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Water Analysis: Emerging Contaminants and Current Issues

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Review Contents

This biennial review covers developments in water analysis over the period of 2005−2006. A few significant references that appeared between January and March 2007 are also included. *Analytical Chemistry*'s current policy is to limit reviews to include 200−250 significant references and to focus on new trends. As a result, as was done in the previous 2005 Water Analysis review (*1*), this 2007 review is limited to new, emerging contaminants and environmental issues that are driving most of the current research. Even with a narrow focus, only a small fraction of the quality research publications could be discussed. As a result, this review will not be comprehensive, but will highlight new areas and discuss representative papers in the areas of focus. Any comments you have are welcome (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 discussed in this review. A table of useful websites is also provided (Table 2).

Sampling and Extraction Trends. Trends in sampling and extraction include increased use of stir bar sorptive extraction, hollow-fiber membrane microextraction, and passive samplers. Examples of stir bar sorptive extraction, hollow-fiber microextraction, and passive sampling (with a polar organic chemical integrative sampler) presented in this review include the extraction of estrogens, polybrominated diphenyl ethers (PBDEs), and pharmaceuticals, respectively. Stir bar sorptive extraction involves the use of a sorbent-coated stir bar, which is stirred in the aqueous sample to extract the analytes of interest. The analytes can then be thermally desorbed and analyzed by gas chromatography (GC)/mass spectrometry (MS). Hollow-fiber microextraction is similar to traditional solid-phase microextraction (SPME), except that a polypropylene hollow-fiber membrane is attached to the tip of a syringe that contains an extraction solvent. The membrane is then used to sample the aqueous sample, and the solvent is drawn back into the syringe, the fiber discarded, and the solvent injected directly into a GC or liquid chromatography (LC) instrument. The polar organic chemical integrative sampler (POCIS) contains membranes that allow polar contaminants to be passively extracted from water and wastewater. This extraction technique provides a time-weighted-average sampling, where transient contaminants can be detected that might have been missed in a grab sampling approach. Two different sorbent systems are used inside the POCIS membranes—one designed for general use that contains a mixture of different sorbents and one designed for pharmaceuticals that contains Oasis HLB as the sorbent. Traditional SPME, which eliminates the need for organic solvents in extraction, has now become commonplace, and examples are presented throughout this review.

Chromatography Trends. New chromatography trends include the use of two-dimensional (2-D) GC, hydrophilic interaction chromatography (HILIC), and ultra-performance liquid chromatography (UPLC). 2-D GC enables enhanced separations of complex mixtures through greater chromatographic peak capacity and allows homologous series of compounds to be easily identified. It also enables the detection of trace contaminants that would not have been identified through traditional GC. Time-of-flight (TOF)-MS is often used as the detector for 2-D GC because of its rapid acquisition capability. An example of 2-D GC presented in this review includes the analysis of complex mixtures of naphthenic acids. HILIC is a new LC technique that provides improved separations and MS sensitivity for highly polar compounds. The stationary phase in HILIC columns has a polar end group (such as an amino group), and retention is based on the affinity of the polar analyte for the charged end group of the column stationary phase. An example of HILIC in this review is the measurement of a veterinary pharmaceutical in runoff waters. UPLC is another new LC technique that uses small-diameter particles (typically 1.7 μm) in the stationary phase and short columns, which allow higher

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Table 1. List of Acronyms

APCI	atmospheric pressure chemical ionization
BP-3	benzophenone-3
CCL	Contaminant Candidate List
DAD	diode array detection
DBPs	disinfection byproducts
DIPE	diisopropyl ether
E1	estrone
E2	17β-estradiol
E3	estriol
EE2	17α-ethinylestradiol
ECD	electron capture detection
EDCs	endocrine disrupting compounds
EDB	ethylene dibromide
ELISA	enzyme-linked immunosorbent assay
EPA	Environmental Protection Agency
ESA	ethane sulfonic acid
ESI	electrospray ionization
ETBE	ethyl *tert*-butyl ether
FAIMS	high-field asymmetric waveform ion mobility spectrometry
FT	Fourier-transform
FTOHs	fluorinated telomer alcohols
GC	gas chromatography
HAAs	haloacetic acids
HILIC	hydrophilic interaction chromatography
IC	ion chromatography
ICP	inductively coupled plasma
LC	liquid chromatography
LT2ESWTR	Long Term 2 Enhanced Surface Water Treatment Rule
4-MBC	4-methylbenzylidene camphor
MCL	maximum contaminant level
MIMS	membrane introduction mass spectrometry
MRM	multiple reaction monitoring
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
PCBs	polychlorinated biphenyls
PBDEs	polybrominated diphenyl ethers
PFCs	perfluorinated compounds
PFBS	perfluorobutanesulfonate
PFCAs	perfluorocarboxylic acids
PFHS	perfluorohexanesulfonate
PFNA	perfluorononanoic acid
PFOA	perfluorooctanoic acid
PFOS	perfluorooctane sulfonate
SPE	solid-phase extraction
SPME	solid-phase microextraction
TAME	*tert*-amyl methyl ether
TBA	*tert*-butyl alcohol
THMs	trihalomethanes
TOF	time-of-flight
TOX	total organic halide
UCMR	Unregulated Contaminants Monitoring Rule
UPLC	Ultra-performance liquid chromatography
VOCs	volatile organic compounds

pressures and, ultimately, narrower LC peaks (5−10 s wide). In addition to providing narrow peaks and improved chromatographic separations, UPLC can also dramatically shorten analysis times, often to 10 min or less. Waters Corp. was the first company to develop this technology, but other companies are now offering similar systems. An example of UPLC presented in this review is the measurement of 29 pharmaceuticals in wastewater in less than 10 min.

