, such as pyrolysis-GC/MS, which does not provide information on the original, intact molecule. The availability of MALDI- and ESI-MS, along with the use of high-resolution Fourier transform (FT)-ion cyclotron resonance (ICR)-MS and MS/MS, is allowing the analysis of intact humic materials for the first time by mass spectrometry.

Pesticides continue to be of interest. However, current research is focusing more on those pesticides considered to be endocrine disrupting, on pesticide degradation products, and on occurrence/degradation of chiral isomers. Alachlor (and other acetanilide pesticides) and triazine and their degradation products are on the U.S. Environmental Protection Agency's (EPA) Contaminant Candidate List (CCL), a list of unregulated contaminants that are to be monitored in drinking water systems and considered for future regulation (based on their occurrence and health effects). Chiral chromatography (using chiral GC or LC columns or CE) is being used to study the occurrence and environmental fate of pesticides that are chiral. Typically, one pesticide enantiomer is the active one, and the other is inactive. In addition, one pesticide enantiomer is typically degraded differently in the environment (their fate is not the same). Therefore, with the manufacture and use of pesticides containing racemic mixtures, there was the potential for one form of the pesticide to accumulate in the environment and cause unintended effects on nontarget species. Because earlier fate research studied racemic mixtures, there was also the potential for an incorrect assessment of the pesticide's half-life in the environment; i.e., the rate of degradation may give the impression that the pesticide would completely degrade, when only one form may be degrading. It is also interesting that the ability to separate pesticide enantiomers has also led pesticide manufacturers to offer a particular enriched chiral isomer commercially. Thus, there is expected to be increased use of single chiral forms of pesticides.

Endocrine disrupting chemicals (EDCs) are also an important issue. Although EDCs can hardly be considered an "emerging" issue (there has been concern about EDCs since the early 1990s), most EDC research has been conducted only in the last six years, and the last two years has seen substantial growth. As time goes on, more chemicals are being discovered to be endocrine disrupting. In the United States, the Food Quality Protection Act and the Safe Drinking Water Act Amendments (published in 1996) helped to promote new research on EDCs. These two legislative acts require that the U.S. EPA develop a screening and testing strategy for estrogenic substances and other EDCs. Publication of the book *Our Stolen Future* in 1996 also helped to publicize this area of concern, much as Rachel Carson's book, *Silent Spring*, helped to launch the beginnings of the environmental movement in the 1960s. One area of very recent interest related to this area is the study of pharmaceuticals and hormones in water. In addition to concern about potential estrogenic effects to wildlife, there is also concern about potential estrogenic effects in humans, through the introduction of pharmaceuticals/hormones into drinking water sources. Due to improved analytical methods (typically LC/MS) that can measure highly polar pharmaceuticals at the low levels required, there has been an explosion of research in this area, with researchers not only measuring their occurrence in waters but also studying their fate in wastewater treatment plants. Several studies are, in fact, showing that there has been incomplete removal at wastewater treatment plants and that many of these pharmaceuticals/hormones are present in source waters.

The discovery of nitrosodimethylamine (NDMA) as a disinfection byproduct (DBP) in drinking water treatment (and also as a source water contaminant) has received much interest due to its known cancer potency. Other recently identified DBPs—such as bromonitromethanes, iodotrihalomethanes, iodo acids, and brominated forms of MX [3-chloro-4-(dichloromethyl)-5-hydroxy-2(5*H*)-furanone]—are also receiving attention and were included in a recent U.S. Nationwide DBP Occurrence Study. Lower detection limits, improved analytical instrumentation and methods, and new derivatization procedures are allowing significant advances in an area that has been active for almost 30 years. Organotins are receiving renewed attention partly because of new studies showing

that they can leach out of poly(vinyl chloride) (PVC) pipe into drinking water at continuous ppb levels. Organotins were originally identified mostly in coastal waters, due to their widespread use in antifouling paints for ships. New research is indicating that there is a potential threat of human exposure through drinking water. Although not considered as great a toxicological risk, methyl *tert*-butyl ether (MTBE) is also still receiving significant study, due to its impact on groundwater sources (and entry into drinking water) from leaking underground gasoline storage tanks. Perchlorate contamination in groundwater has also recently been shown to be significant, and its presence in some fertilizers is a concern. Arsenic research has also increased exponentially, with the development of improved analytical methods permitting the study of specific species of arsenic in water, foods, and biological samples (including human urine).

Algal toxin research has also grown significantly, with the ability of mass spectrometry to measure these polar, higher molecular weight compounds. Many algal toxins are peptide related; e.g., microcystins are cyclic peptides produced by blue green algae. Algal toxins have been responsible for large fish kills, poisoning of shellfish, other animal deaths, and illness in people, and they are listed on EPA's Contaminant Candidate List. All of these emerging contaminants and issues will be discussed in this review, along with new regulations and regulatory methods that relate to water analysis.

GENERAL REVIEWS

This section includes general reviews relating to water analysis. Reviews that relate to specific areas (e.g., pharmaceuticals, chiral compounds, or microorganisms) can be found in those specific sections. Many reviews have been published over the last two years that relate to water analysis. The previous Water Analysis review published in 2001 contained 191 references and discussed advances in research for pesticides, endocrine disrupting chemicals and pharmaceuticals, drinking water disinfection byproducts, surfactants, textile dyes, algal toxins, microorganisms, natural organic matter, inorganic pollutants, field-portable methods, and new regulations and regulatory methods for water (*1*) Clement et al. published the 2001 biennial review on Environmental Analysis, which included 638 references and covered environmental review articles, solid-phase extraction applications, air monitoring and analysis applications, water analysis applications, solid sample analysis applications, biota analysis applications, radionuclides, quality assurance topics, and biomarkers (*2*). This article includes a table with an extensive listing of review articles, along with short descriptions of each review's focus/contents, which is a handy list for those readers who want more detail for specific techniques or applications. The 2003 Environmental Analysis review also appears in this issue of *Analytical Chemistry* and will contain some work related to water analysis, but with more of an emphasis on trends in analytical techniques.

Zwiener and Frimmel published a review on Water Quality in 2001 (*3*). In this review, the authors discussed concerns involving demands for water and water sustainability, as well as European regulations, impacts of chemicals and other pollutants on water quality, new sampling and extraction procedures, and new analytical methods for measuring organic pollutants. Emerging contaminants and current issues in environmental mass spectrometry was the focus of a 2002 *Analytical Chemistry* review of the 2000−2001 literature, which included many of the emerging contaminants discussed in this review, except with a broader focus for contaminants (included emerging air and soil contaminants), and a narrower focus on mass spectrometry methods (*4*). A more comprehensive mass spectrometry review, entitled Mass Spectrometry in Environmental Sciences was published in 2001 in *Chemical Reviews* and covered the last 25 years of developments in environmental mass spectrometry, including early, historical work in the 1970s and developments until the year 2000 (*5*).

Budde, a leader in environmental mass spectrometry for many years, published a book in 2001, *Analytical Mass Spectrometry: Strategies for Environmental and Related Applications* (*6*). This book begins with a wonderful historical overview of environmental legislation and environmental and technical developments that contributed to the widespread use of mass spectrometry. The development of the Priority Pollutant List is discussed, as are the development of U.S. Environmental Protection Agency Methods. Later in the book, analytical strategies are discussed for the quantification of target analytes and the identification of unknowns, with detailed descriptions of GC/MS, LC/MS, exact mass measurements, and enhancing analyte selectivity and lowering detection limits. It is impossible to do this book justice in the small space allotted here. Suffice it to say that this book is an excellent reference for the practicing mass spectrometrist (not just for those involved in environmental measurements) and also for students and others who want to learn about quantitative analysis and other techniques involving mass spectrometry. Niessen edited a book in 2001 on the *Current Practice of Gas Chromatography−Mass Spectrometry* (*7*), which provides a perspective on how GC/MS is used by researchers in a wide variety of different applications, including environmental applications.

Reemtsma reviewed the use of LC-atmospheric pressure chemical ionization (APCI) mass spectrometry for water analysis (*8*, *9*). In part I of this review (*8*), the achievements of LC/MS for expanding the types of water constituents that can be studied are detailed, as well as the use of separation techniques, such as LC, IC, CE, and size exclusion chromatography (SEC). In part II, obstacles for LC/MS are discussed, including the difficulty in identifying unknown compounds and the difficulty in quantifying target analytes in complex samples (*9*). Suggestions are offered to address some of these problems through the use of tandem mass spectrometry, time-of-flight (TOF)-MS, and improved chromatographic separations or sample cleanup procedures.

Two reviews involving the use of atomic spectrometry were published in the last two years (*10*, *11*). In a 2002 review published in *Analytical Chemistry*, Bing et al. provided a general overview of the subject, covering innovations being made in atomic absorption spectrometry, atomic fluorescence spectrometry, atomic emission spectrometry, glow discharge atomic spectrometry, and ICPMS from 1999 to 2001 (*10*). In a 2003 review published in the *Journal of Analytical Atomic Spectrometry*, Hill et al. focus on the application of atomic spectrometry for environmental analysis (*11*). Included in this review are important developments in 2001−2002, for the analysis of air, water, soil, plants, and geological materials. Beauchemin reviewed inductively coupled plasma spectrometry, including advances made in sample preparation and sample introduction, as well as issues associated with spectroscopic and

Table 3. New U.S. Regulations

rule/regulation	website
Stage 1 D/DBP Rule	www.epa.gov/safewater/mdbp/dbp1.html
LT1ESWTR and LT2ESWTR	www.epa.gov/safewater/lt2/lt2_preamble.pdf
Groundwater Rule	www.epa.gov/ogwdw/gwr.html
Filter Backwash Recycle Rule	www.epa.gov/safewater/mdbp/mdbp.html
Arsenic Rule	www.epa.gov/safewater/arsenic.html
Radon Rule	www.epa.gov/ogwdw/radon/proposal.html
Contaminant Candidate List (CCL)	www.epa.gov/ogwdw/ccl/cclfs.html
Unregulated Contaminants Monitoring Rule (UCMR)	www.epa.gov/safewater/ucmr.html

Table 4. New Regulatory Methods

method	analytes	refs
EPA Method 8323	organotins	20
EPA Method 552.3	haloacetic acids (all nine chloro/bromoacetic acids) and dalapon	*a*
EPA Method 317.0	bromate, chlorite, bromide, chlorate	21
EPA Method 326.0	bromate, chlorite, bromide, chlorate	22
EPA Method 531.2	*N*-methylcarbamoyloximes and *N*-methyl carbamates	*b*
EPA Method 529	RDX	24
EPA Method 415.3	TOC, DOC, specific UV absorbance	*a*
EPA Method 200.5	22 elements (Al, Sb, As, Ba, Be, B, Cd, Ca, Cr, Cu, Fe, Pb, Mg, Mn, Ni, Se, Si, Ag, Na, Sn, V, Zn)	24
EPA Method 1605	*Aeromonas*	*b*

[a] Method due in mid-2003. [b] Method available at www.epa.gov/ogwdw/methods/sourcalt.html.

Table 5. DBPs Regulated under the Stage 1 D/DBP Rule

DBP	MCL (mg/L)
total THMs[a]	0.080
HAAs[b]	0.060
bromate	0.010
chlorite	1.0

[a] Total THMs are the sum of the concentrations of chloroform, bromoform, bromodichloromethane, and dibromochloromethane. [b] The HAAs are the sum of monochloro-, dichloro-, trichloro-, monobromo-, and dibromoacetic acids.

nonspectroscopic interferences and developments in instrumentation for isotope ratio work (*12*). Finally, Mester et al. reviewed applications of SPME for trace element speciation (*13*). This review also includes an overview of SPME operation.

NEW REGULATIONS/REGULATORY METHODS

New U.S. Regulations. Several developments in new regulations and regulatory methods have taken place in the last two years that impact water analysis. Table 2 includes websites that can be used to obtain additional details on the regulations and regulatory methods. Table 3 lists the new regulations, and Table 4 summarizes the new regulatory methods. An excellent review of new and proposed drinking water regulations was published in 2002 by Pontius (*14*). Included in this review are the scope and status of new regulations, as well as schedules for key regulations that are currently under development by the U.S. EPA. All of the drinking water contaminants—chemical and microbial—that are currently regulated for drinking water, along with maximum contaminant levels (MCLs), maximum contaminant level goals, and best available technologies for removing them, are provided in this review. Pontius also discusses the possibility of contaminants being deliberately introduced into a water supply and cites a comprehensive review of the sources, fate, and toxicity of chemical warfare agent degradation products (*15*), as well as a review of biological agents that can be a threat to drinking water systems (*16*). The U.S. EPA has an excellent website that can be used to obtain details on regulations and regulatory methods: www.epa.gov. This website has a search function to allow easy access to this information, and it has links to the *Federal Register*, where the complete published rules can be obtained. A direct link to the *Federal Register* can also be made with the following address: www.gpo.gov/su_docs/aces/aces140.html. The specific EPA website for microbial and disinfection byproduct rules can be found at www.epa.gov/safewater/mdbp/mdbp.html.

The Stage 1 and Stage 2 D/DBP Rule. The Stage 1 Disinfectants (D)/Disinfection By-products (DBP) Rule took effect on January 1, 2002, for large surface water treatment systems, lowered permissible levels of trihalomethanes (THMs) to 80 μg/L, and regulates five of the haloacetic acids (HAAs), bromate, and chlorite for the first time in drinking water (Table 5) (www.epa.gov/safewater/mdbp/dbp1.html). The Stage 2 D/DBP Rule is expected to be proposed in mid-2003. This rule will maintain the Stage 1 Rule MCLs for THMs and HAAs but will require that MCLs be based on locational running annual averages (i.e., each location in the distribution system will need to comply on a running annual average basis). The reason for this change is that the running annual averages (used with the Stage 1 D/DBP Rule) permitted some locations within a water distribution system to exceed MCLs, as long as the average of all sampling points did not exceed the MCLs. As a result, consumers served by a particular section of the distribution system could receive water that regularly exceeded the MCLs. The Stage 2 D/DBP Rule is intended to target those higher DBP levels and reduce the variability of exposure for people served by different points in the distribution system. The Stage 2 D/DBP Rule will maintain the MCLs for bromate and chlorite; however, the U.S. EPA plans to review the bromate MCL as part of their six-year review process.

The LT1ESWTR and LT2ESWTR Rules. The final Long Term 1 Enhanced Surface Water Treatment Rule (LT1ESWTR) was published in January 2002 (*17*) and strengthened microbial controls for water systems by extending the previous interim ESWTR (which applied only to large water systems) to small systems serving fewer than 10 000 people. A Long Term 2 Enhanced Surface Water Treatment Rule (LT2ESWTR) is expected to be proposed in mid-2003 and will further improve control of microbial pathogens (including specifically *Cryptosporidium*)

in drinking water and address risk tradeoffs with disinfection byproducts (additional details are available at www.epa.gov/safewater/lt2/lt2_preamble.pdf).

The Groundwater Rule. This rule was initially proposed in 2000 and is expected to be finalized in 2003. This rule will establish a targeted risk-based regulatory strategy for all groundwater systems through a multiple-barrier approach, which includes periodic sanitary surveys of groundwater systems, hydrogeologic assessments to identify wells sensitive to fecal contamination, source water monitoring for systems drawing from sensitive wells without treatment, correction of significant deficiencies and fecal contamination, and compliance monitoring to ensure disinfection treatment is reliably operated when it is used (*14*). Additional details can be found at www.epa.gov/ogwdw/gwr.html.

The Filter Backwash Recycle Rule. This rule was issued in June 2001 and requires all public water systems using surface water or groundwater under the direct influence of surface water to review their backwash water recycling practices to ensure that they do not compromise microbial control. Under this rule, recycled spent filter backwash water, sludge thickener supernatant, and liquids from dewatering processes must be returned to a location such that all processes of a system's conventional or direct filtration are employed. Systems must comply by no later than June 8, 2004 (*14*).

The Arsenic Rule. In January 2001, the U.S. EPA lowered the arsenic MCL from 50 to 10 μg/L; however, two months later, the new EPA Administrator announced that EPA would withdraw this pending arsenic standard in order to seek independent reviews of the science behind the standard and the estimates of costs to communities to implement the rule (www.epa.gov/safewater/arsenic.html). After seeking the advice of independent, expert panels convened by the National Academy of Sciences, the National Drinking Water Advisory Council, and the EPA Science Advisory Board regarding recommendations on the science, cost of compliance, and benefits analysis, the rule was finally agreed upon and the original proposed standard of 10 μg/L was kept. This rule became effective February 22, 2002, and drinking water systems must comply with this new standard by January 23, 2006.

The Radon Rule. This rule is expected to finalized in December 2003; the proposed rule (which was published in 1999) would establish an MCL of 300 pCi/L for radon in potable water. An alternative MCL (at a higher level of 4000 pCi/L) could also be used if a multimedia mitigation program is put in place to also reduce radon levels in indoor air. The proposed standards will apply only to community water systems that regularly serve 25 or more people and that use groundwater or mixed ground and surface water. They will not apply to systems that rely on surface water where radon levels are typically very low, and they will not apply to private wells. Radon exposures from drinking water are normally much lower (1−2%) than radon exposures from air; however, radon can be released into the air from tap water, and there is an increased risk of lung cancer associated with this exposure route. Additional information can be found at www.epa.gov/ogwdw/radon/proposal.html.