Detection Trends. Trends in detection include increased use of TOF- and quadrupole (Q)-TOF-MS. TOF-MS, and Q-TOF-MS provided added MS resolution over traditional quadrupole, triple quadrupole, or ion trap-MS. Typically, 10 000−12 000 resolution can be obtained, which provides exact mass data and enables the identification of transformation products of emerging contaminants. An example of this includes the identification of new pesticide degradation products. LC/electrospray ionization (ESI) and atmospheric pressure chemical ionization (APCI)-MS methods continue to dominate the new methods developed for emerging contaminants, and the use of multiple reaction monitoring (MRM) with MS/MS has become commonplace for quantitative environmental analysis. The use of LC/MS/MS allows the identification of highly polar organic pollutants without derivatization, down to nanogram per liter levels in aqueous samples, including surface water, wastewater, groundwater, and drinking water. And, the use of MRM provides increased selectivity and sensitivity, greatly reducing the chemical background in LC/MS analyses. Researchers are also increasingly using isotopically labeled standards (deuterated or ^{13}C-labeled) to allow more accurate quantitation in a variety of sample matrixes (especially for wastewater, where matrix effects can be substantial). In addition, enzyme-linked immunosorbent assays (ELISAs) continue to be developed for emerging contaminants, which allows an inexpensive alternative to MS. However, false positives can often be obtained with ELISAs, so they are generally used as a rapid screening technique that is followed up with a more precise analysis (such as LC/MS/MS).

Online Analysis. There is also a trend toward more online analysis of contaminants. For example, Emmert's group at the University of Memphis has developed a new online membrane technique for measuring disinfection byproducts (DBPs) in drinking water. Online/real-time methods like this one offer an advantage of continuous monitoring and early detection of potential problems. In addition, new derivatization techniques continue to be published (mostly for GC/MS analysis). For example, 2,4-difluoroaniline and *N,N*-dicyclohexylcarbodiimide were used to derivatize perfluorocarboxylic acids for GC/MS analysis, and octafluoropentyl chloroformate was used to derivatize highly polar alcohol, carboxylic acid, and amine DBPs in drinking water for GC/MS analysis.

Detection Limits. New analytical methods continue to push detection limits lower. Just a few years ago, microgram per liter detection limits were common. Today, it is unusual to see detection limits that are not at least low-nanogram per liter. There are even some examples in this review of picogram per liter detection limits. As instruments and extraction techniques continue to improve, and new types of instruments are developed, detection limits will likely continue to drop, allowing the detection of analytes not previously possible. Another advantage of lower detection limits is in the study of transformation processes. For example, the study of wastewater treatment to remove pharmaceuticals is greatly aided by a technique that can measure low- or subnanogram per liter detection limits. Pharmaceuticals are generally present at nanogram per liter to low-microgram per liter levels in wastewater influents, and detection limits at the low- or subnanogram per liter level allow the percentage removal to be determined.

Emerging Contaminants. Five new emerging contaminants are added to this water analysis review this year: benzotriazoles,

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/safewater/methods/methods.html	link to U.S. EPA and non-EPA drinking water methods
www.epa.gov/safewater/methods/sourcalt.html	methods developed by U.S. EPA's Office of Ground Water and Drinking Water
www.epa.gov/nerlcwww	microorganism methods
www.epa.gov/nerlcwww/ordmeth.htm	drinking water and marine water methods developed by U.S. EPA's Office of Research & Development
www.epa.gov/safewater/dwinfo	local drinking water quality reports (U.S.)
www.gpoaccess.gov/fr	direct link to the Federal Register
www.epa.gov/ncer/grants	U.S. EPA's STAR Grants solicitations

naphthenic acids, ethylene dibromide (EDB), 1,4-dioxane, and nanomaterials. Benzotriazoles are complexing agents that are used as anticorrosives (e.g., in engine coolants, aircraft deicers, or antifreezing liquids) and for silver protection in dish washing liquids. They are soluble in water, resistant to biodegradation, and are only partially removed in wastewater treatment. Naphthenic acids are a growing problem in Alberta, Canada, where they are residual contaminants left over from the extraction of crude oil from oil sands. These naphthenic acids are highly toxic and endocrine disrupting and are present at 80−120 mg/L levels in residual tailing waters that result from extraction with hot water. EDB was previously used as a gasoline additive (a lead scavenger in leaded gasoline), and despite the phase-out of leaded gasoline in the early 1970s in the United States, EDB is among the most commonly detected contaminants in groundwater. EDB is classified as a probable human carcinogen and is highly persistent in water. 1,4-Dioxane is also a widespread contaminant in groundwater and is a probable human carcinogen. Dioxane is a high production chemical and is used as a solvent stabilizer. Finally, nanomaterials are currently one of the hottest topics in research today. They are already being used in a variety of commercial products (particularly cosmetics), and there is significant concern about their potential human and ecological effects. Nanomaterials are the focus of a new initiative at the U.S. Environmental Protection Agency (EPA), where research on their ecological fate, transport, and health effects will be investigated. Nanomaterials research in environmental samples is in its infancy (there is not much published at this time), but this area is included in this review because it is expected to be an area of intense growth in the next 2−3 years.

Other areas covered in this review again include perfluorooctanoic acid (PFOA), perfluorooctanesulfonate (PFOS), and other perfluorinated compounds, pharmaceuticals, hormones, endocrine disrupting compounds (EDCs), sunscreens/UV filters, DBPs, flame retardants, pesticide degradation products and new pesticides, algal toxins, perchlorate, methyl *tert*-butyl ether (MTBE), and microorganisms. These continue to be intense areas of research. A trend for these ongoing research areas is the study of the transformation of some of these compounds in drinking water or wastewater treatment. For example, the chlorination and ozonation of pharmaceuticals, personal care products, and pesticides are represented in this review, as researchers try to find ways to remove these contaminants from source waters. However, new research is discovering that most of these compounds are not completely mineralized, but are transformed into other compounds that may be less toxic or more toxic than the parent compounds.

Finally, new regulations and regulatory methods are again included in this review. Four new U.S. regulations were promulgated for drinking water, and several new regulatory methods have been published in the last 2 years, covering contaminants, such as perchlorate, pesticides, brominated flame retardants, nitroaromatics, nitramines, and nitrate esters. The second drinking water Contaminant Candidate List (CCL) has been published, and the third CCL is currently under development. These new regulations and regulatory methods will be discussed.