The Contaminant Candidate List. In 1996, the Safe Drinking Water Act Amendments required the U.S. EPA to publish a CCL every five years to identify potential substances for future regulation. Monitoring data will be collected from drinking water utilities to determine whether a contaminant occurs at a frequency and in concentrations to warrant further analysis and research on potential health effects and possible regulation. From the CCL, a minimum of five candidates must be selected to be considered for regulation within a five-year period. The first CCL was published in March 1998 and contains both chemical and microbial contaminants. Chemical contaminants include many pesticides (such as triazine and its degradation products), volatile contaminants (such as tetrachloroethane), metals (such as aluminum, boron, manganese, and vanadium), an explosive (RDX), and other chemical contaminants, such as organotins, perchlorate, methyl bromide, MTBE, and algal toxins (a complete list of CCL chemical and microbial contaminants is given in Table 6). Further details on the CCL can be found at www.epa.gov/ogwdw/ccl/cclfs.html. A *Handbook of CCL Microbes in Drinking Water* has also been published recently by the American Water Works Association Research Foundation (*18*).

Table 6. The Drinking Water Contaminant Candidate List

Chemical Contaminants[a]	
1,1,2,2-tetrachloroethane	disulfoton
1,2,4-trimethylbenzene	diuron
1,1-dichloroethane	EPTC (*s*-ethyldipropyl-thiocarbamate)
1,1-dichloropropene	fonofos
1,2-diphenylhydrazine	hexachlorobutadiene
1,3-dichloropropane	*p*-isopropyltoluene (*p*-cymene)
1,3-dichloropropene	linuron
2,4,6-trichlorophenol	manganese
2,2-dichloropropane	methyl bromide
2,4-dichlorophenol	methyl-*teert*-butyl ether
2,4-dinitrophenol	metolachlor
2,4-dinitrotoluene	metribuzin
2,6-dinitrotoluene	molinate
2-methyl-phenol (*o*-cresol)	naphthalene
acetochlor	nitrobenzene
Alachlor ESA and other acetanilide pesticide degradation products	organotins
aldrin	perchlorate
aluminum	prometon
boron	RDX
bromobenzene	sodium
DCPA monoacid degradate	sulfate
DCPA diacid degradate	terbacil
DDE	terbufos
diazinon	triazines and their degradation products (including, but not limited to, cyanazine and atrazine-desethyl)
dieldrin	vanadium
Microbiological Contaminants	
acanthamoeba	cyanobacteria (blue-green algae), other freshwater algae, and their toxins
adenoviruses	echoviruses
Aeromonas hydrophila	Helicobacter pylori
caliciviruses	*Microsporidia* (enterocytozoon and septata)
coxsackieviruses	*Mycobacterium avium* intracellulare (MAC

[a] Note that algal and cyanobacterial (blue-green algae) toxins are listed with microbial contaminants.

The Unregulated Contaminants Monitoring Rule (UCMR). The 1996 Safe Drinking Water Act and Amendments also require the U.S. EPA to publish a list of no more than 30 unregulated

Table 7. Unregulated Contaminants Monitoring Rule

List 1 Contaminants	
2,4-dinitrotoluene	molinate
2,6-dinitrotoluene	MTBE
acetochlor	nitrobenzene
DCPA monoacid; DCPA diacid	perchlorate
4,4′-DDE	terbacil
EPTC	
List 2 Contaminants	
1,2-diphenylhydrazine	diuron
2-methylphenol	fonofos
2,4-dichlorophenol	linuron
2,4-dinitrophenol	nitrobenzene
2,4,6-trichlorophenol	prometon
diazinon	terbufos
disulfoton	*Aeromonas*

contaminants that public water suppliers are to monitor to provide data that can be used to determine whether a contaminant occurs at a frequency and in concentrations to warrant further analysis and research on potential health effects. Such data could result in the contaminant being added to the CCL.

The final UCMR was published in 1999 (*19*) and divided contaminants to be monitored into three lists: (1) List 1, Assessment Monitoring, consists of 12 contaminants (Table 7) for which analytical methods were available; (2) List 2, Screening Survey, consists of 14 contaminants for which new analytical methods will be used (Table 7); and (3) List 3, Prescreen Testing, consists of 9 contaminants for which analytical methods are being researched (*14*). Only the contaminants on List 1 must be monitored by all large drinking water systems (serving more than 10 000 people), and by a representative sample of approximately 800 systems serving 10 000 or fewer people (*14*). Monitoring for List 2 contaminants will be conducted at randomly selected large and small systems-with one round of sampling for chemical contaminants and one round for *Aeromonas* (*14*). The effective implementation date for Assessment Monitoring was January 1, 2001; large systems must conduct this monitoring over any 12-month period from January 1, 2001 to December 31, 2003. Additional information can be found at www.epa.gov/safewater/ucmr.html.

New Regulatory Methods. Several new regulatory methods have been developed over the last two years by the U.S. EPA. Some of these are directed toward the measurement of CCL chemicals in drinking water, some are directed toward the measurement of UCMR analytes, and others are directed toward the upcoming Stage 2 D/DBP Rule. First, a micro-LC/ESI-ion trap-MS method developed by Jones-Lepp (*20*) for determining organotins in water has recently become an official EPA method (Method 8323, Determination of Organotins by Micro-Liquid Chromatography-Electrospray Ion Trap Mass Spectrometry) and can be found at www.epa.gov/epaoswer/hazwaste/test/new-meth.htm#8323. This method, which permits the measurement of mono-, di-, and tributyltin and mono-, di-, and triphenyltin at subnanogram per liter detection limits, was developed to avoid the use of hydrolysis and derivatization and to lower background interferences that are common with traditional methods.

EPA Method 552.3, Determination of Haloacetic Acids and Dalapon in Drinking Water by Liquid−Liquid Microextraction, Derivatization, and Gas Chromatography with Electron Capture Detection (due in mid-2003), provides comparable sensitivity, accuracy, and precision to previously approved methods, but has the added benefit of allowing laboratories to more easily measure three additional haloacetic acids (bromodichloroacetic acid, chlorodibromoacetic acid, tribromoacetic acid) at the same time the regulated HAA5 compounds (chloro-, bromo-, dichloro-, dibromo-, and trichloroacetic acid) are being measured. EPA Method 317.0, Revision 2.0 (published in 2001), Determination of Inorganic Oxyhalide Disinfection By-Products in Drinking Water Using Ion Chromatography with the Addition of a Postcolumn Reagent for Trace Bromate Analysis (*22*), permits 0.12 μg/L detection limits for bromate and 0.45, 0.54, and 0.62 μg/L for chlorite, bromide, and chlorate, respectively (www.epa.gov/ogwdw/methods/sourcalt.html). EPA Method 326.0 (published in 2002), Determination of Inorganic Oxyhalide Disinfection By-Products in Drinking Water Using Ion Chromatography Incorporating the Addition of a Suppressor Acidified Postcolumn Reagent for Trace Bromate Analysis (*22*), provides procedures for determining bromate, bromide, chlorite, and chloride in water (www.epa.gov/ogwdw/methods/sourcalt.html). This method is an alternative to EPA Method 317.0, and while it is slightly more complex than Method 317.0, the reagents are more readily available, and reagent purity is less of a problem Method 326.0 is a modification of an earlier method published by Salhi and von Gunten (*23*), which incorporated an acidic solution of potassium iodide containing catalytic amounts of molybdenum(VI) as the postcolumn reagent. EPA Method 326.0 modifications include optimized flow rates, reaction temperature, and delivery of the postcolumn reagent. This method permits a detection limit of 0.17 μg/L bromate.

EPA Method 531.2, Measurement of *N*-Methylcarbamoyloximes and *N*-Methylcarbamates in Water by Direct Aqueous Injection HPLC with Postcolumn Derivatization, permits the measurement of 11 of these analytes in finished drinking waters at detection limits ranging from 26 to 65 ng/L (www.epa.gov/ogwdw/methods/sourcalt.html). EPA Method 529, Determination of Explosives and Related Compounds in Drinking Water by Solid-Phase Extraction with Capillary Gas Chromatography/Mass Spectrometry (GC/MS) (completed in 2002), was developed to allow the determination of RDX (which is a CCL analyte) and other related compounds (*24*). EPA Method 415.3, Determination of Total Organic Carbon, Dissolved Organic Carbon and Specific UV Absorbance at 254 nm in Source Water and Drinking Water (due in mid-2003), was developed for inclusion in the Stage 2 D/DBP Rule and contains procedures that will eliminate discrepancies in total organic carbon (TOC) measurements that are commonly observed when TOC instruments based on different technologies are used. EPA Method 200.5 (due in mid-2003), Determination of Trace Elements in Drinking Water by Axially Viewed Inductively Coupled Plasma-Atomic Emission Spectrometry, was developed for measuring 22 elements (e.g., aluminum, arsenic, copper, iron, lead, etc.) in drinking water (*24*). Method detection limits range from 0.02 to 3.3 μg/L.

A new EPA method has also been developed for measuring a specific microbial contaminant. EPA Method 1605 (published in 2001), *Aeromonas* in Finished Water by Membrane Filtration using Ampicillin-Dextrin Agar with Vancomycin, permits the measurement of the microorganism *Aeromonas*, which may be found in nonchlorinated or low-flow regions of drinking water distribution

systems. Method 1605 involves membrane filtration with a selective medium, which allows most species of *Aeromonas* to grow (and partially inhibits growth of nontarget species). *Aeromonas* is then identified by the production of acid from dextrin fermentation and the presence of yellow colonies on ampicillin−dextrin agar medium with vancomycin. Yellow colonies are counted and confirmed by testing for the presence of cytochrome *c* (oxidase test) and the ability to ferment trehalose and produce indole (www.epa.gov/microbes). This method was developed for the measurement of *Aeromonas* in drinking water for the UCMR regulation (Table 7).

A few methods have also been further refined in support of the UCMR survey or the CCL. Bassett et al. made an improvement in EPA Method 532 for measuring phenylurea pesticides in support of the UCMR (*25*). Using EPA Method 532, phenylurea pesticides were found to degrade rapidly in the presence of residual chlorine disinfectant in drinking waters. The degradation was prevented by adding tris buffer, and copper sulfate was used to prevent the regrowth of microorganisms. Tris buffer had the added benefit of keeping the copper sulfate preservative in solution, even in groundwater samples that would ordinarily precipitate the copper sulfate. Winslow et al. made modifications to EPA Method 526 to stabilize organophosphorus and other pesticides for measurement for the UCMR survey (*26*). A mixture of tris and tris hydrochloride buffer was used to minimize hydrolysis, and ascorbic acid was used to quench residual chlorine to prevent degradation of analytes that were unstable in the presence of chlorine. Magnuson et al. developed a method for cyanuric acid, which is a potential degradation product of triazine herbicides (*27*). Following a microscale liquid−liquid extraction of cyanuric acid from water, the extract is taken to dryness, and an aqueous solution of quaternary ammonium cationic surfactant is added. When injected into the electrospray interface, the surfactant and the cyanuric acid form a stable association complex, which allows a detection limit of 130 μg/L for a 1-mL sample using ESI-MS detection. Shoemaker developed a new method for measuring acetanilide herbicide degradation products using SPE with LC/ESI-MS (*28*). Twelve acetanilide degradation products were extracted by SPE from a 100-mL water sample and exhibited recoveries of >90%.

DISINFECTION BYPRODUCTS

In addition to new regulations involving DBPs (e.g., the Stage 2 D/DBP Rule), there are also new, emerging issues with DBPs (*29*). New human exposure research is revealing that ingestion is not the only important route of exposure—inhalation from showering and dermal absorption (from bathing and other activities) can often provide equivalent exposures or increased exposures to certain DBPs (*29*, *30*). Therefore, these exposure routes are now being recognized in new epidemiologic studies that are being conducted. Epidemiology studies are beginning to focus more on reproductive and developmental effects—which recent studies have been shown to be important.

Toxicologically Important DBPs. Also, DBPs beyond those that are currently regulated are becoming important. For example, brominated DBPs are now being recognized as toxicologically important because brominated DBPs are proving to be much more carcinogenic than their chlorinated analogues (*31*), and preliminary studies indicate that iodinated compounds may be more toxic than their brominated analogues (*31*, *32*). Brominated and iodinated DBPs are formed by the reaction of the disinfectant (such as chlorine) with natural bromide or iodide present in source waters. Coastal cities, whose groundwaters and surface waters can be impacted by saltwater intrusion, and some inland locations, whose surface waters can be impacted by natural salt deposits from ancient seas or oil field brines, are examples of locations that can have high bromide and iodide levels. A significant proportion of the U.S. population and that of several other countries now live in coastal regions that are impacted by elevated bromide and iodide; therefore, exposures to brominated and iodinated DBPs are important. Early evidence in epidemiologic studies also gives indication that brominated DBPs may be associated with the new reproductive and developmental effects, as well as cancer effects.

Specific DBPs that are of current interest include bromonitromethanes, iodo-THMs, brominated forms of MX (MX is 3-chloro-4-(dichloromethyl)-5-hydroxy-2(5*H*)-furanone), and NDMA (which is not brominated but is classified as a probable carcinogen). The bromonitromethanes (including dibromonitromethane, tribromonitromethane, and bromonitromethane) have been recently shown to be extremely cytotoxic and genotoxic to mammalian cells (*34*). For example, dibromonitromethane is at least 1 order of magnitude more genotoxic to mammalian cells than MX and is more genotoxic than all of the regulated DBPs, except for monobromoacetic acid.

Bromonitromethanes, iodo-THMs, and brominated forms of MX (so-called BMXs), as well as other "high-priority" DBPs, were the focus of a recently completed U.S. Nationwide DBP Occurrence Study (*35*−*37*). This study focused on approximately 50 high-priority DBPs that were selected from an extensive prioritization effort of all DBPs that had ever been reported (Table 8) (*35*). DBPs were prioritized according to predicted adverse health effects (cancer) by a multidisciplinary group of experts, including toxicologists, structure−activity specialists, and chemists (*38*). The high priority DBPs include brominated, chlorinated, and iodinated species of halomethanes, brominated and chlorinated forms of haloacetonitriles, haloketones, haloacids, and halonitromethanes, as well as analogues of MX. This new nationwide occurrence study represents the first such comprehensive study where the selected DBPs to be measured were chosen because of predicted adverse health effects. Standards were first obtained for these high-priority DBPs (many of which had to be synthesized), rugged analytical methods were developed, and these DBPs were quantified in waters across the United States. Waters treated with all four disinfectants that are commonly used in the United States (chlorine, ozone, chlorine dioxide, chloramines) were included in this study, as were high-bromide source waters.

Results of this nationwide occurrence study revealed the presence of many of the high-priority DBPs in the waters across the United States (including iodo-THMs, MX and BMX compounds, bromonitromethanes, haloaldehydes, haloketones, and haloamides, which is a new class of DBP for which there was no previously existing quantitative occurrence data). In addition, five iodo acids (iodoacetic acid, iodobromoacetic acid, iodobromopropenoic acid (two isomers), and 2-iodo-3-methylbutenedioic acid) were identified as DBPs in waters treated with chloramines (*35*,

Table 8. High-Priority DBPs Included in Nationwide DBP Occurrence Study

MX and MX Analogues	
3-chloro-4-(dichloromethyl)-5-hydroxy-2(5*H*)-furanone (MX)	3-chloro-4-(dibromomethyl)-5-hydroxy-2(5*H*)-furanone (BMX-2)
3-chloro-4-(dichloromethyl)-2-(5*H*)-furanone (red-MX)	3-bromo-4-(dibromomethyl)-5-hydroxy-2(5*H*)-furanone (BMX-3)
(E)−2-chloro-3-(dichloromethyl)-butenedioic acid (ox-MX)	(*E*)-2-chloro-3-(bromochloromethyl)-4-oxobutenoic acid (BEMX-1)[b]
(E)−2-chloro-3-(dichloromethyl)-4-oxobutenoic acid (EMX)	(*E*)-2-chloro-3-(dibromomethyl)-4-oxobutenoic acid (BEMX-2)[b]
2,3-dichloro-4-oxobutenoic acid (mucochloric acid)	(*E*)-2-bromo-3-(dibromomethyl)-4-oxobutenoic acid (BEMX-3)[b]
3-chloro-4-(bromochloromethyl)-5-hydroxy-2(5*H*)-furanone (BMX-1)	
Haloacids	
3,3-dichloropropenoic acid	
Halomethanes	
chloromethane	dibromoiodomethane[b]
bromomethane (methyl bromide)[a]	chlorodiiodomethane[b]
dibromomethane	bromodiiodomethane[b]
bromochloromethane	iodoform[b]
bromochloroiodomethane	chlorotribromomethane
dichloroiodomethane	carbon tetrachloride
Halonitromethanes	
bromonitromethane	bromochloronitromethane[b]
chloronitromethane[b]	bromodichloronitromethane[b]
dibromonitromethane	dibromochloronitromethane[b]
dichloronitromethane[b]	tribromonitromethane (bromopicrin)[b]
Haloacetonitriles	
bromoacetonitrile	bromodichloroacetonitrile
chloroacetonitrile	dibromochloroacetonitrile
tribromoacetonitrile	
Haloketones	
chloropropanone	1,1,1,3-tetrachloropropanone
1,3-dichloropropanone	1,1,3,3-tetrachloropropanone
1,1-dibromopropanone	1,1,3,3-tetrabromopropanone[b]
1,1,3-trichloropropanone	1,1,1,3,3-pentachloropropanone
1-bromo-1,1-dichloropropanone	hexachloropropanone
Haloaldehydes	
chloroacetaldehyde	bromochloroacetaldehyde[b]
dichloroacetaldehyde	tribromoacetaldehyde [b]
Haloacetates	
bromochloromethyl acetate	
Haloamides	
monochloroacetamide[b]	dibromoacetamide[b]
monobromoacetamide[b]	trichloroacetamide[b]
dichloroacetamide	
Nonhalogenated Aldehydes and Ketones	
2-hexenal	methyl ethyl ketone (2-butanone)[c]
5-keto-1-hexanal[c]	6-hydroxy-2-hexanone [c]
cyanoformaldehyde	dimethylglyoxal (2,3-butanedione)
Volatile Organic Compounds (VOCs) and Miscellaneous DBPs	
1,1,1,2-tetrabromo-2-chloroethane	methyl *tert*-butyl ether[a]
1,1,2,2-tetrabromo-2-chloroethane[b]	benzyl chloride

[a] Not a DBP but included because it is an important source water contaminant. [b] DBP not originally prioritized (identified in drinking water after initial prioritization) but included due to similarity to other priority compounds. [c] DBP not given a high priority but included for completeness sake to provide more representation to ozone DBPs for occurrence.

36). This is the first report of iodo acids being found as DBPs for any disinfectant. The identities of iodoacetic acid and 3,3-iodobromopropenoic acid have been confirmed through the analysis of authentic chemical standards; standards for the other iodo acids are currently being synthesized. Preliminary studies of iodoacetic acid have shown that it is potent in mammalian cell and mouse embryo assays (*32, 33*). In addition, MX levels were higher than previous levels reported, with levels of >100 ng/L frequently observed, and a high of 310 ng/L. BMX-1 [3-chloro-4-(bromochloromethyl)-5-hydroxy-2(5*H*)-furanone] and BEMX-3 [(*E*)-2-bromo-3-(dibromomethyl)-4-oxobutenoic acid] were observed as high as 170 and 200 ng/L, respectively (at a plant that disinfected a high-bromide water with chlorine dioxide, chlorine, and chloramines) (*35*). Individual halonitromethanes ranged from 0.1 to 3 μg/L, with dichloronitro-, bromochloronitro-, bromodichloronitro-, and dibromochloronitromethane being the most prevalent forms observed. The fully brominated forms, bromo-, dibromo-, and tribromonitromethane, were also measured in drinking waters up to 3 μg/L. In some cases, preozonation (used before chloramination) was found to increase the formation of brominated trihalonitromethanes (including tribromonitromethane). Individual iodo-THMs were found consistently at microgram per liter levels and as high as 15 μg/L at one location that used chloramines for primary disinfection. The total iodo-THMs reached 81% of the THM4 (four regulated THMs) at this one location (*35*). As a whole, the haloaldehydes represented the third largest class in concentration (behind THMs and HAAs) measured in the study. A particularly important observation from this study was that while the use of alternative disinfectants minimized the four regulated THMs, certain other DBPs were formed at significant concentrations. For example, bromonitromethanes were highest at a plant using preozonation; iodo-THMs were highest at a plant using chloramines; dihaloaldehydes were highest at a plant using chloramines and ozone; and MX and BMXs were highest at a plant using chlorine dioxide (followed by chlorine chloramines) that treated waters high in natural organic matter and bromide (*35*−*37*). Chlorine dioxide itself did not form MX or BMXs, rather chlorine dioxide did not destroy MX precursors, which enabled the formation of MX and BMX during intermediate chlorination and postchloramination in these waters.

Analytical techniques that were used to measure these high-priority DBPs include methylation with GC-electron capture detection (ECD) for the MX analogues and haloacids, pentafluorobenzylhydroxylamine (PFBHA) derivatization with GC-ECD for carbonyl compounds, liquid−liquid extraction-GC-ECD for haloamides and haloacetates (*39*), and liquid−liquid extraction-GC-ECD, SPE-GC/MS, and purge-and-trap-GC/MS for halonitromethanes, iodo-THMs, other halomethanes, haloaldehydes, haloketones, and haloacetonitriles (*35, 40*). Bromopicrin and other trihalonitromethanes (which include bromodichloro- and chorodibromonitromethane) require particular analytical conditions for their analysis. These compounds are thermally unstable and decompose under commonly used injection port temperatures during GC or GC/MS analysis (*41*). The major decomposition products are haloforms (such as bromoform), which result from the abstraction of a hydrogen atom from the solvent by thermally generated trihalomethyl radicals. A number of other reaction products are also formed by radical reactions with the solvent and other radicals. In addition, trihalonitromethanes can decompose in a hot GC/MS transfer line and can exhibit unusual mass spectra, due to H/Br exchanges by some of their fragment ions. To successfully detect and quantify these compounds in drinking water, a GC injection temperature of 170 °C and a GC/MS transfer line at 225 °C must be used (*41*).

Many of the high-priority DBPs are also being measured as part of a large collaborative research effort involving scientists from the National Laboratories/Centers of the U.S. EPA's Office of Research and Development—the National Health and Environmental Effects Research Laboratory, the National Exposure Research Laboratory, the National Risk Management Research Laboratory, and the National Center for Environmental Assessment (*42*). This effort involves the joint chemical and toxicological evaluation of mixtures of DBPs produced by different water treatment processes. A comprehensive chemical evaluation of the drinking waters is being made, including the quantitation of most of the high-priority DBPs included in the nationwide occurrence study. The toxicological evaluation focuses on reproductive and developmental end points, with assays for other important end points and target organs, such as mutagenicity, carcinogenicity, hepatotoxicity, nephrotoxicity, immunotoxicity, neurotoxicity, developmental neurotoxicity, and pharmacokinetics, included to the extent possible (*42*).

Other studies involving MX have also been recently reported. Wright et al. measured MX concentrations and mutagenic activity in tap water samples from 36 surface water systems throughout Massachusetts (*43*). MX levels up to 80 μg/L were found (which were higher than previous limited reports before the U.S. Nationwide Occurrence Study). When the effect of chemical treatment on the formation of MX was studied, chloramination and filtration were found to be the best for reducing the mutagenic activity and DBP formation. The method used for this study involved the extraction of MX using XAD-8 resin adsorption, elution with ethyl acetate, methylation with acidic methanol, and analysis by GC/MS. Zwiener and Kronberg developed a new method using GC with ion trap-MS/MS as an alternative to high-resolution mass spectrometry for measuring MX (and MX analogues, including BMXs) in drinking water (*44*). This method provided a detection limit of 2 ng/L for MX and <1 ng/L for BMXs and was as selective as previously published methods. Zou et al. used GC/MS to identify a new DBP (2-chloro-5-oxo-3-hexene diacyl chloride) in chlorinated drinking water and in chlorinated fulvic acid solutions (*45*). This compound has a retention time similar to that of the methylated derivative of MX and the same characteristic ions (m/z 199, 201, and 203), which could cause interferences for selected ion monitoring-MS measurements of MX.

DBP Reviews. Three reviews have been published on DBPs in the last two years. Richardson et al. published a review of new epidemiology, toxicology, exposure, and chemistry research in a feature article entitled Disinfection By-products: The Next Generation (*29*). A tutorial review discussing the role that GC/MS and LC/MS have played in the discovery of new drinking water DBPs was also published (*46*). In addition to summarizing previous work, this article also discusses future directions for this area. In 2002, Urbansky and Magnuson published a review in *Analytical Chemistry*, which discusses the formation of DBPs, analytical methods used to identify them, and future research directions (*47*).

Identification of New DBPs. New DBPs continue to be discovered, and new chemical disinfectants continue to be investigated. For example, Taguchi reported the identification of two new halogenated DBPs in drinking water treated with chlorine (*48*). These DBPs, tentatively identified as 1-aminoxy-1-chlorobutan-2-ol and 1-aminoxy-1-bromobutan-2-ol, represent the first DBPs reported with an aminoxy structure. GC with low- and high-resolution electron ionization (EI)- and chemical ionization (CI)-MS, and MS/MS were used for their identification. Monarca et al. measured mutagenicity and reported DBPs from a new chemical disinfectant—peracetic acid—that has been previously used for wastewater disinfection and is being considered for use in drinking water treatment (*49*). Using GC with low- and high-resolution EI- and CI-MS, DBPs identified from peracetic acid disinfection were compared to those formed by chlorine and chlorine dioxide with the same source water. Peracetic acid formed mainly carboxylic acids (which are not mutagenic), whereas waters treated with the other disinfectants showed the presence of mutagenic/carcinogenic halogenated DBPs.

There has also been an exploration of new methods for determining highly polar DBPs that are believed to be present in treated drinking water but are missed with current methods. Zwiener et al. refined a previously published 2,4-dinitrophenylhydrazine (DNPH) derivatization-LC/MS method through the use of tandem MS (*48*). Using this method, aldehydes, ketones, hydroxybenzaldehyde, and dicarbonyl DBPs were identified in chlorinated drinking water. Another paper published a new tailor-made derivatization agent to be used with LC/MS to identify highly polar carbonyl DBPs (*49*). This reagent—4-(dimethylamino)-6-(4-methoxy-1-naphthyl)-1,3,5-triazine-2-hydrazine—allows polar carbonyl DBPs to be detected by LC/APCI-MS at nanogram per liter levels, with no preconcentration or extraction. The derivatization process requires only 0.5 mL of drinking water and only 10 min for reaction, which can be done directly in an LC autosampler vial. The derivatizing agent was also designed to allow optimal detection by UV or fluorescence spectroscopy, with the incorporation of a strong chromophore and a strong fluorophore. Because of the sensitivity of these derivatives to APCI-MS, the increased signal-to-noise values helped to overcome the chemical background inherent with LC/MS, reducing chemical backgrounds to flat, baseline levels and easily allowing the detection of chromatographic peaks, without the need for reconstructed ion chromatograms. This allows unknown peaks (DBPs) to be targeted for identification.

New Methods for Known DBPs. New analytical methods for known DBPs have also been developed. Cancho et al. published a headspace-SPME-GC-ECD method utilizing PFBHA derivatization for measuring aldehydes in drinking water (*50*). This method allowed microgram per liter determinations, showed good agreement of results with a previously published EPA method (EPA Method 556), and was used to measure aldehydes at a treatment plant in Barcelona, Spain (*50*). Loos and Barcelo developed a SPE-ion pair-LC/ESI-MS method for measuring HAAs in drinking water (*51*). Triethylamine was used as the ion pairing reagent, and detection limits in the low microgram per liter range were achieved. Using this method, high microgram per liter concentrations of chlorinated and brominated HAAs were found in samples from Barcelona tap water, swimming pool water, and surface waters from Portugal. Xie also reported a new method for HAAs using liquid—liquid microextraction, acidic methanol derivatization, and GC/MS detection (*52*). This method was capable of measuring all nine chloro/bromoacetic acids at

microgram per liter levels and provided cleaner baselines and fewer interfering peaks than EPA Method 552.2, which uses GC-ECD detection. Riter et al. constructed an external interface for use with a trap-and-release membrane introduction mass spectrometry (MIMS) system for measuring inorganic chloramines and chlorobenzenes in water (*53*). Chloramine is an alternative disinfectant that is becoming popular in the United States and other countries. This new interface allows independent control of the temperature of the membrane and eliminates the dependence of membrane heating efficiency on its position in the ion source.

Degradation of DBPs. Degradation of DBPs has been the focus of a few papers. Urbansky wrote a review covering the fate of HAAs in drinking water (*54*). Potential decarboxylation and nucleophilic substitution pathways are discussed; however, it was acknowledged that these processes are very slow (e.g., half-life of trichloroacetic acid estimated to be 20 years at 25 °C). Zhang and Minear studied the decomposition of trihaloacetic acids and the formation of corresponding trihalomethanes in drinking water (*55*). These decompositions occurred via a decarboxylation pathway, and rate constants were 0.0011, 0.0062, and 0.040 day^{-1} at 23 °C for bromodichloro-, dibromochloro-, and tribromoacetic acid, respectively. The effects of pH in the range of 6−9 and the drinking water matrix on trihaloacetic acid decomposition were found to be insignificant. Decomposition rate constants were also predicted for iodo-HAAs. It is interesting to note that the primary thermal decomposition pathway mentioned earlier for trihalonitromethanes also results in halomethanes as the dominant decomposition products (*41*). Also, it is interesting that, at the time of this prediction of decomposition rate constants for iodo-HAAs, they had not been found in drinking water; however, as noted earlier for the Nationwide Occurrence Study, iodo-HAAs and other iodo acids have now been found at one location in the United States (*35*). Reckhow et al. studied the formation and degradation of dichloroacetonitrile in drinking water (*56*). Dichloroacetonitrile is a DBP that is common for chlorine or chloramine disinfection. Although dichloroacetonitrile has been known to undergo base-catalyzed hydrolysis from previous studies, the pathway of decomposition and dependence on pH, reaction time, and chlorine dose were not completely understood. Results of this study revealed a decomposition scheme with three pathways of hydrolysis: attack by (1) hydroxide, (2) hypochlorite, and (3) water (*56*). Depending on pH, reaction time, and chlorine residual, any one of these three pathways may predominate. Also, the kinetic model showed that the dichloroacetonitrile initially formed during treatment was often many times the actual measured concentration (due to significant decomposition).

Human Exposure Studies. Important new human exposure studies are also being conducted for DBPs. These studies are not only useful to demonstrate exposure/uptake of DBPs in the human body but they can also ultimately provide more accurate information about an individual's exposure, as compared to using water consumption questionnaires and quarterly water treatment plant data, which have been traditionally used in epidemiologic studies. Previous research revealed that showering and bathing can result in higher blood levels of THMs than ingesting 1 L of water. In the last two years, additional research has revealed other important findings. Xu et al. recently published a study of the permeation of THMs, HAAs, and haloketones through human skin (*57*). This study showed that compounds in these three classes had different permeabilities—indicating DBPs can have different dermal absorptions. Of the THMs, bromoform had the highest permeation and chloroform the least; THMs were 10 times more permeable than haloketones; and the permeability of HAAs was very low. It was proposed that ionization may be the most significant factor limiting the permeability of the HAAs. The dose of THMs by dermal absorption was estimated to be 40−70% of the dose from the ingestion of drinking water, while for haloketones, it was 10% and insignificant for HAAs. Froese et al. performed a human exposure trial to evaluate trichloroacetic acid (TCAA) excretion in urine as a biomarker of exposure to DBPs (*58*). A modified version of EPA Method 552.2 was used, in which urine was acidified, salted, extracted with MTBE, methylated, and analyzed by GC-ECD. Considerable inter- and intraindividual variability in both TCAA ingestion and excretion was observed. This variability raised questions about generalizations of DBP exposures from routine water quality monitoring data. A major contribution to the observed variability was the variability of TCAA levels in the water and the volume of water consumed for each individual and across all individuals in the study. The excretion half-life of TCAA (2.3−3.7 days) was longer than any of the THM biomarkers, and the presence of TCAA could be linked to tap water ingestion (excretion levels were low after prolonged exposure to TCAA-free bottled water). Also, the TCAA in urine was sufficiently stable to allow monitoring, making it a promising biomarker of ingestion exposure to DBPs in drinking water. Kuklenyik et al. developed a fast and sensitive assay for quantifying TCAA in urine, with the goal of having a good method to evaluate the potential of TCAA as a biomarker for assessing chronic ingestion exposure to HAAs from drinking water (*59*). This method used SPE cleanup followed by isotope dilution-LC/MS/MS detection. The limit of detection was 0.5 ng/mL (ppb) for 1 mL of urine, and the entire sample preparation and analysis could be performed in 15 min or less. Miles et al. used a purge-and-trap-GC/isotope dilution-MS method (with ng/L detection limits) to measure THM concentrations in tap water and blood of women living in two different states in the United States that have substantial differences in DBP speciation (one state with a higher level of brominated THMs, the other with more chlorinated THMs) (*60*). THMs in the blood rose significantly as a result of showering, and the resulting THM distribution in the blood corresponded to that observed in the tap water.

Other New DBP Research. Predictive work involving DBPs has also been a subject of research. Roberts et al. developed a simple predictive model based on fundamental chemistry and the Information Collection Rule data to project HAA9 occurrence (all nine chloro/bromoacetic acids) in U.S. drinking waters (*61*). According to the model, total HAA9 concentrations in finished drinking water are likely to be similar to the total THM concentrations (THM4—the four chloro/bromo-THMs) and may be appreciably higher than would be anticipated based on measurement of only the five regulated HAAs.