GENERAL REVIEWS

This section includes general reviews relating to water analysis. Reviews that relate to specific areas (e.g., perfluorinated compounds, pharmaceuticals, DBPs, etc.) can be found in those specific sections. Many reviews have been published over the last 2 years that relate to water analysis, and several of these focus specifically on emerging contaminants. The previous water analysis review published in 2005 contained 200 references and discussed advances in research for new regulations and regulatory methods for water and emerging contaminants, including, drinking water DBPs, PFOA and other perfluorinated compounds, pharmaceuticals, hormones, endocrine disruptors, chiral contaminants, sunscreens/UV filters, brominated flame retardants, pesticide degradation products, chemical warfare agents, MTBE, algal toxins, organotins, perchlorate, arsenic, natural organic matter (NOM), and microorganisms (*1*).

Emerging environmental contaminants were the focus of a recent issue of *Environmental Science & Technology* (December 1, 2006), where current research on emerging chemical and microbial contaminants was highlighted. This is a must-read issue, and several of those papers will be discussed in this review. The guest editors of this issue also published an excellent perspective on "What is emerging?" as a lead-off editorial to this issue, which points out that the longevity of a contaminant's "emerging" status is typically determined by whether the contaminant is persistent or has potentially harmful human or ecological effects (*2*). It is often the case that emerging contaminants have actually been present in the environment for some time (in some cases, decades), but they are discovered through a wider search of potential contaminants (as in the case of ethylene dibromide, in

Table 3. New U.S. Regulations

rule/regulation	website
Stage 2 D/DBP Rule	www.epa.gov/safewater/stage2
Second Unregulated Contaminants Monitoring Rule (UCMR-2)	www.epa.gov/safewater/ucmr/ucmr2
First UCMR	www.epa.gov/safewater/ucmr/ucmr1
Contaminant Candidate List (CCL)	www.epa.gov/safewater/ccl
LT2ESWTR	www.epa.gov/safewater/lt2
Ground Water Rule	www.epa.gov/safewater/gwr
Arsenic Rule	www.epa.gov/safewater/arsenic
Radon Rule	www.epa.gov/safewater/radon/proposal.html

this current review) or through the use of new technologies (such as LC/MS) that have enabled their discovery and measurement in the environment for the first time (as in the case of many pharmaceuticals). Petrovic and Barcelo presented a nice perspective on emerging environmental contaminants and emphasized that the term "emerging contaminants" does not necessarily mean new substances (i.e., newly introduced) but can also include naturally occurring compounds with previously unrecognized adverse effects on ecosystems (*3*). In fact, algal toxins and hormones, two classes of emerging contaminants included in the current water analysis review fall into this category of being naturally occurring, yet can have adverse ecological impacts. Petrovic and Barcelo also provide a list of several compounds considered to be emerging and discuss LC/MS instrumentation for their analysis, along with the identification point (IP) system used for identification and confirmation of environmental contaminants in the European Union. In another paper, Muir and Howard discuss a procedure for determining whether there are other persistent organic pollutants that should be addressed beyond those currently being studied (*4*). The authors point out that only a small fraction of the approximately 30 000 chemicals widely used in commerce are currently being investigated, and they list 30 chemicals with high predicted bioconcentration factors and low rates of biodegradation, along with 28 chemicals with long-range atmospheric transport potential, that could be candidates for environmental monitoring.

Emerging contaminants are also the focus of a new consortium of laboratories under a project called NORMAN (Network of Reference Laboratories and Related Organizations for Monitoring and Bio-Monitoring of Emerging Environmental Pollutants) (www.norman-network.net/index_php.php). The objectives of NORMAN are to create a network of expert reference laboratories and organizations to improve the exchange of information and data on emerging environmental contaminants and encourage the validation and harmonization of analytical methods for these analytes.

Mass spectrometry techniques for emerging contaminants were the focus of another biennial review published in *Analytical Chemistry* in 2006 (*5*). This review (covering the period of 2004−2005) included many of the same emerging contaminants discussed in the present review, but with a focus on mass spectrometry techniques, and it included environmental matrixes in addition to water (e.g., biological, air, sediment, and water samples). Koester et al. published the biennial *Analytical Chemistry* review on environmental analysis (covering the period of 2003−2004), which included a review of sample collection and extraction methods (including semipermeable membrane devices, SPME, hollow-fiber, liquid-phase microextraction, and new materials for solid-phase extraction (SPE)), separation and detection techniques (including novel chromatographic stationary phases, chiral separations, and two-dimensional GC, TOF-MS, inductively coupled plasma (ICP)-MS, and nuclear magnetic resonance (NMR) spectroscopy (*6*). A helpful table is also included for analytes of emerging interest, which lists the sample preparation methods and detection techniques for each analyte. This article not only reviews key papers published in those areas, but also gives detailed discussions on the advantages and disadvantages of the analytical techniques, making this article a must-read for analytical chemists desiring the latest developments in environmental analysis.

Peck reviewed analytical methods for determining persistent ingredients in personal care products, which included synthetic musk fragrances, antimicrobials, UV filters, insect repellents, and parabens (*7*). LC/Q-TOF in environmental analysis was also the focus of another review article that highlighted the utility of Q-TOF mass spectrometers for identifying unknown contaminants and degradation products in environmental samples (*8*). Microextraction of polar analytes from environmental samples was the focus of another review by Quintana and Rodriguez (*9*). SPME, stir bar sorptive extraction, and liquid-phase microextraction were discussed, as well as derivatization strategies to enable GC analysis. Emerging chiral compounds were the focus of a review by Wong, who summarized their analytical chemistry, environmental occurrence, and environmental fate (*10*). Passive sampling techniques were the focus of reviews by Namiesnik et al. (*11*) and Vrana et al. (*12*). Passive sampling techniques, such as semipermeable membrane devices, are becoming increasingly popular as tools to enable time-weighted-average samples, rather than traditional grab samples, which could miss an important contaminant input. Finally, Ramos et al. discussed developments in the field of miniaturized sample preparation for environmental analysis (*13*), and Butler et al. published their annual review on atomic spectrometry (*14*), which includes an update on techniques currently being used to measure metal species in environmental samples.

NEW REGULATIONS/REGULATORY METHODS

New U.S. Regulations. Several developments in new regulations and regulatory methods have taken place in the last 2 years that impact water analysis. Table 3 includes websites that can be used to obtain additional details on the regulations. Table 4 summarizes the new regulatory methods.