Studies involving the formation/decomposition of DBPs in the distribution system have also been published. Most measurements of DBPs have been done at drinking water treatment plants, and there is a scarcity of information on the chemistry of particular

DBPs in the distribution system. The distribution system is important because human exposure occurs from the distribution system (and not at the plant itself), where concentrations can increase or decrease and DBPs can hydrolyze. Rossman et al. conducted a distribution system study in a controlled, simulated pipe environment and compared the rate of chlorine consumption and the levels of THMs and HAAs to the same water held in glass bottles (*62*). Results showed that the rate of chlorine consumption in the pipe was much greater, and that there was no decrease in the amounts of HAAs produced, but that the THM levels increased by an average of 15%. Separate tests confirmed that this increase was due to a reservoir of organic precursor material associated with deposits on the pipe wall. Stability of DBPs in actual distribution systems and in simulated distribution systems was also a component of the U.S. Nationwide DBP Occurrence Study mentioned earlier (*35*). In most cases where chloramination was used, the DBPs were relatively stable. However, when free chlorine was used, THMs and other DBPs, including HAAs, increased in concentration both in the actual distribution system and in simulated distribution system tests. Haloacetonitriles generally were stable (at the distribution system pH levels encountered in this study—6.8−9.4) and increased in concentration, but many haloketones were found to degrade in the distribution system and in tests. Halonitromethanes and dihaloacetaldehydes were found to be stable in these systems and in tests. Although controlled laboratory studies had suggested instability of halogenated furanones, particularly MX, in water, MX and MX analogues were sometimes stable, and sometimes they degraded somewhat in the distribution system and tests. When MX analogues showed some degradation, they were generally still present at detectable levels, indicating that they do not completely degrade in the distribution system. Many times, the BMXs were stable.

A new area of DBP research involves probing high molecular weight halogenated material that is formed upon disinfection. ESI-MS and MALDI-MS are allowing researchers to study this more in-depth for the first time. Zhang and Minear designed studies with ^{36}Cl-labeled chlorine as the disinfectant to allow the high molecular weight, chlorine-containing DBPs to be better detected and characterized (*63*). Ultrafiltration/SEC, ESI-MS, and MS/MS were used to provide information on the high molecular weight total organic halides formed by chlorinating aquatic humic substances. The molecular weight distribution of chlorinated DBPs was highly dispersed, with an average molecular weight of ∼2000. The Cl/C ratios of the high molecular weight DBPs were roughly constant (0.025), which is much lower than for lower molecular weight DBPs.

Ultrafiltration membranes have also been used to separate untreated, raw water dissolved organics into different molecular weight fractions to study their disinfection byproducts. For example, Chang et al. studied the reaction of chlorine dioxide with four isolated molecular weight fractions of natural organic matter from raw source waters (<1000, 1000−5000, 5000−10 000, and >10 000) (*64*). Results showed that the lower molecular weight organic matter fractions (<5000) contributed to the most DBPs per unit carbon for THMs and total HAAs. Another recent study showed that dissolved organic matter concentrated by reverse osmosis and treated with chlorine produced the same amount of THMs, HAAs, haloacetonitriles, and haloketones (within 95% confidence intervals) as disinfected waters that were not preconcentrated prior to treatment (*65*). This is an important finding because concentration following disinfection can result in the loss of volatile DBPs; this preconcentration procedure could potentially allow the toxicological study of drinking water concentrates with minimal loss.

Finally, an important study was conducted by Kimbrough and Suffet showing that bromide can be removed electrochemically in source waters for drinking water (*66*). Generally, treatment or removal studies are not included in this review; however, this treatment appears to be extremely promising and may be a solution to the production of highly toxic/carcinogenic brominated DBPs that can be produced when source waters are high in bromide. Electrochemical treatment was showed to oxidize bromide to bromine, which subsequently volatilized from the water. When the electrolyzed water was chlorinated, it produced measurably lower amounts of THMs and proportionately fewer brominated THMs (*66*).

Nitrosodimethylamine. NDMA, which has recently been discovered to be a DBP from chloramines or chlorine disinfection, is also very important, as it is recognized as a probable human carcinogen. NDMA was initially discovered in chlorinated drinking waters from Ontario, Canada, and has recently been found in other locations and in laboratory studies. The observation of NDMA in U.S. waters is largely due to improved analytical techniques that have allowed its determination at low nanogram per liter concentrations. Recent measurements have shown it is generally present at 10 ng/L or less in chlorinated drinking water, and it can be formed at 100 ng/L or higher in wastewater treated with chlorine (*67*). Following its discovery in California well water, the State of California issued an action level of 0.002 μg/L (2 parts per trillion) for NDMA, which was subsequently revised to 0.01 μg/L, due to the analytical difficulty in measuring it at the original proposed level. The California Department of Health Services has a website that provides further background and details about NDMA (www.dhs.ca.gov/ps/ddwem/chemicals/NDMA/NDMAindex.htm). This site also provides a link to the U.S. National Toxicology Program (NTP) 2000 report on NDMA. NDMA is currently not regulated in the United States for drinking water. It is being considered for the Contaminant Candidate List in the United States but is currently not listed.

An isotope dilution-GC/MS method reported can measure as little as 3 ng/L NDMA in drinking water (*68*). Another method reports ∼0.5-ng detection limits for derivatized NDMA using high-pressure thin-layer chromatography with fluorescence detection (*69*). GC/MS and GC/MS/MS have also recently been used to study the formation of NDMA during chlorination (*70*). This study revealed that NDMA can form by the reaction of dimethylamine and other secondary amines (potential NDMA precursors) and that this process may involve the slow formation of 1,1-dimethylhydrazine by the reaction of monochloramine and dimethylamine, followed by rapid oxidation to NDMA and other products, including dimethylcyanamide and dimethylformamide. Other pathways, such as the reaction of sodium hypochlorite with dimethylamine, can also lead to NDMA formation. However, the rate of NDMA formation is 10-fold slower than that observed when monochloramine reacts with dimethylamine, and it showed a

strong pH dependence due to competing reactions. In another paper, Choi and Valentine also studied the formation of NDMA, using dimethylamine as a model precursor (*71*). ^{15}N-Labeled monochloramine was used to track the incorporation of nitrogen into the nitroso group, and mass spectrometry was used to analyze the products. This work showed that the nitrogen from monochloramine was the source of a nitrogen atom in the nitroso group of NDMA, and its formation increased with increasing monochloramine concentration. The proposed NDMA formation pathway involves the formation of 1,1-dimethylhydrazine (from the reaction of dimethylamine with monochloramine), followed by oxidation by monochloramine to NDMA. In a separate paper, Choi et al. reported mechanistic studies of NDMA formation in chlorinated drinking water (*72*). In this study, dimethylamine was used as a model precursor and was found to react with free chlorine in the presence of ammonia to form NDMA.

Two recent studies have focused on methods to eliminate NDMA from drinking water. One study showed that ultraviolet direct photolysis could remove NDMA from water, with dimethylamine, nitrite, and nitrate formed as the major degradation products (*73*). Another study showed that treatment with a high-energy electron beam could eliminate NDMA (*74*).

Bromate. Although the issue of bromate formation is not new (there have been more than 10 years of research on bromate and it is now regulated by the U.S. EPA and in other countries), there are a few papers worthy of note that significantly lower detection limits. First, Delcomyn et al. developed a new IC-postcolumn reaction method for measuring bromate in drinking water (*75*). This postcolumn reaction converts bromate to tribromide, which can be detected by UV spectrometry at 0.05 μg/L detection limits. No pretreatment of samples is required with this method, other than filtration and quenching of the oxidant residual. Ingrand et al. developed laboratory and field methods for measuring bromate in water (*76*). This paper offers improved procedures for an existing IC method to remove interferences and provides alternative laboratory methods including IC/ICPMS, IC-postcolumn reaction-UV, ion pair chromatography-postcolumn reaction-fluorescence, and flow injection-ICPMS. These alternative methods yielded detection limits of 1.6 (for the fluorescence method) or 0.1−0.3 μg/L (for the other methods). Finally, Liu et al. developed a simple sample preconcentration method using microwave concentration, which was coupled with IC for measuring bromate at 0.1 μg/L detection limits (*77*).

PHARMACEUTICALS, HORMONES, AND ENDOCRINE DISRUPTING COMPOUNDS

Pharmaceuticals, hormones, and EDCs have become major issues in environmental chemistry, due to their presence in environmental waters (following incomplete removal in wastewater treatment or point-source contaminations) and concern about possible estrogenic and other effects, both to wildlife and humans. Pharmaceuticals that have been detected directly or as their metabolites include antibiotics (such as erythromycin, sulfamethoxazole, and trimethoprim), analgesics and antiinflammatory drugs (such as aspirin, ibuprofen, and diclofenac), lipid regulators (such as clofibric acid, bezafibrate, and gemfibrozil), β blockers (such as bisoprolol, betaxolol, and metoprolol), antiepileptic drugs (such as carbamazepine), oral contraceptives (such as 17α-ethynyl estradiol and mestranol), and steroids and hormones (such as *cis*-androsterone, coprostanol, 17α-estradiol, 17β-estradiol, estrone, progesterone, and testosterone). Although their environmental concentrations are generally very low (low ng/L), these levels would be sufficient to induce estrogenic responses and cause reproductive and developmental effects in wildlife. Many pharmaceuticals and hormones are highly polar—which necessitates the use of either LC/MS or an efficient derivatization procedure combined with GC/MS for their analysis.

Pharmaceuticals. Interest in this area is evidenced by reviews that have recently been published. Ternes reviewed analytical methods for determining pharmaceuticals in aqueous environmental samples (*78*). Methods include those using SPE, derivatization, detection, and confirmation by GC/MS, GC/MS/MS, and LC/ESI-MS/MS. A wide variety of pharmaceuticals can be determined in the nanogram per liter range. Ternes discusses the advantages and disadvantages of GC/MS and LC/MS methods. Zwiener et al. reviewed the occurrence and fate of pharmaceuticals in the aquatic environment and their significance for drinking water production (*79*). Heberer reviewed the occurrence, fate, and removal of pharmaceuticals in environmental waters (*80*). He reports on measurements of more than 80 pharmaceuticals and their metabolites in studies from Austria, Brazil, Canada, Croatia, England, Germany, Greece, Italy, Spain, Switzerland, The Netherlands, and the United States. One of these surveys completed by the U.S. Geological Survey in 2002 involved the first nationwide reconnaissance of pharmaceutical residues, hormones, and other organic wastewater constituents in the United States; results showed that many of these compounds were detected in rivers and streams, indicating that many survived wastewater treatment and biodegradation (*81*).

Pharmaceuticals are a concern for drinking water because recent studies have shown that wastewater treatment does not always remove them and that they can enter drinking water source waters (either surface water or groundwater sources) and survive drinking water treatment. It has not yet been determined whether levels found in drinking water pose a human health risk, but finding these compounds in drinking waters and surface waters has created concern due to potential low levels of action and their potential widespread occurrence. There have been reports going back to 1997 for pharmaceuticals being found in drinking water, and over the last two years, reports continue. Reddersen et al. reported finding three phenazone-type pharmaceuticals and three metabolites in wells in Berlin, Germany, at concentrations up to the low microgram per liter level (*82*). The metabolites were identified as 1-acetyl-1-methyl-2-dimethyl-oxamoyl-2-phenylhydrazide (AMDOPH), 1-acetyl-1-methyl-2-phenylhydrazide, and dimethyloxalamide acid−(*N*′-methyl-*N*-phenyl)hydrazide. The pharmaceutical residues are believed to originate from former production spills of a pharmaceutical plant located in a city north of Berlin. With the exception of AMDOPH, all of the other pharmaceuticals were effectively removed during conventional drinking water treatment; AMDOPH was found at concentrations of 0.9 μg/L in finished drinking water. A follow-up toxicity study indicated that concentrations were not high enough to contribute to any adverse human health effects (*82*). Ibuprofen, diclofenac, phenazone, clofibric acid, carbamazepine, primidone, sulfamethoxazole, sulfamethazine, dehydroerythromycin, and sotalol were also found in groundwaters in Germany (*80*, *83*). Sulfamethoxazole and

sulfamethazine have also been detected in groundwaters in the United States (*80*).

Drewes et al. evaluated different wastewater treatment technologies (activated carbon, trickling filter, nanofiltration, reverse osmosis) at full-scale facilities in Arizona and California that would lead to indirect potable reuse (*84*). Nanofiltration and reverse osmosis were found to remove all drugs studied; other removal techniques showed varying results; and antiepileptic drugs, carbamazepine and primidone, were the most difficult to remove. Zwiener et al. discussed possible removal strategies in drinking water treatment (*79*). Flocculation was not determined to be suitable for the removal of pharmaceuticals; activated carbon adsorption could result in significant removals; and advanced oxidation processes (using ozone and hydrogen peroxide at a level of 5 and 1.8 mg/L, respectively) had the potential to remove pharmaceuticals (clofibric acid, ibuprofen, and diclofenac were studied) (*79*). In a discussion of future needs, Zwiener et al. (*79*) cite analytical method development and investigation of the behavior of pharmaceuticals in drinking water treatment as two of the most important research needs concerning drinking water. In 2002, Heberer measured aminophenazone, carbamazepine, clofibric acid, diclofenac, gemfibrozil, ibuprofen, indomethacine, ketoprofen, naproxen, oxazepam, phenazone, phenobarbital, phenytoine, primidone, propyphenazone, sulfadiazine, sulfamethizole, sulfamethoxazole, and salicylic acid at levels up to micrograms per liter in influent and effluent samples from sewage treatment plants and discovered that, under recharge conditions, several of these pharmaceuticals were also present at concentrations up to 7.3 μg/L in groundwater samples (*85*). Four different analytical methods were used to enable this broad analysis of pharmaceuticals. All methods used SPE and GC/MS, and sometimes GC/MS/MS, for detection. A few of the pharmaceuticals were also detected at the nanogram per liter level in tap water from Berlin. Derivatizing agents used to enable analysis by GC/MS included pentafluorobenzyl bromide, *N*-(*tert*-butyldimethylsilyl)-*N*-methyltrifluoroacetamide, or a mixture of *N*-methyl-*N*-(trimethylsilyl)-trifluoroacetamide, trimethylsilylimidazole, and dithioerytrol. Jux et al. developed a derivatization-GC/MS method for simultaneously determining polar pharmaceuticals in water (*86*). This method was used to measure gemfibrocil (a lipid blood regulating compound), clofibric acid (a metabolite of lipid regulated compounds), and antirheumatics (diclofenac, ibuprofen, ketoprofen, indomethacin, fenoprofen) in 27 rivers and ponds in Germany. Diclofenac was detected in 10 of the 27 water samples in concentrations up to 15 μg/L, but none of the pharmaceuticals was present in finished drinking waters from Cologne and the surrounding area.

Pedersen et al. used GC/MS to investigate xenobiotic organic compounds in runoff from fields irrigated with treated wastewater (*87*). Nontarget compounds identified in this study included pharmaceuticals, personal care products, flame retardants, plasticizers, and pesticide transformation products. Pharmaceuticals and personal care products identified include *p*-toluenesulfonamide, benzophenone, and *N*,*N*-diethyltoluamide. La Farre et al. used a combined method involving toxicity and SPE with LC/ESI-MS to determine pharmaceuticals in water (*88*). The analgesic drugs investigated include ibuprofen, ketoprofen, naproxen, and diclofenac and the decomposition product of aspirin (salicylic acid), along with one lipid lowering agent, genifibrozil. Microtox and ToxAlert toxicity tests with *Vibrio fischeri* were used to determine the 50% effective concentration and toxicity units for each compound. Detection limits ranged from 15 to 56 ng/L. This method was applied to wastewater and surface water samples from Catalonia, Spain. Ternes et al. developed a LC/ESI-MS/MS method for determining nine pharmaceuticals in groundwater, river water, and wastewater down to the low nanogram per liter range (*89*). The analytes included antiphlogistics, psychiatric drugs, and antidiabetic drugs. Recoveries exceeded 80%, and quantification limits were as low as 50 ng/L in wastewater and 10 μg/L in groundwater. Using this method, caffeine and propyphenazone were found in municipal wastewater at levels of 147 and 1.3 μg/L, respectively. Ahrer et al. compared two methods—LC/ESI-MS and CE/MS—for determining drug residues in water (*90*). For the LC separations, a methanol gradient was used to separate a number of drugs, such as paracetamol, clofibric acid, penicillin, naproxen, bezafibrate, carbamazepine, diclofenac, ibuprofen, and mefenamic acid. Sample pretreatment for the LC/MS method involved the use of SPE; pretreatment for the CE/MS method involved the combination of liquid−liquid extraction and SPE. LC/MS offered high selectivity and good detection limits of 1 ng/L and below for samples that are concentrated by SPE. Due to high standard deviations of recoveries with CE/MS, a standard addition method was required for CE/MS, which gave detection limits of 4.8−19 ng/L.

Antimicrobial agents have also been the subject of studies. For example, Lindstrom et al. investigated the occurrence and environmental behavior of the bactericide triclosan and its methyl derivative (transformation product) in surface waters and wastewaters (*91*). Passive sampling with semipermeable membrane devices were used to collect samples of triclosan and methyl triclosan in lakes from Switzerland, and the analytical method involved derivatization with diazoethane and GC/MS analysis. Levels up to 74 and 2 ng/L were found, for triclosan and methyl triclosan, respectively. Both compounds were found to be emitted from wastewater treatment plants, and methyl triclosan is postulated as having been formed by biological methylation. A regional mass balance of one of the lakes showed significant removal of triclosan by processes other than flushing. Laboratory experiments showed that dissociated triclosan can be rapidly degraded in water when exposed to sunlight (half-life <1 h); however, methyl triclosan and nondissociated triclosan were not photolabile. Lindsey et al. used SPE and LC/ESI-MS to analyze sulfonamide and tetracycline antimicrobials in groundwater and surface waters (*92*). Six sulfonamides and five tetracyclines, which are commonly used for veterinary purposes and agricultural feed additives and are suspected to leach into groundwaters and surface waters, were investigated. The LC/ESI-MS method allowed submicrogram per liter detection limits; several of the antimicrobials were found in groundwaters and surface waters from the United States at levels ranging from 0.06 to 1.34 μg/L.

The degradation and treatment of pharmaceuticals have also been investigated. Zwiener et al. identified metabolites from the biodegradation of ibuprofen (hydroxyibuprofen, carboxyibuprofen, carboxyhydratropic acid) (*93*). GC/EI-MS/MS and on-line methylation were used to identify these metabolites, which accounted for <10% of the initial concentration of ibuprofen.

Degradation experiments with biofilm reactors and batch experiments with activated sludge revealed the hydroxyibuprofen as the major metabolite under oxic conditions and carboxyibuprofen under anoxic conditions. Carboxyhydratropic acid was found under oxic and anoxic conditions mostly with activated sludge. Balcioglu and Otker investigated the treatment of antibiotics in wastewater using ozone and ozone/hydrogen peroxide to enhance their biodegradability (*94*). These processes provided significant reductions in chemical oxygen demand and aromaticity.

Hormones and Endocrine Disrupting Compounds. EDCs are not a new issue, necessarily, but have recently become a major area of concern worldwide. In addition to the U.S. Food Protection Act and the Safe Drinking Water Act and Amendments, there is a European Union Directive (2001) that addresses many of the EDCs as priority substances. The endocrine system is an intricate system of hormones that regulate development, growth, reproduction, and behavior. Certain synthetic and natural chemicals have the ability to mimic these hormones and, thus, can interfere with or disrupt the normal function. EDCs can alter hormonal function by binding to hormone receptors directly or by indirectly relaying molecular messages through a complex array of cellular proteins that activate genes and alter cell growth and division. In wildlife, EDCs are suspected of being responsible for the decline in certain species (e.g., possible increased sterility in the American alligator), change of sex in fish and shellfish, and other problems. EDCs are also suspected in declining sperm counts in humans, although this has not been proven. Both natural estrogens and anthropogenic EDCs can reach the aquatic environment through wastewater discharges. Fish and wildlife can be exposed, and humans can become exposed through the intake of this water into drinking water treatment plants. Chemicals that have been determined to be estrogenic include synthetic estrogens (such as commonly used birth control pills), steroids, pesticides, phthalates, alkylphenol ethoxylate surfactants, dioxins, polychlorinated biphenyls (PCBs), and natural estrogens, such as phytoestrogens that are found in many plants, including soybeans, wheat, rice, carrots, beans, potatoes, cherries, and apples. Trussell published a nice review in 2001 on EDCs in the *Journal of the American Water Works Association*, where he explains in detail the endocrine system and specifically how EDCs interfere with natural receptors (*95*). Trussell also makes recommendations on how the water industry should actively respond to this issue.

Reviews of hormones and other EDCs have focused on analytical methods and occurrence. De Alda and Barcelo reviewed analytical methods for determining estrogens and progestogens in wastewater and discuss the difficulty in measuring these compounds at nanogram per liter levels in complex matrixes (such as wastewater) (*96*). This review covers analytical methods used for determining these compounds in wastewater and discusses key procedural steps—from sampling to analysis—and the techniques most commonly used in those measurements. Petrovic et al. provide an overview of mass spectrometry methods for measuring EDCs in environmental waters (*97*). EDCs discussed in this review include alkylphenols, polychlorinated compounds (dioxins, furans, biphenyls), polybrominated diphenyl ethers, phthalates, and sex hormones. Ying et al. reviewed the occurrence and fate of hormone steroids in the environment (*98*). This review reports the detection of estrogenic steroids in sewage treatment plant effluents, with up to 70 ng/L observed for estrone, 64 ng/L for 17β-estradiol, 18 ng/L for estriol, and 42 ng/L for 17α-ethynylestradiol. In river water from Japan, Germany, Italy, and The Netherlands, 17β-estradiol has been found at levels up to 27 ng/L, and 17β-estradiol ranging from 6 to 66 ng/L has been found in groundwater in northwest Arkansas. This groundwater contamination has been associated with land applications of poultry litter and cattle manure waste.

A variety of different analytical methods have been used to measure EDCs, including ELISA, LC, GC/MS, LC/MS, and MS/MS, as well as immunosorbents used with LC/MS. Some of these methods are providing not only low nanogram per liter detection but also as low as picogram per liter detection. Benijts et al. developed a LC/ion trap-MS method for three natural estrogens—estrone, estradiol, and estriol—and two synthetic estrogens—ethynylestradiol and diethylstilbestrol (*99*). This negative ionization-MS method gave limits of detection ranging from 3.2 to 10.6 ng/L for all compounds, with a limit of quantitation between 10.6 and 35.0 ng/L. Ferguson et al. reported a method for measuring steroid estrogens in wastewater using immunoaffinity extraction coupled with LC/ESI-MS (*100*). The use of highly selective immunosorbents removed interfering sample matrix compounds present in wastewater, which would otherwise cause severe ionization suppression of the estrogens during electrospray. The signal-to-noise ratio was also increased for the analytes, and extremely low detection limits of 0.18 and 0.07 ng/L were achieved for 17β-estradiol and estrone, respectively. This method was then applied to the analysis of estrogens in two wastewater effluents; recoveries were >90%, and the selectivity of the method was demonstrated by excluding a structurally related analyte, 17α-ethynylestradiol (which is not immunogenic) in the immunoextraction purification step. Concentrations of 17β-estradiol and estrone were found to be between 0.77 and 6.4 ng/L and 1.6 and 18 ng/L, respectively. Huang and Sedlak developed an ELISA method for measuring 17β-estradiol and 17α-ethynylestradiol in municipal wastewater and surface water (*101*). GC/MS/MS was used for confirmation. Detection limits were approximately 0.1 ng/L in wastewater effluent and 0.05 ng/L in surface water.

New LC methods include those developed by de Alda and Barcelo (*102*) and Penalver et al. (*103*). The first method used a fully automated on-line SPE-LC-diode array method, which allowed the simultaneous determination of six estrogens—estradiol, estriol, estrone, ethynylestradiol, mestranol, and diethylstilbestrol—and three progestogens—progesterone, norethindrone, and levonorgestrel (*102*). These nine hormones were chosen because of their abundance in the human body, their estrogenic potency, and their use in contraceptive pills. Up to 16 samples could be analyzed in a completely automated, unattended manner. This method was applied to the analysis of various water samples, including drinking water, groundwater, surface water, and sewage treatment plant effluents. Detection limits ranged from 10 to 20 ng/L, with good precision and accuracy. The second LC method involved the use of SPME coupled to LC with both UV and electrochemical detection for measuring bisphenol A, β-estradiol, α-estradiol, 17α-ethynylestradiol, estrone, 4-*tert*-butylphenol, diethylstilbestrol, mestranol, 4-nonylphenol, and 4-*tert*-octylphenol (*103*). Detection limits ranged from 0.3 to 1.1 μg/L using UV detection and from 60 to 80 ng/L using electrochemical detection. Using this method,

β-estradiol was found in wastewater treatment plant effluents at concentrations between 1.9 and 2.2 μg/L.

GC/MS methods developed for estrogenic compounds include those by Kuch and Ballschmiter (*104*), Xiao et al. (*105*), Nakamura et al. (*106*), Spengler et al. (*107*), and Ding and Chiang (*108*). Kuch and Ballschmiter used SPE with GC-negative chemical ionization (NCI)-MS to measure estrogens and endocrine disrupting phenolic compounds in surface and drinking water (*104*). The phenols and steroids were initially derivatized to their pentafluorobenzoylate esters, and detection limits of 20−200 pg/L were achieved for estrone, 17α-estradiol, 17β-estradiol, 17α-ethynylestradiol, bisphenol A, 4-nonylphenol, and 4-*tert*-octylphenol. This method was used to identify these analytes in sewage treatment plant effluents, river water, and drinking waters in Germany, where several of these analytes were found. In drinking water, bisphenol A ranged from 300 pg/L to 2 ng/L, 4-nonylphenol from 2 to 15 ng/L, 4-*tert*-octylphenol from 150 pg/L to 5 ng/L, and the steroids from 100 pg/L to 2 ng/L. This work clearly showed that endocrine disrupting estrogens were not completely removed in wastewater treatment and that they could also survive drinking water treatment. Xiao et al. also reported a GC/NCI-MS method using derivatization with pentafluorobenzoyl chloride and SPE to measure estrogens in environmental water and wastewater effluents (*105*). Detection limits were 0.2 ng/L or below for estrone, ethynylestradiol, 17β-estradiol, and estriol. Using this method, wastewater and river water in the U.K. were analyzed; the most abundant estrogen was estrone with concentrations ranging from 6.4 to 29 ng/L in effluents and 0.2 to 17 ng/L in water from the River Thames. Nakamura et al. also developed a method using GC/NCI-MS (for 17α-estradiol, 17β-estradiol, estrone, ethynylestradiol, and estriol) but with pentafluorobenzylbromide as the derivatizing agent (*106*). Detection limits ranged from 0.10 to 0.28 ng/L in river water. Spengler et al. developed a GC/MS method using standard addition for measuring natural and synthetic estrogens 17β-estradiol, estrone, 17α-ethynylestradiol, and mestranol; phytoestrogens genistein and β-sitosterol; and xenoestrogens benzyl butyl phthalate, dibutyl phthalate, bisphenol A, 4-nonylphenol, 4-nonylphenoxyacetic acid, 4-nonylphenol diethoxylate, and α-endosulfan in sewage treatment plant effluents (*107*). Using this method, effluents from 18 sewage treatment plants in Germany were investigated. The median concentration of steroidal estrogens ranged between 0.4 and 1.6 ng/L; the metabolites of the nonylphenol polyethoxylates ranged between the upper nanogram per liter range to the lower microgram per liter range. Finally, Ding and Chiang evaluated different derivatization procedures for determining estrogenic chemicals with GC/MS (*108*). Different silylating agents (mostly trimethylsilylating agents) were compared. Steric hindrance of multiple hydroxyl groups and ethynyl groups was the cause of most of the differences in derivatization efficiency. Trimethylchlorosilane produced the highest efficiencies for compounds with multiple hydroxyl groups (e.g., 17β-estradiol and estriol). Mass spectra of these derivatives were presented and fragmentation pathways discussed. Quantitation limits ranged from 5 to 10 ng/L.

Because of their widespread use and potential for endocrine disruption, alkylphenol ethoxylate surfactants have become a focus of interest in environmental chemistry. One method was published for determining halogenated derivatives of alkylphenol ethoxylates and their metabolites that are formed during chlorine disinfection (*109*). Using SPE-LC/MS, brominated and chlorinated nonylphenol ethoxylates, octylphenol ethoxylates, nonylphenols, and nonylphenoxycarboxylates were determined, with detection limits ranging from 20 to 100 ng/L for water. This method was also used to measure halogenated surfactant byproducts in sludge from a drinking water treatment plant in Barcelona, Spain, where levels in the hundreds of micrograms per kilogram bromononylphenol and bromononylphenol ethoxylates were found. This method is the first one developed to simultaneously determine alkylphenol ethoxylates and their halogenated byproducts, along with their degradation products. In an occurrence study of polyethoxylate surfactants, Petrovic et al. used SPE-LC/MS to analyze alcohol ethoxylates, nonylphenol ethoxylates, coconut diethanol amides, nonylphenoxy monocarboxylates, nonylphenol, octylphenol, and linear alkylbenzenesulfonates in coastal sediment and water samples from harbors along the Spanish Mediterranean coast (*110*). Results revealed the presence of considerably high concentrations of nonylphenyl ethoxylates and nonylphenol near points of discharge of industrial and urban wastewaters. Nonylphenol was found in 47% of the water samples and in 77% of the sediment samples.

GC/MS methods (with derivatization) have also been used to measure nonylphenol and nonylphenol ethoxylates in water. Diaz et al. developed a derivatization-headspace-SPME-GC/MS method for analyzing nonylphenol, nonylphenol mono- and diethoxylates (short-chain ethoxylates) and their acidic metabolites in water (*111*). Samples were methylated with dimethyl sulfate/NaOH; Carbowax−divinylbenzene was found to be the best SPME fiber, allowing 20−1500 ng/L detection limits.

Immunoassays have also been developed for measuring EDCs. Matsunaga et al. developed a fully automated immunoassay system for measuring EDCs in water, which allows the rapid measurement of samples (*112*). Monoclonal antibodies chemically conjugated to bacterial magnetic particles were used to measure alkylphenol ethoxylates, bisphenol A, and linear alkylbenzenesulfonates with luminescence detection. Detection limits ranged from low nanogram per liter to low microgram per liter. Zhao et al. developed a new ELISA method for measuring bisphenol A and other bisphenols (*113*). Cross-reactions of other common phenolic compounds (such as phenol, hydroquinol, and *p*-hydroxybenzoic acid) were all lower than 1%; detection limits were 0.1 μg/L.

CHIRAL CONTAMINANTS

A major development, particularly in pesticide research, is the use of chiral chromatography to analyze individual chiral isomers. Chemically, chiral isomers are very similar, having the same boiling points, melting points, and typically the same solubility, reactivity, and other chemical properties. Microbially and biologically, however, they can behave very differently. Typically, one form is active against the insects and pests that the pesticide is designed to attack, and the other form is inactive. Likewise, in the environment, one form can be actively degraded by microbes, and the other form can accumulate. It was not until recent developments allowed the separation and low-level detection of these isomers that their environmental behavior could be studied. However, early research is showing that the environmental

behavior of chiral compounds is not straightforward—it is not always possible to predict the enantiospecific transformation. Microbial populations in environmental matrixes can change, and even reverse, the enantiomeric ratios (so microbial processes may not always show selective degradation of the same enantiomer). Some environmental processes are not enantioselective toward a particular chemical, even if microorganisms are involved. Sometimes microbial degradation rates are sufficiently rapid for both enantiomers, so that enantioselective degradation is not important. Some compounds are degraded much faster chemically (abiotically) than microbially, so that enantioselective degradation is not important, and sometimes enantiomerization can occur, where one enantiomer is microbially converted to the other (*114*).

The ability to separate enantiomers and produce a single enantiomeric isomer has not been lost on pesticide manufacturers. This ability has allowed manufacturers to sell a new, patented enantiomeric form of a pesticide, creating new markets for their products. The development of enantiomerically enriched pesticides may actually be a benefit for the environment, as less material could potentially be applied to crops, less may be accumulated in the environment, and there may be fewer unintended side effects on nontarget species.

Ward published a 2000 *Analytical Chemistry* review on chiral separations (*115*). This review provided details on the types of chiral phases used for separations and various separation techniques (including CE, supercritical fluid chromatography, GC, and LC). Chiral selectors now include cyclodextrins, proteins, crown ethers, polysaccharides, polyacrylamides, polymeric chiral surfactants, macrocyclic antibiotics, and ergot alkaloids. Cyclodextrins still remain the most popular chiral selectors used for environmental applications. Hegeman and Laane published a review on the enantiomeric enrichment of chiral pesticides in the environment (*116*), and Issaq published a review of capillary electrophoresis, which included the use of CE for chiral separations (*117*). Shamsi et al. published the development of polymeric molecular micelles as pseudostationary phases for CE (*118*). Molecular micelles offer the following advantages as chiral selectors over cyclodextrins: (1) different functionalities, including a variety of chiral headgroups, can be incorporated into the polymers to offer a variety of selectivities; (2) amino acid-based polymeric surfactants with D and L optical configurations can be easily synthesized in high purity and characterized using a variety of analytical techniques; and (3) elucidating chiral interaction mechanisms can be easier with molecular micelles (derivatized cyclodextrins have varying degrees of substitution, which is not always accurately known). Molecular micelles can also be used in combination with MS detection.

Although there are now numerous papers in the literature studying the environmental fate and effects of chiral compounds, only a few representative examples are provided here. There are also several studies of fate of chiral pesticides in soils, but because the scope of this review is on water analysis, only those involving fate in water or papers of a general nature are noted here. Muller et al. used LC, polarimetric measurements, and enantioselective GC to isolate and identify metolachlor stereoisomers in technical products (*119*). Chiral-GC was then used to study the kinetics of thermally induced interconversion of the isomers. When on-column and split/splitless injection techniques were compared, split/splitless injection was found to result in significant isomerization prior to separation; therefore, it was not recommended for accurate isomer analysis. Poiger et al. used enantioselective GC/MS to verify a switch from commercial use of racemic metolachlor to (*S*)-metolachlor in Switzerland (*120*). Samples from a lake that receives inputs from agricultural activities were measured from 1997 to 2001. Results showed that pre-1998 inputs were from the racemic herbicide, but after 1998, a clear excess of *S*-isomers was observed, with samples collected in 2000−2001 having almost exclusively (*S*)-metolachlor. These data confirmed the switch to the *S*-isomer for agricultural purposes, and also that there is a rapid environmental response to this change.