The U.S. EPA's website is a good source for obtaining details on regulations and regulatory methods: www.epa.gov. This

Table 4. New Regulatory Methods

method	analytes	website
EPA Method 331.0	perchlorate (LC/ESI-MS/MS)	www.epa.gov/safewater/methods/sourcalt.html
EPA Method 314.1	perchlorate (IC)	www.epa.gov/safewater/methods/sourcalt.html
EPA Method 6850	perchlorate (LC/ESI-MS/MS)	www.epa.gov/epaoswer/hazwaste/test/new-meth.htm
EPA Method 6860	perchlorate (IC/ESI-MS/MS)	www.epa.gov/epaoswer/hazwaste/test/new-meth.htm
EPA Method 527	brominated flame retardants, pesticides	www.epa.gov/safewater/methods/sourcalt.html
EPA Method 8260C	>100 VOCs (including fuel oxygenates)	www.epa.gov/epaoswer/hazwaste/test/new-meth.htm
EPA Method 8330B	nitroaromatics, nitramines, nitrate esters	www.epa.gov/epaoswer/hazwaste/test/new-meth.htm

Table 5. DBPs Regulated under the Stage 1 and Stage 2 D/DBP Rules

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.

Table 6. Second Unregulated Contaminants Monitoring Rule (UCMR-2) Contaminants

List 1. Assessment Monitoring
1,3-dinitrobenzene
2,2′,4,4′-tetrabromodiphenyl ether (BDE-47)
2,2′,4,4′,5-pentabromodiphenyl ether (BDE-99)
2,2′,4,4′,5,5′-hexabromobiphenyl (245-HBB)
2,2′,4,4′,5,5′-hexabromodiphenyl ether (BDE-153)
2,4,6-trinitrotoluene (TNT)
dimethoate
hexahydro-1,3,5-trinitro-1,3,5-triazine (RDX)
terbufos sulfone
perchlorate
2,2′4,4′,6-pentabromodiphenyl ether (BDE-100)

List 2. Screening Survey
acetochlor
acetochlor ESA
acetochlor OA
alachlor
alachlor ESA
alachlor OA
metolachlor
metolachlor ESA
metolachlor OA
N-nitrosodiethylamine (NDEA)
N-nitrosodimethylamine (NDMA)
N-nitrosodi-*n*-butylamine (NDBA)
N-nitrosodi-*n*-propylamine (NDPA)
N-nitrosomethylethylamine (NMEA)
N-nitrosopyrrolidine (NPYR)

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.gpoaccess.gov/fr. Currently, there are primary drinking water regulations for 92 contaminants, including 11 DBPs, 53 organic contaminants, 16 inorganic contaminants, 4 radionuclides, 7 microorganisms, and turbidity (www.epa.gov/safewater/contaminants). The U.S. EPA has a website where local drinking water quality reports can be obtained (www.epa.gov/safewater/dwinfo).

Four major drinking water rules were issued in 2005: the Stage 2 Disinfectants (D)/DBP Rule, the second Unregulated Contaminants Monitoring Rule (UCMR-2), the Long Term 2 Enhanced Surface Water Treatment Rule (LT2ESWTR), and the Ground Water Rule. Other Rules that were proposed or were effective within the last 2 years are also included in the sections below.

Stage 2 D/DBP Rule. The Stage 2 D/DBP Rule is an extension of the Stage 1 Rule, which took effect on January 1, 2002, for large surface water treatment systems and 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 (www.epa.gov/safewater/stage2). The Stage 2 D/DBP Rule maintains the Stage 1 Rule maximum contaminant levels (MCLs) for THMs and HAAs (Table 5), but requires that MCLs be based on locational running annual averages (i.e., *each location* in the distribution system must 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 maintains the MCLs for bromate and chlorite; however, the U.S. EPA plans to review the bromate MCL as part of their 6-year review process (additional details area available at www.epa.gov/safewater/stage2).

Second Unregulated Contaminants Monitoring Rule. The UCMR-2 was proposed on August 22, 2005 (www.epa.gov/safewater/ucmr/ucmr2), and is an updated form of the original UCMR (www.epa.gov/safewater/ucmr/ucmr1) that was issued in 1999. The UCMR-2 requires drinking water utilities to monitor for 26 chemicals over a 12-month period in 2007−2011. Table 6 lists the contaminants to be monitored under the UCMR-2. Several of these contaminants are PBDE flame retardants and nitrosamine DBPs that are discussed in this review. This rule allows the U.S. EPA to obtain occurrence data for priority unregulated contaminants that are being considering for regulation. The occurrence data are being stored in the National Drinking Water Contaminant Occurrence Database (NCOD) and will be used with health effects data to determine whether any should be regulated. This rule helps to support the Safe Drinking Water Act and Amendments, which requires that, at least once every 5 years, the U.S. EPA identify a list of no more than 30 unregulated contaminants to be monitored. The UCMR-2 is divided up into List 1 and List 2 contaminants (Table 6). Contaminants for which standard analyti-

cal methods are available fall under List 1, and all large water systems that serve more than 10 000 people, as well as a nationally representative sample of 800 small water systems, are required to measure these contaminants in drinking water for a continuous 12-month period during July 2007−June 2010 (quarterly for surface water systems and twice, at 6-month intervals, for groundwater systems). List 2 contaminants cover those for which analytical methods were recently developed, and for which these technologies are not widely used (and laboratory capacity may be limited). For List 2 contaminants, a Screening Survey will be conducted for approximately 320 public water systems serving more than 100 000 people, by a randomly selected sample of 320 water systems serving between 10 001 and 100 000 people, and by 480 small water systems. The Screening Survey systems are required to monitor during a continuous 12-month period during July 2007−June 2009 (quarterly for surface water systems, and twice, at 6-month intervals for groundwater systems). A total of 1100 systems will be participating in the Screening Survey, which will enable sufficient data to be generated to provide an overall national estimate of exposure.

Long Term 2 Enhanced Surface Water Treatment Rule. The final LT2ESWTR was published on January 5, 2006, and is an extension of the former Long Term 1 Rule. This rule improves the control of microbial pathogens (including specifically *Cryptosporidium*) in drinking water and addresses risk trade-offs with disinfection byproducts (additional details are available at www.epa.gov/safewater/disinfection/lt2).