Chiral PCBs and polybrominated biphenyls (PBBs) have also been the focus of research, as 19 of the 209 possible congeners are chiral. Edwards and Shamsi used a conventional chiral micelle (using hydroxypropyl-γ-cyclodextrin) with a polymeric chiral surfactant (polysodium *N*-undecanoyl-D-valinate) to analyze chiral PCBs with electrokinetic chromatography (*121*). Addition of the hydroxypropyl-γ-cyclodextrin to the background electrolyte containing the chiral surfactant improved chiral resolution for the PCBs and reduced the analysis time ($<$50 min). Berger et al. investigated the separation properties of different chromatographic methods for enantioselective separation of chiral PBBs (*122*). A commercial flame retardant material (Firemaster BP-6(R)) was characterized by fractionating the mixture by LC and analyzing it by GC-ECD, electron-capture negative ion mass spectrometry, and LC with diode array detection (using chiral GC and LC columns). Twelve individual PBBs were isolated, and 6 of the 12 were separated into atropisomers on a LC column containing permethylated β-cyclodextrin on silica.

Finally, the occurrence and enantiomeric degradation of α- and γ-hexachlorocyclohexane isomers were studied by Law et al. (*123*). Concentrations were measured in the arctic, Great Lakes, Canada, temperate regions, and temperate and arctic wetlands and streams. Hexachlorocyclohexane enantiomers were analyzed using GC-negative ion mass spectrometry and GC-ECD with chiral GC columns. The highest concentrations of γ-hexachlorocyclohexane were found in cold, large, and oligotrophic lakes, such as those in the arctic, subarctic, and upper Great Lakes, indicating a significant atmospheric deposition and slower loss rates relative to warmer, temperate lakes. Enantioselective degradation was greatest in small, high arctic lakes and streams and in large lakes in the subarctic. Results suggested that enantioselective degradation was optimized by maximal contact between the chemical and sediment substrates in nutrient-poor waters, where oligotrophic bacteria may act as biofilms.

METHYL *TERT*-BUTYL ETHER

MTBE contamination is a relatively recent concern, due to its introduction into groundwater and surface waters through leaking underground gasoline storage tanks and discharges of fuel from boats and other watercraft. MTBE has been used as a gasoline additive since its introduction in 1979 and, by 1998, was added to ~30% of all gasoline sold in the United States. MTBE has been responsible for taste and odor problems in drinking water, and there are also concerns about possible adverse health effects. The U.S. EPA is now requiring monitoring of oxygenate compounds in groundwater at leaking underground storage tank sites and

intends to publish a secondary standard for MTBE based on taste and odor. This new standard would represent the first time that the U.S. EPA developed a secondary MCL based on taste and odor of a specific chemical. In addition, MTBE has been included in the final Unregulated Contaminant Monitoring Rule that will require all large public water systems and a statistical sampling of small and medium public water systems to monitor and report the presence of MTBE in their water supplies (www.epa.gov/OGWDW/mtbe.html). The U.S. EPA is continuing to study both the potential health effects and the occurrence of MTBE, and it is currently on the CCL for which EPA is considering setting health standards. Stocking et al. provided a background and perspective on the establishment of MCLs and secondary MCLs by states and the federal government. They also published results of a consumer study designed to determine the odor threshold of MTBE in drinking water (determined to be 15 μg/L) (*124*).

The occurrence of MTBE has been the focus of studies both in the United States and in Europe. A national U.S. survey on the frequency of detection, concentration, and distribution of MTBE in source waters is due to be completed in 2003 (http://wwwsd.cr.usgs.gov/nawqa/vocns/nat_survey.html). This study is being conducted by the U.S. Geological Survey and the Metropolitan Water District of Southern California and is sponsored by the American Water Works Association Research Foundation. This study includes samples from ~1000 untreated groundwater and surface water sources for drinking water used by community water systems in the United States. In a study of California waters, Williams measured MTBE in drinking waters from 1995 to 2000 (*125*). In this survey, MTBE was detected in 1.3% of all drinking water samples, 2.5% of drinking water source waters, and 3.7% of drinking water systems. For those drinking waters with detectable levels of MTBE, 75% of them were below California's primary health-based standard of 13 μg/L. Achten et al. reported the occurrence of MTBE in drinking water from Germany from 1999 to 2001 (*126*). In this study, MTBE was found at an average of 88 ng/L in well water and riverbank filtered waters, and at a mean level and maximum level of 35 and 71 ng/L, respectively, in tap water from the metropolitan Frankfurt area. Headspace-SPME with GC/MS detection was used and provided detection limits of 10 ng/L. In a companion paper (using the same analytical method), Achten et al. reported the concentrations of MTBE in river water and wastewater from Germany (*127*). MTBE concentrations in river water fell in the range of 50−200 (32%), 10−50 (28%), and 200−1000 ng/L (26%), which are approximately 3−17 times lower than concentrations found in California waters. Wastewater treatment plant influent samples contained concentrations of 100−300 ng/L. MTBE has also been found in urban and rural precipitation in Germany at a maximum concentration of 85 ng/L (*128*). Lacorte et al. found MTBE in groundwaters from Catalonia, Spain, in 20 of 21 samples collected from vulnerable areas, with a maximum concentration of 666 μg/L (*129*). Seven samples had levels that would exceed the maximum permissible levels for taste and odor proposed by the U.S. EPA (20−40 μg/L).

Methods that have been used to measure MTBE include headspace (*129*, *130*), purge and trap (*129*, *131*, *132*), or SPME (*126*−*128*) combined with GC or GC/MS detection. Methods using purge-and-trap-GC/MS and SPME-GC/MS have yielded the lowest detection limits—at low nanogram per liter levels. Lacorte et al. compared headspace-GC with flame ionization detection (FID) and purge-and-trap-GC/MS for measuring MTBE in groundwaters (*129*). Recoveries achieved ranged from 94 to 100%, precision from 4.6 to 12.2%, and limits of detection from 0.3 to 5.7 μg/L for headspace-GC-FID, and 0.001 μg/L (1 ng/L) for purge-and-trap-GC/MS. Halden et al. compared three purge-and-trap GC or GC/MS methods for measuring MTBE and other oxygenates in gasoline-contaminated groundwater (*132*). Consistently good results were obtained with EPA Method 8240B/60B (a GC/MS method) and ASTM Method D4815 (a GC-FID method); however, EPA Method 8020A/21B (GC with photoionization detection) frequently yielded false-positives (for 12−50% of the samples) and inaccurate results for *tert*-butyl alcohol (a degradation product of MTBE) when samples contained high concentrations of gasoline.

Stable isotopes have been used to differentiate specific source markers for MTBE. A GC-isotope ratio-MS method developed by Smallwood et al. (*133*) showed differences in the carbon isotope compositions of MTBE for 10 gasoline samples from three different parts of the United States, which could allow MTBE sources to be traced.

Several methods have been proposed for the removal of MTBE from contaminated water. These include bioremediation (*134*), granular activated carbon (GAC) (*135*), air-stripping, ozonation, or ozone/hydrogen peroxide treatment (*136*), and phytoremediation. Aerobic biodegradation can mineralize MTBE into CO_2, but it has been shown to be a slow process (*134*). GAC is more effective, but high natural organic matter content in the water can decrease the rate of adsorption of granular activated carbon and its ability to remove MTBE (*135*). Oxidation of MTBE by ozonation and ozone/hydrogen peroxide treatment was found to be effective, with major degradation products identified as *tert*-butyl formate, *tert*-butyl alcohol, 2-methoxy-2-methylpropionaldehyde, acetone, methyl acetate, hydroxyisobutyraldehyde, and formaldehyde (*136*). However, if bromide levels are high (e.g., 50 μg/L), only 35−50% of MTBE could be eliminated using ozone/hydrogen peroxide without exceeding the current drinking water standard for bromate (10 μg/L).

ALGAL TOXINS

The increase in frequency and intensity of harmful algal blooms has led to increased incidence of the poisoning of shellfish, large fish kills, and deaths of livestock and wildlife, as well as illness and death in humans. Toxins produced by these algae have been implicated in these adverse effects. Algal toxins that impact human health are generally categorized as neurotoxins or hepatotoxins that are produced by dinoflagellates, diatoms, or cyanobacteria (blue-green algae). Dinoflagellate and diatom toxins impact humans primarily through the consumption of seafood, and cyanobacterial toxins can impact humans through drinking water contamination. For example, saxitoxins, which have heterocyclic guanidine structures, are produced by dinoflagellates and cyanobacteria and cause paralytic shellfish poisoning. Anatoxins, which have heterocyclic structures, are produced by cyanobacteria and are neurotoxic. Microcystins, nodularins, and cylindrospermopsin, which have cyclic peptide structures, are produced by cyanobacteria and are hepatotoxic. "Red tide" toxins, which have heterocyclic polyether structures, are produced by red tide dinoflagel-

lates (mostly from *Gymnodinium breve*) and are neurotoxic. The National Oceanic and Atmospheric Administration (NOAA) has a nice website that provides the structures of these algal toxins and further details (www.chbr.noaa.gov/CoastalResearch). Algal toxins are currently on the U.S. EPA's CCL list. Many of these toxins are peptide-related, have relatively high molecular weights, and are highly polar, which hindered their environmental measurement until the recent application of ESI- and APCI-MS techniques.

Methods developed for algal toxins include ELISA, protein phosphatase inhibition assays, LC-photodiode array/UV, LC/ELISA, LC/MS, LC/MS/MS, MALDI-MS, and ESI-high-field asymmetric waveform ion mobility spectrometry (FAIMS)-MS. Using these methods, detection limits ranging from low nanogram per liter to low microgram per liter can be achieved. Rapala compared a colorimetric phosphatase inhibition assay, a commercial ELISA test, and different LC methods using UV detection for detecting microcystins and nodularin (*137*). The most important factor that decreased toxin recovery in sample treatment was the use of C18 cartridges and polypropylene containers; on the other hand, good recoveries were possible when hydrophilic−lipophilic balanced cartridges were used for concentrating the samples. Toxins could be detected at submicrogram per liter and low microgram per liter levels, but concentrations of hydrophobic microcystin variants were lower when analyzed with the ELISA test than with other methods (*137*). Bouaicha et al. developed a colorimetric and fluorometric protein phosphatase inhibition method for determining microcystin-LR in drinking water (*138*). This method did not involve complex cleanup or preconcentration procedures and allowed 0.25 and 0.1 μg/L detection for colorimetric and fluorometric methods, respectively, which is well below the World Health Organization provisional guideline of 1 μg/L for drinking water. Of the two methods, the protein phosphatase inhibition assay was the least expensive and therefore may be more attractive than the colorimetric method for routine measurements.

In an international intercomparison exercise, Fastner et al. evaluated the comparability of current microcystin analysis methods (*139*). Methods evaluated included LC-photodiode array/UV (which is the most widespread method for microcystin analysis), ELISA, protein phosphatase inhibition assay, and LC/MS. Thirty-one laboratories from 13 countries participated in the study. The LC-photodiode array/UV method was found to have the most variability—both the extraction and the analysis of microcystins appeared to contribute to this variability. Zeck et al. coupled LC with ELISA and achieved extremely high sensitivity and specificity for detecting microcystins and nodularin in water (*140*). Using this method, the World Health Organization guideline of 1 μg/L could be met without sample preconcentration. This method was also compared to LC/UV and ESI-time-of-flight-MS.

Although there has been some epidemiologic evidence linking symptoms of human poisoning to cyanobacterial toxins, the presence of specific algal toxins in finished drinking water had not been proven analytically until a recent discovery of cyanobacterial toxins in finished drinking waters in Florida (*141*−*143*) and in a survey of U.S. and Canadian drinking waters sponsored by the American Water Works Association Research Foundation (AWWARF) (*144*). In the 1999 survey of Florida surface waters and finished drinking waters, 75 of the 167 surface water bodies sampled contained toxic cyanobacteria blooms, and microcystins, anatoxin-a, and cylindrospermopsin were found and quantified in finished drinking waters at levels that exceed proposed human health guidelines (*142*). Microcystins were the most commonly found toxins in Florida waters, occurring at levels up to 12.5 μg/L. Anatoxin-a was found in three finished drinking water samples up to 8.46 μg/L, and cylindrospermopsin was found in nine finished waters at levels ranging from 8.07 to 97.12 μg/L. Cylindrospermopsin had been previously found in a drinking water reservoir in Australia, following a poisoning episode of 138 children and 10 adults that accompanied a *Cylindrospermopsis* bloom; the Burns et al. finding represents the first identification of this toxin in North America (*142*). In this study, algal toxins were characterized and quantified using ELISA, a protein phosphatase inhibition assay, LC with fluorescence and UV detection, and LC/MS/MS.

In the survey of U.S. and Canadian source waters and finished drinking waters (conducted from 1996 to 1998), 80% of the 677 utility water samples collected were positive for microcystins, and 4.3% were higher than the World Health Organization drinking water standards (*144*). Only two of the finished drinking water samples exceeded this guideline. Results revealed that the majority of source waters with cyanobacteria do contain microcystins but that most treatment plants had adequate procedures to reduce them to safe levels in finished water. There was also an indication that the presence of taste-and-odor compounds (e.g., geosmin and methylisoborneol) could be used as indicators of algal toxins, as a high percentage of the water samples testing positive for microcystins also were positive for taste-and-odor compounds. An immunoassay was used for the detection of microcystins. A summary of this project is available on the web at http://www.awwarf.org/exsums/256htm.

Another AWWARF report authored by Newcombe provides information on the use of ozone and GAC for removing algal toxins from drinking water (*145*). In this study, ozone was found to be effective for removing anatoxin-a and microcystins but did not readily destroy saxitoxins. GAC filtration alone was effective for removing saxitoxins, but not for microcystins; however, when the GAC filter was made biologically active, microcystins could be effectively removed. A summary of these results is available on the web at http://www.awwarf.org/exsums/446.htm.

ORGANOTINS

Organotins are widely used in antifouling paints for ships and have been measured widely in coastal waters and sediment. Their toxicity generally follows the order, trialkyl > dialkyl > monoalkyl, but the dialkyl form is much more neurotoxic, with an effect in brain cells as low as 30 ppb. The discovery that dibutyltin leaches from PVC pipe at 1 μg/L levels created a new concern for drinking water (*20*). There have also been reports of organotins in Canadian drinking water that was supplied by PVC pipe. European countries have proposed banning the use of PVC to transport potable water, due to the leaching of organotin from PVC plastic products, and organotins are currently included on the U.S. EPA's CCL (www.epa.gov/ogwdw/ccl/cclfs.html).

Dibutyltin is used as a heat stabilizer in PVC pipe and is highly toxic. Because PVC pipe is widely used as a domestic water supply

carrier from main water lines into homes, the potential for widespread exposure to dibutyltin is enormous. A variety of analytical methods have been developed to measure organotins in environmental samples, including GC with mass spectrometry, atomic absorption spectrometry (AAS), flame photometry, ICP, or microwave-induced plasma atomic emission spectrometry, as well as LC coupled to mass spectrometry, AAS, ICPMS, and fluorescence detection. Headspace-SPME sampling is also becoming more popular, as this allows for easy and rapid extractions that avoid the use of solvents. Several methods can detect low nanogram per liter levels of organotins in water. One of the more creative methods developed includes the use of a poly(dimethylsiloxane)-coated stir bar for extracting organotins from water, with subsequent analysis by thermal desorption-GC/ICPMS (*146*). This method permits extremely low detection limits of 0.1 pg/L.

A micro-LC/ESI-ion trap-MS method developed by Jones-Lepp (*20*) has recently become an official EPA method (Method 8323, Determination of Organotins by Micro-Liquid Chromatography-Electrospray Ion Trap Mass Spectrometry) and can be found at www.epa.gov/epaoswer/hazwaste/test/new-meth.htm#8323. This method, which permits the measurement of mono-, di-, and tributyl tin, and mono-, di-, and triphenyltin at subnanogram per liter detection limits, was developed to avoid the use of hydrolysis and derivatization and to lower background interferences that are common with traditional methods.

Several other LC/MS methods have also been reported for measuring organotins in water (both freshwater and seawater). Gimeno et al. developed an on-line SPE-LC/APCI-MS method, which allowed 5 ng/L detection limits in seawater for diuron, irgarol 1050, and dichlofluanid and 250 ng/L for folpet (*147*). This method was used to measure these antifouling agents in coastal waters in Catalonia, Spain, over a 5-month period. Diuron and irgarol 1051 were detected at levels ranging from 27 to 420 ng/L for diuron and from 15 to 511 ng/L for irgarol 1051. Wu et al. developed an automated in-tube-SPME-LC/ESI-MS method for measuring tributyltin in water (*148*). This method had a linear response over the range of 0.5−200 μg/L, with a detection limit of 0.05 μg/L.