Ground Water Rule. This rule was published in November 2006 and seeks to provide increased protection against microbial pathogens in public water systems that use groundwater sources. It is expected to impact approximately 100 million people in the United States. The new rule establishes a multiple-barrier approach, which includes periodic 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. Additional details can be found at www.epa.gov/safewater/gwr.

Arsenic Rule. The Arsenic Rule was issued in 2001, which lowers the arsenic MCL from 50 to 10 μg/L (www.epa.gov/safewater/arsenic). This rule became effective February 22, 2002, and since January 23, 2006, drinking water systems have had to comply with this new standard.

Radon Rule. The Radon Rule was issued in 2005 and established an MCL of 300 pCi/L for radon in water. An alternative MCL (at a higher level of 4000 pCi/L) can also be used if a multimedia mitigation program is put in place to also reduce radon in indoor air. The proposed standards apply only to community water systems that regularly serve 25 or more people and that use groundwater or mixed groundwater and surface water. They do not apply to systems that rely on surface water where radon levels are typically very low, and they do not apply to private wells. Radon exposures from drinking water are much less (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/safewater/radon/proposal.html.

Contaminant Candidate List. The Safe Drinking Water Act Amendments (1996) required the U.S. EPA to publish a CCL every 5 years to identify potential substances for future regulation. Monitoring data are 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 5-year period. The first CCL (CCL1) was published in March 1998 and contained 50 chemical and 10 microbial contaminants. Chemical contaminants included 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 (www.epa.gov/safewater/ccl). In July 2003, determinations regarding whether to regulate were made for eight chemical contaminants (aldrin, dieldrin, hexachlorobutadiene, manganese, metribuzin, naphthalene, sodium, sulfate) and one microbial contaminant (*Acanthanmoeba*). The U.S. EPA decided against regulation for these contaminants (www.epa.gov/safewater/ccl/pdfs/reg_determine1/fs_ccl1_regdetermine_july03.pdf).

The second Contaminant Candidate List (CCL2) was published on February 23, 2005 (www.epa.gov/safewater/ccl/ccl2.html). Table 7 lists the CCL2 contaminants, which are the same as the original CCL1 list, except that the contaminants mentioned above (for which regulatory determinations were made) have been removed. The third CCL is currently under development and expected to be released in 2008. For the CCL3 effort, there is a major change in the way that it is being developed. EPA is undertaking a broader and more comprehensive screening process of potential contaminants and has a new mechanism for allowing the general public, stakeholders, agencies, and industry to nominate chemicals, microorganisms, or other materials for consideration. Instructions for nominating contaminants for the CCL3 can be found at www.epa.gov/safewater/ccl/ccl3.html. In the new process, a broadly defined "universe" of potential drinking water contaminants is being identified, assessed, and reduced to a preliminary CCL (PCCL) using simple screening criteria that indicate public health risk and the likelihood of occurrence in drinking water. The PCCL contaminants will be assessed in more detail using available occurrence and toxicity data, and a draft CCL3 will be proposed. Further details on the CCL can be found at www.epa.gov/safewater/ccl/cclfs.html.

New Regulatory Methods. A few new regulatory methods have been developed over the last 2 years by the U.S. EPA. Most of these are directed toward the measurement of CCL chemicals in drinking water under the UCMR; a few are for hazardous waste measurements.

Nitrosodimethylamine (NDMA) and Other Nitrosamines. In 2004, a new EPA method was created for measuring NDMA and six additional nitrosamines in drinking water, in support of the UCMR (EPA Method 521, Determination of Nitrosamines in Drinking Water by Solid-Phase Extraction and Capillary Column Gas Chromatography with Large Volume Injection and Chemical Ionization Tandem Mass Spectrometry (MS/MS)) (www.epa.gov/nerlcwww/m_521.pdf). This method enables the measurement of

Table 7. Second Drinking Water Contaminant Candidate List (CCL2)

Chemical Contaminants[a]
1,1,2,2-tetrachloroethane
1,2,4-trimethylbenzene
1,1-dichloroethane
1,1-dichloropropene
1,2-diphenylhydrazine
1,3-dichloropropane
1,3-dichloropropene
2,4,6-trichlorophenol
2,2-dichloropropane
2,4-dichlorophenol
2,4-dinitrophenol
2,4-dinitrotoluene
2,6-dinitrotoluene
2-methylphenol (*o*-cresol)
Acetochlor
alachlor ESA and other acetanilide pesticide degradation products
aluminum
boron
bromobenzene
DCPA monoacid degradate
DCPA diacid degradate
DDE
diazinon
disulfoton
diuron
EPTC (s-ethyldipropylthiocarbamate)
fonofos
p-isopropyltoluene (*p*-cymene)
linuron
methyl bromide
methyl *tert*-butyl ether (MTBE)
metolachlor
molinate
nitrobenzene
organotins
perchlorate
prometon
RDX
terbacil
terbufos
triazines and their degradation products (including, but not limited to cyanazine and atrazine-desethyl)
vanadium

Microbiological Contaminants
adenoviruses
Aeromonas hydrophila
caliciviruses
coxsackieviruses
Cyanobacteria (blue-green algae), other reshwater algae, and their toxins
echoviruses
Helicobacter pylori
Microsporidia (Enterocytozoon and Septata)
Mycobacterium avium intracellulare (MAC)

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

NDMA and six other nitrosamines (*N*-nitrosomethylethylamine, *N*-nitrosodiethylamine, *N*-nitroso-di-*n*-propylamine, *N*-nitroso-di-*n*-butylamine, *N*-nitrosopyrrolidine, *N*-nitrosopiperidine) in drinking water at detection limits ranging from 1.2 to 2.1 ng/L. Coconut charcoal is used as the solid-phase extractant, and sample preparation steps are simple and inexpensive. In 2006, Munch and Bassett published an article detailing the development of this method (*15*).

Perchlorate. Four new methods have been created for perchlorate in the past 2 years. Two methods were developed for the analysis of perchlorate in drinking water, in support of the UCMR, and two methods were developed for measuring perchlorate in hazardous waste samples (including water samples).

The new drinking water methods include EPA Methods 314.1 and 331.0. These methods were created to overcome matrix interferences in high ionic strength waters and also to lower detection limits to levels that are of human health concern. An earlier EPA method for measuring perchlorate (EPA Method 314.0) had a minimum reporting level of 4 μg/L and was vulnerable to sensitivity loss and false positive identifications in high ionic strength waters. Method 331.0, Determination of Perchlorate in Drinking Water by Liquid Chromatography Electrospray Ionization Mass Spectrometry (www.epa.gov/safewater/methods/sourcalt.html) uses O-18 labeled perchlorate and MRM with a triple quadrupole mass spectrometer, which provides selectivity for the measurement of perchlorate. This method allows 0.02 μg/L detection limits. Wendelken et al. published an article in 2006 that discusses details of the method, including method uncertainties and recovery data in simulated drinking water (*16*). Method 314.1, Determination of Perchlorate in Drinking Water Using Online Column Concentration/Matrix Elimination Ion Chromatography with Suppressed Conductivity Detection (www.epa.gov/safewater/methods/sourcalt.html), utilizes a concentrator column to retain perchlorate, while potentially interfering anionic contaminants (chloride, carbonate, sulfate) are washed from the column to waste. The concentrator column is then switched inline with the ion chromatography (IC) system, which also utilizes a guard column, an analytical column, a suppressor device, and conductivity detection. This new IC method allows 0.2 μg/L detection limits of perchlorate in water. Wagner et al. published an article in 2006 describing the method details (*17*).

The new hazardous waste methods include EPA Methods 6850 and 6860 (www.epa.gov/epaoswer/hazwaste/test/new-meth.htm). Method 6850, Perchlorate in Water, Soils, and Solid Wastes Using High Performance Liquid Chromatography/Electrospray Ionization/Mass Spectrometry, and Method 6860, Perchlorate in Water, Soils, and Solid Wastes Using Ion Chromatography/Electrospray Ionization/Mass Spectrometry, can be used to measure perchlorate in surface waters, groundwater, wastewater, salt water, and soils. Both methods are performance-based, such that performance criteria should be developed on a project-specific basis. These methods allow flexibility, where a variety of chromatographic conditions and analysis options (including MS/MS) have been validated and are provided with the methods.

Pesticides and Brominated Flame Retardants. A new method was published in 2005 for the measurement of pesticides and flame retardants that are listed on the UCMR-2. EPA Method 527, Determination of Selected Pesticides and Flame Retardants in Drinking Water by Solid Phase Extraction and Capillary Column Gas Chromatography/Mass Spectrometry (www.epa.gov/safewater/methods/sourcalt.html), allows sub- to low-ppb level detection for five flame retardants, hexabromobiphenyl (HBB-157), 2,2′,4,4′,5,5′-hexabromodiphenyl ether (BDE-153), 2,2′,4,4′,5-pentabromodiphenyl ether (BDE-99), 2,2′,4,4′,6-pentabromodiphenyl ether (BDE-100), and 2,2′,4,4′-tetrabromodiphenyl ether (BDE-47), and the following 21 pesticides, atrazine, bifenthrin, bromacil,

chlorpyrifos, dimethoate, esbiol, esfenvalerate, fenvalerate, hexazinone, kepone, malathion, mirex, norflurazon, nitrofen, oxychlordane, parathion, prometryne, propazine, terbufos-sulfone, thiobencarb, and vinclozolin. This method uses solid-phase extraction of a 1-L water sample, followed by GC/MS analysis using internal standards. Further details on this method can also be found in a 2005 article by Pepich et al. (*18*).

Volatile Organic Compounds (VOCs). EPA Method 8260C, Volatile Organic Compounds By Gas Chromatography/Mass Spectrometry (GC/MS), was developed in August 2006 for hazardous waste samples (including groundwater and surface waters) and includes a variety of different sample extraction/introduction techniques, with purge-and-trap and direct aqueous injection options for aqueous samples (www.epa.gov/epaoswer/hazwaste/test/new-meth.htm). This method is applicable to >100 VOC analytes, which includes fuel oxygenates, MTBE, ethyl *tert*-butyl ether (ETBE), *tert*-amyl methyl ether (TAME), *tert*-butyl alcohol (TBA), and diisopropyl ether (DIPE), one nitrosamine, (*N*-nitroso-di-*n*-butylamine), and several common contaminants (e.g., trichloroethene).

Nitroaromatics, Nitramines, and Nitrate Esters. EPA Method 8330B, Nitroaromatics, Nitramines, and Nitrate Esters by High Performance Liquid Chromatography (LC), was updated in November 2006 for hazardous waste samples and uses a direct injection procedure for water samples (www.epa.gov/epaoswer/hazwaste/test/new-meth.htm). The 17 analytes covered by this method are either used in the manufacture of explosives or propellants or are impurities in their manufacture, or their degradation products. This method includes compounds, such as 2,4,6-trinitrotoluene (TNT), nitrobenzene, and 3,5-dinitroaniline.

New EPA Methods Currently under Development. New methods are currently being developed for measuring organotins, perfluorinated compounds (PFCs), and 1,4-dioxane in drinking water. These methods are expected to be available within the next 2 years.

PFOA, PFOS, AND OTHER PERFLUORINATED COMPOUNDS

PFCs—also referred to as fluorotelomer acids, alcohols, and sulfonates—have been manufactured for more than 50 years and have been used to make stain repellents (such as polytetrafluoroethylene and Teflon) that are widely applied to fabrics and carpets. They are also used in the manufacture of paints, adhesives, waxes, polishes, metals, electronics, and caulks, as well as grease-proof coatings for food packaging (e.g., microwave popcorn bags, french fry boxes, hamburger wrappers, etc.). PFCs are unusual chemically, in that they are both hydrophobic (repel water) and lipophobic (repel lipids/grease), and they contain one of the strongest chemical bonds (C−F) known. Because of these properties, they are highly stable in the environment (and in biological samples), and they are expected to have unique profiles of distribution in the body. During 2000−2002, an estimated 5 million kg/yr was produced worldwide, with 40% of this in North America. Two of these PFCs, PFOS and PFOA, are currently receiving a great deal of attention as emerging contaminants in the United States. PFOS was once used to make the popular Scotchgard fabric and carpet protector, and since 2002, it is no longer manufactured due to concerns about widespread global distribution in the blood of the general population and in wildlife, including remote locations in the Arctic and North Pacific Oceans. However, other fluorinated surfactants like PFOA are still manufactured. Like PFOS, PFOA appears to be ubiquitous at low levels in humans, even in those living far from any obvious sources (*1*).