GC/MS methods also continue to be reported for organotins. Ikonomou et al. developed a GC-high-resolution-EI-MS method for simultaneously determining nine organotins in water, sediment, and tissue (*149*). Analytes measured in this method include monobutyl-, dibutyl-, tributyl-, tetrabutyl-, monophenyl-, diphenyl-, and triphenyl-, dicyclohexyl-, and tricyclohexyltins. Using selected ion monitoring, detection limits of 7−29 ng/L for water and 0.35−1.45 μg/L for tissue/sediments were achieved. Organotins were derivatized with sodium tetraethylborate, which converted these ionic compounds into nonpolar derivatives that could be extracted into hexane for analysis by GC/MS. Tsunoi et al. used Grignard derivatization with GC/MS/MS to determine six organotins (mono-, di-, and tributyltins and mono-, di-, and triphenyltins) in river water and seawater (*150*). Several Grignard reagents were investigated and compared to achieve optimal derivatization and MS detection. Pentylmagnesium bromide was the best reagent and allowed detection limits of 0.20−0.35 pg (as Sn).

Several methods are now utilizing headspace-SPME for sampling. Mester developed a method using chloride generation, headspace-SPME, and ICP-TOF-MS for measuring tributyltin in aqueous samples (*151*). This method permits the identification of tributyltin without the need for chromatography. A detection limit of 5.8 ng/L (as Sn) was achieved. Headspace sampling is possible because the organometallic halide form of tributyltin has a relatively high volatility. A multicapillary GC-atomic emission detection (AED) method published by Botana et al. provides rapid measurement of mono-, di-, and tributyltin in water (*152*). Samples are ethylated and concentrated on a SPME fiber placed in the headspace for 2 min. Then, using multicapillary GC with AED, the ethylated species are separated and selectively quantified in only 90 s. Detection limits of 1−5 ng/L were shown. Crnoja et al. developed a headspace-SPME-GC/AED method (using in situ propylation) for simultaneously measuring organotin and organolead compounds in water (*153*). Derivatizations were carried out using sodium tetrapropylborate (which has recently become commercially available). Detection limits of 0.2 ng/L (as metal) could be achieved with headspace sampling and a 20-mL sample volume.

Methods using fluorescence detection have also been developed for measuring organotins. Gonzalez-Toledo et al. published a SPE-LC-fluorescence method for determining dibutyl-, diphenyl-, tributyl-, and triphenyltin species at low nanogram per liter concentrations in water (*154*). Analytes were isolated from seawater by SPE and analyzed both off-line and on-line by LC with postcolumn derivatization and fluorometric detection. Preconcentration factors up to 250 could be achieved, and recoveries ranged from 75 to 110%.

Finally, Wei and Miller published the measurement of 10 hydrolysis products of organotin compounds formed in water (*155*). Most measurements of organotins have been of the parent molecules, so this paper is unusual in that it specifically targeted these hydrolysis products. Positive ion electrospray mass spectrometry and MS/MS were used for their analysis, and structures for parent and fragment ions could be assigned based on the comparison of calculated isotopic patterns.

PERCHLORATE

Perchlorate has recently become an important environmental issue since its discovery in 1997 in a number of water supplies in the western United States (*156*). The development of sensitive analytical techniques has revealed perchlorate concentrations ranging from 5 to 20 μg/L in groundwaters from the southwestern United States (*157*). High quantities of perchlorate have been disposed of since the 1950s in Nevada, California, and Utah, which is believed to have contributed to the contamination. Ammonium perchlorate has been used as an oxygenate in solid propellants used for rockets, missiles, and fireworks, and there is also possible contamination that can occur through the use of fertilizers (that contain Chilean nitrate). Health concerns arise from perchlorate's ability to disrupt the thyroid gland's use of iodine in metabolic hormones, which could affect normal metabolism, growth, and development. In addition, perchlorate is not removed by conventional water treatment processes. Due to these concerns, the U.S. EPA has placed perchlorate on the CCL for further study.

Urbansky published a review of the practices and advances for quantifying perchlorate in environmental samples (*156*). This review discusses the strengths and weaknesses of gravimetry, spectrophotometry, electrochemistry, IC, capillary electrophoresis,

and MS for measuring perchlorate and looks forward to where sample pretreatment and analysis methods are headed. Of these techniques, IC was recognized as the best technique for measuring perchlorate in drinking waters because of its low detection limits (<5 μg/L), ease of use, selectivity, and availability. Since this review, other methods utilizing ESI-MS/MS, ion pair extraction-ESI-MS, and ESI-FAIMS-MS have been developed.

In one of the more extensive occurrence studies of perchlorate contamination in water, Gullick et al. examined 40 U.S. surface waters in 11 states and 367 groundwater wells in 17 states (*158*). In this study, no perchlorate was detected in the surface waters but was identified in nine wells in California or New Mexico at levels ranging from <4 to 7 μg/L, which were below the health advisory guideline value of 18 μg/L suggested by the California Department of Health Services. This study provided further support to previous reports that perchlorate contamination is a localized problem, affecting sites near military-related facilities or other major sources of perchlorate (*158*).

The removal of perchlorate from contaminated waters has also been the focus of a few studies. Proposed removal technologies include sorption onto GAC, biological reduction, and biological removal. Na et al. showed that preloading of GAC with iron−oxalic acid can improve the GAC adsorption capacity by 42% (*159*). When the preloaded GAC becomes saturated with perchlorate, 65−74% of the GAC's original adsorption capacity can be restored by chemically regenerating the GAC with sodium borohydride. Nerenberg et al. investigated the use of a hydrogen-oxidizing hollow-fiber membrane−biofilm reactor system for perchlorate removal (*160*). Hydrogen was chosen as the electron donor because it presents no toxicity, is inexpensive, and is unlikely to persist as a source of biological instability in distribution systems. Results showed that biological perchlorate reduction occurred concurrently with nitrate reduction and that perchlorate could be removed to below the preliminary regulatory standards with no chemical addition other than hydrogen gas. Brown et al. evaluated the use of a biologically active carbon filter to remove perchlorate from drinking water (*161*). When influent nitrate concentrations were present, up to 2 mg/L acetate or ethanol was required to achieve and sustain the removal of 50 μg/L perchlorate. Most of the remaining acetate and ethanol were subsequently removed in the biological filtration. If breakthrough of perchlorate occurred, nine days were required to reestablish complete perchlorate removal. When dissolved oxygen levels were >2.5 mg/L, a cleaning procedure was required every 50 days (4800 bed volumes) to maintain perchlorate removals. Given these caveats, it was demonstrated that perchlorate could be removed using biologically active carbon filtration for influent perchlorate levels ranging from 10 to 300 μg/L.

ARSENIC

Arsenic has been a politically charged issue the last two years. Unlike many other contaminants that are anthropogenic, arsenic contamination of waters generally comes from natural sources, through the erosion of rocks, minerals, and soils. For several years, the U.S. EPA has conducted research on arsenic (occurrence, health effects, bioavailability) and intended to lower the existing standard in drinking water of 50 μg/L to a level that would better protect human health. The general toxicity of arsenic is well known, but studies have also linked long-term exposure of arsenic (at lower, nontoxic levels) to a variety of cancers in humans. In January 2001, the U.S. EPA lowered the standard (MCL) from 50 to 10 μg/L; however, two months later, the new EPA Administrator announced that EPA would withdraw this pending arsenic standard in order to seek independent reviews of the science behind the standard and the estimates of costs to communities to implement the rule (http://www.epa.gov/safewater/arsenic.html). After seeking the advice of independent, expert panels convened by the National Academy of Sciences, the National Drinking Water Advisory Council, and the EPA Science Advisory Board regarding recommendations on the science, cost of compliance, and benefits analysis, the rule was finally agreed upon and the original proposed standard of 10 μg/L was kept. This rule became effective on February 22, 2002, and drinking water systems must comply with this new standard by January 23, 2006.

On the nonpolitical front, arsenic research issues that have become important are determining individual species of arsenic (rather than total arsenic as had been done in the past) and their occurrence in water, foods, and biological samples. Different arsenic species have different toxicities and chemical behavior in aquatic systems, so it is important to be able to identify and quantify them.

Several new analytical methods have been developed for measuring different arsenic species. These methods include SPME and SPE used with GC/MS, LC/ESI-MS, LC/ICPMS, and IC/ICPMS. The number of papers describing the development or use of LC/ICPMS techniques has grown significantly in the past two years. Martinez-Bravo et al. developed a new method using on-line, anion exchange-LC/ICPMS for measuring arsenic, selenium, and chromium(IV) species in water (*162*). Detection limits of 40−60 ng/L were obtained for the arsenic species, arsenite, arsenate, monomethylarsonic acid, and dimethylarsinic acid. Day et al. used drinking water samples from different regions of the United States to evaluate the robustness of an anion exchange-LC/ICPMS method (*163*). This method did allow the separation of four arsenic species (arsenite, arsenate, monomethylarsonic acid, dimethylarsinic acid) at method detection limits lower than 100 ng/L. Mazan et al. published a new LC separation method using porous graphite carbon as the stationary phase (*164*). Separations could be achieved in 10 min for arsenite, arsenate, dimethylarsinic acid, and monomethylarsonic acid; detection limits of 10−70 ng/L were possible through the coupling of LC with ICP-MS. Xie et al. coupled LC to a hexapole collision cell ICPMS, which minimized interferences and offered improved detection limits (0.02−0.4 μg/L) for the simultaneous determination of arsenite, arsenate, monomethylarsonic acid, dimethylarsinic acid, and arsenobetaine in water (*165*). The use of an ion exchange column allowed near-baseline separation of the five arsenic species.

Gallagher et al. investigated preservation agents for measuring inorganic arsenic species in drinking water (*166*). Because arsenic can coprecipitate with iron when iron levels are high in groundwaters, analyses of samples shipped back to the laboratory can be inaccurate. The use of ethylenediaminetetraacetic acid (EDTA), which sequesters iron, prevented this coprecipitation and was proposed as a preservation agent. Well waters not treated with

EDTA showed dramatic losses (2−5×) of dissolved arsenic in less than 1 day; however, with EDTA, samples were stable for 10 days. Yan et al. developed a method for inorganic arsenic (arsenite and arsenate) using flow injection on-line sorption preconcentration and separation in a knotted reactor that was coupled to hydride generation (HG)-atomic fluorescence spectrometry (*167*). This method permitted 0.023 μg/L detection for As(III) at a throughput of 32 samples/h. Finally, Erickson reviewed field kits for measuring arsenic in groundwater and discussed advantages and disadvantages of each type (*168*). These field kits have been used in extensive testing of well waters in Bangladesh and West Bengal, India, but have been found not to be very accurate when wells marked as containing moderate and high levels of arsenic were reanalyzed with a more accurate flow injection-HG-atomic absorption spectroscopy method.

NATURAL ORGANIC MATTER

Natural organic matter (NOM) is a complex mixture of substances, such as amino acids, carbohydrates, lipids, lignins, waxes, organic acids, humic acids, and fulvic acids. Humic substances, which are the major component of aquatic, dissolved organic matter, are complex macromolecular structures. The understanding of NOM is important because it impacts such processes as the sorption or transformation/degradation of environmental pollutants, provides sources and sinks for carbon, serves as a carbon and energy source for biota, and controls levels of dissolved oxygen, nitrogen, phosphorus, sulfur, trace metals, and acidity (*169*). Also importantly, NOM serves as the precursor material for the formation of drinking water DBPs. Understanding the structure of NOM could aid in the design of new treatment processes for removing it from drinking water and lessening or preventing the formation of DBPs. Previous research using gel permeation chromatography indicated that, of these humic substances, fulvic acids generally have molecular weights of 200−2000, and humic acids have much higher molecular weights (1000−100 000). However, new information provided by ESI- and APCI-MS is showing much lower molecular weight distributions (e.g., 300−1200 for humic acid). These new data have caused scientists to rethink "truths" about NOM that have been accepted for many years. As such, this area is a fascinating, emerging one. The questions to answer are as follows: (1) Did the earlier measurements using gel permeation chromatography measure individual NOM molecules, or were these colloidal aggregates? (2) Is the earlier data correct, but the new mass spectrometry data instrumentally biased toward low molecular weight—either due to the difficulty in obtaining stable molecules with multiple charges or ionization suppression of larger molecules?

Leenheer and Croué published a nice feature article in 2002 on aquatic organic matter (*169*). In this article, the authors discuss the new mass spectrometry work, along with fractionation of dissolved organic matter and techniques used to probe its structure. A few research groups have been engaged in new mass spectrometry work to probe the structure of NOM. Some ESI-MALDI-MS work was published before this review (in 2000), so work cited here is not inclusive of all research conducted in this area. Leenheer et al. used ESI-ion trap-MS to investigate molecular weight distributions of fulvic acids from the Suwannee River (GA) (*170*). Tandem mass spectrometry was used to determine several fragmentation pathways. Model compounds, including aromatic and aliphatic carboxylic acids that have hydroxyl or carboxylic acid distributions characteristic of humic material, were analyzed for comparison. Poly(carboxylic acid) standards (molecular weight 2000 and 5000) were also analyzed to investigate the ability of ESI to ionize higher molecular weight material (similar to humic material). The smaller carboxylic acids showed losses of water, decarboxylation, or both, and the poly(carboxylic acid) results indicated that there might be a limitation in the detection range of large (>400 Da) polyacids. In the negative ion mode, polyacids formed multiply charged species, with the number of charges dependent on the number of carboxyl groups and on molecular spacing between these groups. For the Suwannee River fulvic acid, the average molecular weight distribution was m/z 591 in the negative ion mode and m/z 617 in the positive ion mode. MS/MS of several ions showed a major daughter ion resulting from the loss of CO_2 from the $(M - H)^-$ parent ion; successive losses of CO_2 (two to five units) were observed, with an average CO_2 unit loss of 3.4. The loss of water from the parent ion was also prominent in the MS/MS spectra.

Kujawinski et al. used ESI-FT-ICR-MS to analyze humic and fulvic acids and resolved individual compounds within these mixtures with a resolving power of approximately 80 000 (*171*). Two different samples were analyzed: dissolved organic matter (primarily fulvic acids) from the Suwannee River and a humic extract from a degraded wood collected on Mt. Rainier, WA. Results showed a cluster of peaks at every nominal mass between m/z 400 and 1200 for Mt. Ranier humic acid and between m/z 300 and 900 for Suwannee River dissolved organic matter. The resolving power was high enough to separate four to eight peaks per nominal mass. Because there were few peaks observed at half the nominal mass, and isotope peaks were one nominal mass higher than the original compound, the ions appeared to be due to singly charged species. Molecular weight distributions were different for the two types of organic matter. A Kendrick mass analysis applied to the data yielded additional information about the degree of oxidation and unsaturation in the molecules. The Kendrick mass deficit plot indicated that there was a significant fraction of Suwannee River humic matter with a larger aliphatic contribution, as compared to the Mt. Ranier sample; this was judged by the greater fraction with lower Kendrick mass defects. Because odd-m/z ions correspond to an even mass ($[M + H]^+$ ions) in the positive ion mode, and because the nitrogen content is generally low in humic acids, it was more likely that odd-m/z compounds contained primarily C, H, and O. It could also be surmised from the data that the high molecular weight compounds were either more aromatic or more oxygenated (or a combination of both) than their lower molecular weight counterparts. Kendrick analysis was also used to determine the CH_2 content. Many compounds fit a series of increasing CH_2 units, with a small number of total units (generally <10). For these humic compounds, it appeared that CH_2 was not a dominant building block.

Although ESI-MS allowed the ionization of humic substances, a number of caveats should be considered when ESI-MS is used to analyze humics (*171*). First, the variations in ionization efficiencies among different classes of compounds within these samples could result in spectra with compound distributions that are not representative of the original sample. For example,

hydrocarbons are not ionized well by electrospray, and their contribution would be missed. Also, the contribution of nitrogen-containing compounds in the humic samples may be overestimated, due to their preferential ionization efficiency in the positive ion mode. Second, the ionization mode (positive or negative) will also affect the distributions observed.

Stenson et al. also used ESI-FT-ICR-MS to study humic and fulvic acid mixtures and operated at resolutions of 60 000 (at high mass) and 120 000 (at low mass) (*172*). Results were the same as for Kujawinski et al.: virtually all ions present in the spectra of Suwannee River fulvic and humic acid were singly charged, thus eliminating inadequate accounting for multiply charged ions as a primary source of any low molecular weight bias. Ionization suppression based on molecular weight is still possible, but this was difficult to determine unequivocally due to the limited mass range of the mass spectrometer and the shortcomings of size-based separations. No direct evidence was found for fragmentation of humics in the source. Patterns in the mass spectra suggested that these humics were made up of molecular families that differ from each other in degree of saturation and functional group substitution (mostly likely CH vs N and CH_4 vs O), and individual members of each family differed in the number of CH_2 groups.