Most Americans have about 5 ppb of PFOA in their blood (www.epa.gov/opptintr/pfoa/pubs/pfoarisk.pdf), and potential health concerns include developmental toxicity (*19*), cancer (*20*), and bioaccumulation (*21*). Research questions include understanding the sources of PFOA and other PFCs, their environmental fate and transport, pathways for human exposure and uptake, and potential health effects. It is currently hypothesized that the widespread occurrence of PFOA and other fluoro acids is likely due to the atmospheric or oceanic transport of the more volatile fluorinated telomer alcohols (FTOHs) and subsequent transformation into PFOA and other fluoro acids via metabolism and biodegradation. Early studies seem to offer support for this hypothesis (*22*−*25*). PFOS, PFOA, and other PFCs are now included in National Health and Nutrition Examination Survey (NHANES) being conducted by the Centers for Disease Control and Prevention (CDC) to provide a better assessment of the distribution of these chemicals in the human population (www.cdc.gov/nchs/nhanes.htm). The National Toxicology Program will also be carrying out toxicity studies on PFOA and several other perfluorcarboxylic acids and perfluorosulfonates to better understand the toxicity of these chemicals and their persistence in human blood (http://ntp.niehs.nih.gov).

In January 2005, the U.S. EPA issued a draft risk assessment of the potential human health effects associated with exposure to PFOA (www.epa.gov/opptintr/pfoa/pubs/pfoarisk.htm), and in January 2006, the U.S. EPA invited PFC manufacturers to participate in a global stewardship program on PFOA and related chemicals (www.epa.gov/oppt/pfoa/pubs/pfoastewardship.htm). Participating companies have agreed to commit to reducing PFOA from emissions and product content by 95% by 2010 and to work toward eliminating PFOA in emissions and products by 2015.

While PFOS and PFOA were the first fluorinated surfactants to receive considerable attention, research is expanding beyond these two contaminants to other perfluorinated acids and alcohols. LC/MS and LC/MS/MS are the most common analytical techniques used for their measurement; however, it can be difficult to obtain clean analytical blanks, due to inherent contamination in LC systems (fluoropolymer coatings on seals, etc.). As a result, GC/MS and GC/MS/MS are sometimes used. Most research being conducted on PFCs is focused on determining their sources, fate, and transport. Previous studies have focused on measurements in biota and wastewaters. Current studies include surface waters, seawaters, and drinking water.

There were several good reviews published on PFCs in the last 2 years. Prevedouros et al. discussed the sources, fate, and transport of perfluorocarboxylates in the environment, with a special focus on PFOA. De Voogt and Saez reviewed analytical methods for measuring PFCs in environmental samples, which included LC/MS(/MS) and GC/MS, along with issues involved in measuring PFCs (*26*). A review of LC/MS/MS methods for PFCs was the focus of another review by Villagrasa et al. (*27*). Finally, Houde et al. reviewed the biological monitoring of PFCs in wildlife and humans, compared concentrations and contamination profiles among species and locations, evaluated the bioaccu-

mulation/biomagnification in the environment, and discussed possible sources (*28*). Knowledge gaps related to transport, accumulation, biodegradation, temporal/special trends, and PFC precursors were also discussed.

Skutlarek carried out one of the first studies of PFCs in drinking water (*29*). In this study, 12 PFCs were measured in drinking waters and in surface waters from Germany with SPE and LC/MS/MS (*29*). A relatively high maximum concentration of PFCs was found in drinking water (598 ng/L), with the major component being PFOA (519 ng/L). An even higher concentration was found in surface waters, with a maximum of 4385 ng/L found (for total PFCs measured) in the Moehne River at Heidberg. PFOA was the major component (3640 ng/L), followed by perfluorohexanoic acid (PFHxA) (247 ng/L), PFOS (193 ng/L), perfluoroheptanoic acid (PFHpA) (148 ng/L), and perfluoropentanoic acid (93 ng/L).

Several researchers are examining precipitation (rainwater) to test for the atmospheric transformation of FTOHs as a source of PFOA and other perfluorocarboxylic acids (PFCAs). To that end, Scott et al. developed a method to measure PFCAs in surface waters and in precipitation using GC/MS with large-volume sampling (*30*). The PFCAs were derivatized with 2,4-difluoroaniline and *N,N*-dicyclohexylcarbodiimide to form 2,4-difluoroanilide derivatives prior to analysis by GC/MS. This enabled detection limits of 0.5 ng/L (and large-volume extraction could achieve 0.01 ng/L). In a companion paper, Scott et al. used this GC/MS method to analyze PFCAs in precipitation from North America (*31*). Significantly higher concentrations of PFOA were found in four states from the northeastern part of the United States and in two southern urban Canadian sites. Delaware had the highest levels (85 ng/L PFOA), and the highly populated urban corridor from New York City to Washington, DC, was suggested to be the main source of PFOA. Longer chain PFCAs (deca-, undeca-, and dodeca-PFCAs) were also detected in two urban Ontario sites. These results supported the hypothesis that FTOHs are oxidized in the atmosphere to produce PFCAs. Support for this atmospheric transformation was also given in a paper by Loewen et al., who used LC/ESI-MS/MS to measure PFCAs and PFOS in rainwater (*32*). Low-nanogram per liter levels of the C-10 and C-12 PFCAs were found in the rainwaters. Simcik and Dorweiler used PFC ratios (C-6−C-10 PFCAs and PFOS) from urban sources (with both atmospheric and nonatmospheric sources) and from remote waters (with only atmospheric sources) to identify tracers of atmospheric sources of PFCs (*33*). The ratio of PFHpA to PFOA increased with increasing distance from nonatmospheric sources, suggesting that this ratio might be able to be used as a tracer of atmospheric deposition of PFCs to surface waters. Applying this tracer to measurements of Lake Michigan indicated that the primary source of PFCs to Lake Michigan is nonatmospheric, most likely from wastewater treatment plant effluents.