The structure of dissolved organic phosphorus (DOP) species was also probed using ESI-FT-ICR-MS (*173*). This was possible due to a recently developed method for selectively concentrating dissolved organic phosphorus from complex water samples, which allowed a 300-fold concentration of high molecular weight DOP. Model organic phosphorus standards representative of the DOP species expected in aquatic environments were used to evaluate the technique. The method was then applied to a series of high molecular weight (>1000) DOP fractions isolated from sites within the Everglades Nutrient Removal Treatment Wetland (FL). The elemental compositions of several individual DOP compounds were determined by ESI-FT-ICR-MS (e.g., one compound had a composition of $C_{18}H_{30}N_6O_{13}PNa$). Elemental compositions revealed apparent molecular masses of <1000 Da, which is similar to results found for humic acids and could be due to colloidal aggregates of DOP molecules (or DOP molecules linked to humic-like substances through ionic interactions) or due to a low molecular weight bias of electrospray ionization. These compounds appeared to be nonreactive during their residence in the Everglades Nutrient Removal Treatment Wetland. This work represents the first time that specific organic phosphorus compounds within a pool of nonbiologically available DOP have been identified.

Finally, one study of NOM using a nuclear magnetic resonance (NMR) technique will be presented here. Wong et al. used ^{13}C cross-polarization magic-angle spinning NMR spectroscopy and size exclusion chromatography to obtain structural information on hydrophilic and hydrophobic NOM fractions from three sources (two surface waters and one groundwater) (*174*). The purpose of this study was to try to relate NOM structure to treatability. Organic matter was fractionated into two hydrophobic and two hydrophilic groups by adsorption on nonpolar and ion exchange resins. ^{13}C NMR spectra of freeze-dried fractions revealed that the most hydrophobic fraction was high in aliphatic and aromatic carbon, while the slightly hydrophobic fractions had more carbonyl and alkoxyl carbon. The hydrophilic fractions from the groundwater and one of the surface waters exhibited strong alkoxyl signals attributed to carbohydrates. Hydrophilics from the second surface water contained aromatic (phenolic) carbon. Size exclusion data showed high apparent molecular weights from the hydrophobic and charged hydrophilic fractions but low apparent molecular weights for the neutral fraction.

MICROORGANISMS

Outbreaks of waterborne illness in the United States and other parts of the world (including *Escherichia coli*-induced gastroenteritis in Walkerton, Ontario, in 2000, cryptosporidiosis in Milwaukee in 1993, and cholera in Peru beginning in 1991) have necessitated improved analytical methods for detecting and identifying microorganisms in water and other environmental samples. Mass spectrometry had played a minor role in the past through the use of pyrolysis-GC/MS but is beginning to play a more important role, with increased research using MALDI-MS and ESI-MS techniques, which can be used on whole or treated cells. These MS methods offer a very rapid analysis time (~10 min) and specific information that can be used to distinguish different strains of the same organism. In the last two years, further advances have been made, moving beyond simple fingerprinting and empirical matching to modeling and algorithm development, microorganism−protein database development, and complete sequencing of protein biomarkers. There have also been advances in the more traditional biological and biochemical methods, with new polymerase chain reaction (PCR) methods to achieve lower detection limits and new work to improve recoveries of microorganisms from natural waters.

Reviews. Increased interest in mass spectrometry for analyzing microorganisms is evidenced by the number of reviews that have been published in this area. Representative reviews are mentioned here. Fenselau and Demirev published a review of the characterization of intact microorganisms by MALDI-MS with 113 references (*175*). This review included a summary of the instrumentation, sample collection, sample preparation, and algorithms for data analysis. Lay published a review of the use of MALDI-TOF-MS for characterizing bacteria (*176*). This review included applications involving the analysis of RNA and DNA, the detection of recombinant proteins, the characterization of targeted or unknown proteins, bacterial proteomics, the detection of virulence markers, and the rapid characterization of bacteria at the genus, species, and strain level.

Mass Spectrometry Methods. Several authors have published papers on the development of algorithms or pattern recognition software for enabling rapid typing of bacteria and other microorganisms. Bright et al. developed a search engine to rapidly build and search databases of intact cell microorganism mass spectra (*177*). This mass spectral fingerprint comparison algorithm is fully automated and statistically based and was demonstrated using a blind study, which showed a 90% correct identification rate. Wang et al. presented a method to create protein mass tables tailored for bacterial identification (*178*). Their method involved the use of three MS techniques: MALDI-TOF-MS for bacterial extracts, LC fractionation of bacterial extracts followed by off-line MALDI-TOF-MS of individual fractions, and LC/ESI-MS analysis of extracts. Some of the protein components were common to all three detection schemes, but some unique components were found using each of the three techniques, which

allowed the development of mass tables that were more accurate in the identification of the bacterial species. Wahl et al. carried out a double-blind study of microbial mixtures, demonstrating that MALDI-MS could be used successfully for identifying specific bacteria in complex bacterial cultures (*179*). Identifications were correct to the species level in all but one of the samples. It was acknowledged that challenges remain for identifying closely related organisms with the current algorithms available.

New improvements continue to be made for MALDI-MS analyses of microorganisms. Yao et al. presented a simple method involving a proteolytic digestion that could be accomplished directly on the slide, followed by direct analysis by MALDI-MS and MS/MS (*180*). No isolation or fractionation of the microorganisms was needed. Database searching of the MS/MS spectrum allowed the microorganism proteins to be identified and, consequently, the microorganism. In a separate paper, Yao et al. presented a new method based on the construction of databases of organism-specific tryptic peptide masses and demonstrated it for rapid virus identification (*181*). For this work, a sample of an intact virus is digested with a selective protease for a short time, and the digestion products are analyzed by MALDI-TOF-MS without fractionation or purification. In their proof of concept, the Sindbis virus AR 339 was identified by using the masses of the observed tryptic peptide products to query a database composed of tryptic peptide masses generated in silico for six viruses whose genomes have been sequenced. Each of the two algorithms tested (a direct score-ranking algorithm and an algorithm that evaluates the probability of random matching) unambiguously identified the Sindbis virus.

Immunomagnetic separation is a common technique used with traditional microscopic techniques for identifying microorganisms, and in new work, Madonna et al. combined immunomagnetic separation with MALDI-TOF-MS for identifying bacteria (*182*). This method involved mixing a bacterial mixture suspension with commercially available immunomagnetic beads (coated with polyclonal antibodies specific for the target microorganism), a short incubation period (20 min), washing microorganisms, resuspension in deionized water, and direct application to the MALDI probe. Liquid suspensions containing bacterial mixtures could be screened within a 1 h total analysis time.

Biological and Biochemical Methods. Recovery and concentration of microorganisms remains an important research issue, as recoveries can be as low as 10−20% for organisms, including *Cryptosporidium* oocysts. Borchardt evaluated the effectiveness of continuous separation channel centrifugation for concentrating *Cryptosporidium parvum* oocysts, *Giardia lamblia* cysts, *Encephalitozooan intestinalis* spores, and *E. coli* from water (*183*). When these organisms were seeded into different water matrixes at densities ranging from 5 to 10 000 organisms/L and recovered using continuous separation channel centrifugation, recovery efficiencies were usually >90%. Oocyst recovery did not vary with source water turbidity or with centrifuge flow rate, and oocyst viability remained intact. This method could simultaneously concentrate multiple pathogens as small as 1 μm with high and reproducible efficiency.

A new immunocapture-PCR method was also developed for the simultaneous determination of *C. parvum* oocysts and *Giardia intestinalis* cysts in water (*184*). Using this method, as few as 50−100 oocysts and cysts could be detected; this method was demonstrated on 54 surface water samples and allowed the first detection of *Cryptosporidium* and *Giardia* in surface waters from Finland.

Two papers evaluated the relatively new EPA Method 1622 for detecting *Cryptosporidium* and *Giardia* in water, to test the recovery of these organisms in real source waters with environmentally realistic organism spike doses and common turbidity levels found in surface waters. EPA Method 1622 consists of filtration, concentration, immunomagnetic separation, fluorescent antibody and 4,6-diamidino-2-phenylindole counterstaining, and microscopic evaluation. Simmons et al. evaluated this method for detecting *Cryptosporidium* oocysts in streamwaters collected in the United States (*185*). Two filters were compared for the analysis of 11 streamwater samples, and replicate 10-L samples (unspiked and spiked with 100−250 oocysts) were tested to evaluate matrix effects. Oocyst recoveries averaged 22% with a membrane disk and 12% with a capsule filter. Recoveries in reagent water were higher at 39 and 47%, respectively, demonstrating that recoveries observed for real waters will not be as high as expected from tests using reagent water. DiGiorgio et al. evaluated filtration capacities and recovery efficiencies for a standard filter and a high-volume capsule filter for recovering *Cryptosporidium* oocysts and *Giardia* cysts from natural waters (*186*). With high-turbidity water, the high-volume capsule filter could filter approximately twice the volume than the standard filter, but neither could filter 10 L without clogging. With low-turbidity water, oocyst (but not cyst) recoveries were significantly higher with the high-volume capsule filter. In turbid waters, organism recoveries were lower than those in nonturbid waters but were not significantly different for the different filters. Recoveries for *Cryptosporidium* using the high-volume filter ranged from 36 to 75%; *Giardia* recoveries ranged from 0.5 to 53%, and recoveries varied significantly for both by site. Turbidity could not explain the variation in *Cryptosporidium* recoveries. These findings suggest that the background matrix of the ambient water significantly affects recovery using EPA Method 1622.

MISCELLANEOUS APPLICATIONS AND NEW TECHNOLOGIES

There were several papers worth noting that did not fit any of the previous categories. These include papers on such subjects as the development of new types of instrumentation, fast-GC/MS techniques, and new degradation products of environmental contaminants. New fast-GC/MS methods (which use shorter columns and higher helium flow rates) include a fast-GC/TOF-MS method developed by Hirsch et al. for measuring organic compounds, including acidic pesticides and acidic drugs (*187*). Using fast-GC/MS, analysis times can be 5−10 times faster than with conventional GC/MS.

Time-of-flight MS has also made exact mass measurements of contaminants in water a much simpler process (compared to measurements using conventional magnetic sector measurements), without a compromise in sensitivity. As a result, many researchers are now using TOF-mass spectrometers to identify unknown contaminants and determine pollutants at trace levels with increased mass accuracy. For example, Maizels and Budde published a paper showing the utility of LC/ESI-TOF-MS exact mass measurements for the confirmation of 10 nonvolatile or

thermally unstable carbamate, urea, and thiourea pesticides and herbicides (*188*). Resolutions between 3500 and 5000 could be routinely obtained, and the exact masses were important for the identifications, as ESI mass spectra contain few fragment ions. Thurman et al. used LC/ESI-TOF-MS to provide exact mass measurements of acetochlor and alachlor degradates (*189*).

Measurements of pesticide degradation products have become important because sometimes the degradation products can be more prevalent that the parent compounds. Triazine degradation products are listed on the CCL (Table 6). Kolpin et al. used LC/ESI-MS to investigate the occurrence of cyanazine (which is a triazine herbicide) and its degradation products, cyanazine acid, cyanazine amide, deethylcyanazine, and deethylcyanazine acid, in groundwater (*190*). While cyanazine was infrequently detected in the 64 wells sampled across Iowa, cyanazine degradation products were commonly found. Of the total measured concentration, only 0.2% was derived from the parent compound, with deethylcyanazine acid (74.1%) and cyanazine acid (18.4%) comprising 92.5% of the total. These data suggest that, to accurately determine the overall effect on human health and the environment from cyanazine, its degradation products should also be considered. In a study to determine the effectiveness of various treatment schemes for herbicides, Verstraeten et al. measured the changes in concentrations of trazine and acetamide herbicides in groundwater treated with natural bank filtration and by ozonation, filtration, and chlorination (*191*). This study was done in Lincoln, NE, where the city's groundwater supply is affected by infiltration and transport of triazine and acetamide herbicides from the Platte River. Samples collected during the spring, when runoff is the highest, showed an overall reduction of 75% (33% by bank filtration, 41% by ozonation, and 1.5% by chlorination). Herbicide degradation products were reduced by 21% overall. However, increases in cyanazine amide, cyanazine acid, and deethylcyanazine were found after bank filtration. After ozonation, concentrations of deisopropylatrazine, deethylatrazine, didealkylatrazine, atrazine amide-I, hydroxydeethylatrazine, hydroxydeisopropylatrazine, deethylcyanazine acid, and deethylcyanazine increased. Concentrations of cyanazine acid, ethanesulfone, and oxanilic acids of acetamides decreased during ozonation. These results suggest that bank filtration and ozonation of water can shift the assessment of risk from the parent compounds to their degradation products.

Thurman et al. published a study comparing APCI- and ESI-MS for measuring a wide variety of pesticides (*192*). More than 75 pesticides were evaluated, and the data showed that different classes of pesticides were more sensitive using either APCI or ESI. Neutral and basic pesticides (e.g., phenylureas, triazines) were more sensitive using APCI (especially positive ion), whereas cationic and anionic herbicides (e.g., bipyridylium ions, sulfonic acids) were more sensitive using ESI (especially negative ion). These data were plotted on an ionization-continuum diagram, which showed that protonation in the gas phase (proton affinity) and polarity in solution (expressed as proton addition or subtraction—pK_a) was useful for selecting APCI or ESI.

Field-portable methods continue to be important, as they can allow rapid sampling at the contaminated site and a more complete assessment/mapping of contaminated areas. Ballesteros et al. evaluated a field-test kit for determining triazine herbicides in water samples (*193*). The test is a membrane-based ELISA method, which allows a visual estimation of the presence of triazine herbicides in <10 min. Detection limits are 0.1 μg/L for atrazine and 0.5 μg/L for the sum of all triazines. This is the first time that a commercial field-test kit to control water contamination by herbicides performed in compliance with U.S. and European Union requirements regarding the detection level.

In a particularly interesting publication, Wegner and Hamburger used LC/ESI-MS to identify unknown compounds that have caused a persistent foam for 30 years in the Rhine River beneath the Rhine Falls (a waterfall in Switzerland) (*194*). This foam occurs during the summer months and has been a matter of public concern ever since its first appearance, but previous attempts to determine its origin and its composition were not successful. Using LC/ESI-MS, the authors identified triterpene saponins and mono- and digalactosyldiacylglycerolipids, two classes of surface-active metabolites produced by an aquatic plant, in the river water and foam samples. Foam occurrence paralleled saponin concentration and the amount of plant biomass, but not the concentration of synthetic detergents. Therefore, this phenomenon was determined to be due to naturally derived surfactants. No acute toxicity was observed at concentrations 50× higher than those found in the environmental samples; therefore, despite the stark appearance, these compounds may not necessarily pose an ecological or human health risk.

A chemical warfare agent, 2-chlorovinylarsonous acid (a hydrolysis product of lewisite), was the target of a new, automated SPME-GC/MS method (*195*). Under aqueous conditions, lewisite [dichloro(2-chlorovinylarsine)] rapidly hydrolyzes to 2-chlorovinylarsonous acid, which is nonvolatile. The method involves initial derivatization with 1,3-propanedithiol, and the limit of detection was 7.4 pg in 1 mL of urine.

Finally, two other reviews are worthy of note. Eljarrat and Barcelo published a review of trace dioxin determination by mass spectrometry and discussed sample preparation and chromatographic separation, as well as the use of different MS techniques (low- and high-resolution MS, MS/MS, and TOF-MS) (*196*). Different MS techniques were compared in terms of selectivity and sensitivity, and quantification techniques, especially isotope dilution, were also discussed. Conclusions and future perspectives were outlined. Urbansky reviewed the fate of fluorosilicate additives in drinking water (*197*). Hexafluorosilicic acid is the most commonly used additive to provide fluoride in drinking water (for the prevention of tooth decay). Urbansky discussed in detail the dissociation and hydrolysis equilibria of fluorosilicates, as well as the potential distribution of fluoride species (e.g., F^-, HF, HF_2^-, $Si(OH)_2F_2$, SiF_6^{2-}). It was concluded that for drinking water supplies that are fluoridated with sodium silicofluoride (hexafluorosilicate) at 16 ppm of F or less, all of the silicofluoride would be completely hydrolyzed to silicic acid, fluoride ion, and hydrogen fluoride, so that the toxicity of hexafluorosilicate is not an issue. The U.S. EPA limits the addition of fluoride to drinking water at 4 mg/L (the fluoride MCL). However, Urbansky notes that there are still unanswered questions and that additional research should be carried out to measure all species that could be present when hexafluorosilicates are added (including those species that could be formed with metal cations—e.g., aluminum, iron, lead, zinc, etc.—present in a real drinking water matrix).

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Susan D. Richardson *is a research chemist at the U.S. Environmental Protection Agency's National Exposure Research Laboratory in Athens, GA. She received her B.S. degree in chemistry and mathematics from Georgia College in 1984 and her Ph.D. degree in chemistry from Emory University in 1989. At the U.S. EPA, Dr. Richardson leads a team of chemists in developing and applying multispectral analysis techniques (GC/MS, LC/MS, CE/MS, and GC/IR) to environmental problems. Her recent research has focused on the identification/characterization of new disinfection byproducts (DBPs), with special emphasis on alternative disinfectants and polar byproducts. She led the Nationwide DBP Occurrence Study mentioned in this paper and is particularly interested in promoting new health effects research so that the risks of DBPs can be determined and minimized.*

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