Surface waters and seawater were the focus of some occurrence studies published in the last 2 years. Sinclair et al. examined PFCs in nine major water bodies in New York State (*34*). PFOA, PFOS, and perfluorohexanesulfonate (PFHS) were ubiquitous in these waters, with PFOA typically found at higher concentrations than PFOS and PFHS. This study also examined biomagnification factors in fish and birds. Yamashita used LC/ESI-MS/MS to carry out a global survey of PFOS, PFOA, PFHS, perfluorobutane sulfonate (PFBS), perfluorononanoic acid (PFNA), and perfluorooctane sulfonamide in seawater samples (*35*). This paper also provides a nice summary of PFOS and PFOA measurements in the livers of various marine mammals and birds, as well as toxicity effects of PFOS in aquatic organisms. Seawater is a particularly challenging matrix for PFC measurements because of the lower levels (pg/L, parts-per-quadrillion) of PFCs in seawater. This method used Oasis HLB cartridges for extraction of the fluoro acids from seawater, which gave lower background levels and greater recoveries than other SPE cartridges. Method detection limits were in the low-picogram per liter range, and this method was used to measure these PFCs at 19 locations in the Pacific Ocean, 5 locations in the South China Sea and Sulu Sea, 12 locations in the mid-Atlantic Ocean, and 20 locations in the Labrador Sea. PFOS and PFOA were found in 80% of the seawater samples analyzed. Tokyo Bay contained the highest levels of PFOA (192.0 ng/L) and PFOS (57.7 ng/L); levels in the open oceans were lower, in the picogram per liter range. The higher levels of PFOA relative to PFOS in the seawater, coupled with previous findings of higher levels of PFOS in wildlife, suggested that PFOS may be more bioaccumulative than PFOA.

Industrial sources of PFCs were the focus of another study in South Korea carried out by Rostkowski et al. (*36*). SPE with LC/MS/MS was used, and concentrations of PFOS and PFOA ranged from 2.24 to 651 and 0.9 to 62 ng/L, respectively, in stream and lake water. Lake water concentrations were among the highest levels reported in the environment, and the results pointed to local industrial sources of PFOS, PFOA, and other PFCAs. Industrial sources were also indicated in a study by Boulanger et al. (*37*), who used LC/ESI-MS/MS to measure PFOA, PFOS, and six other PFCs in wastewater (*37*). 2-(*N*-ethylperfluorooctanesulfonamido) acetic acid was found in influent (5.1 ng/L), effluent (3.6 ng/L), and river water samples (1.2 ng/L); PFOS and PFOA were found in effluent (26 and 22 ng/L, respectively) and river water (23 and 8.7 ng/L, respectively). Further biotransformation studies indicated that the transformation of precursors in wastewater treatment was not an important source of these PFCs but that direct use and disposal of products containing the end products was likely to be a more important source.

Schultz et al. investigated the PFC mass flows in a municipal wastewater treatment plant (*38*). Results showed that PFOS and perfluorodecanesulfonate increased in mass flow throughout the wastewater plant, with both exhibiting increased mass flows during trickling filtration. All four perfluoroalkylsulfonamides measured demonstrated increased mass flows, which were attributed to the degradation of precursors during the activated sludge process. No trends were observed for the PFCAs, and conventional treatment was not effective for removing them. In fact, PFNA levels increased following wastewater treatment.

New analytical methods were the focus of several other papers. Schultz et al. reported a new large-volume-injection LC/ESI-MS/MS method for measuring PFCs in wastewater (*39*). This method included centrifugation of the sample, followed by a 500-μL injection of the supernatant onto the LC (with a reversed-phase column). Recoveries ranged from 82 to 100% and quantification limits of 0.5 ng/L were achieved. The larger injection volume was needed for this method, as initial attempts to directly inject 10 μL

of the wastewater resulted in analytes being at or below detection limits. This direct injection method also avoids the use of SPE, which showed low and variable recoveries (50−90%) for PFBS, perfluorohexane sulfonate, PFOS, PFHxA, PFHpA, and PFOA. Tseng et al. reported a new method using LC/ion trap-MS for measuring PFCs in water and biological tissues (*40*). SPE was used to extract a 250-mL water sample, and quantitation limits of 0.5−6 ng/L were achieved. Gonzalez-Barreiro et al. developed two new methods for measuring 11 PFCs in water (*41*). The first method utilized liquid−liquid extraction, and the second method utilized SPE extraction, with large volumes of water samples (400−900 mL) being extracted and concentrated. Sodium chloride was added to the water samples to aid in the extraction, and samples were acidified to pH 4 prior to extraction. Identification and quantification was achieved using LC/ESI-MS/MS, and detection limits ranged from 0.26 to 0.62 ng/L.

Finally, Van Leeuwen et al. reported results from the first worldwide interlaboratory study for the analysis of 13 PFCs in three environmental and two human samples (*42*). Good agreement among the laboratories was found for standard and human matrixes, but low agreement (31%) was found for water and other samples, indicating that extraction and cleanup steps may require further improvement.

PHARMACEUTICALS, HORMONES, AND ENDOCRINE DISRUPTING COMPOUNDS

Pharmaceuticals, hormones, and EDCs have become important emerging contaminants, due to their presence in environmental waters (following incomplete removal in wastewater treatment or point-source contaminations), threat to drinking water sources, and concern about possible estrogenic and other effects, both to wildlife and humans. A major concern for pharmaceuticals also includes the development of bacterial resistance (creation of "super bugs") from the release of antibiotics in the environment. It is estimated that approximately 3000 different substances are used as pharmaceutical ingredients today, including painkillers, antibiotics, antidiabetics, β-blockers, contraceptives, lipid regulators, antidepressants, and impotence drugs (*1*). However, only a very small subset of these compounds (~150) has been investigated in environmental studies (*1*). Pharmaceuticals are introduced not only by humans but also through veterinary use for livestock, poultry, and fish farming. Various drugs are commonly given to farm animals to prevent illness and disease and to increase the size of the animals. One lingering question has been whether the low environmental levels of pharmaceuticals (generally ng/L) would cause adverse effects on humans or wildlife. While health effects studies are still limited, estrogenic effects (*1*) and renal effects (*43*) have been reported for 17α-ethinylestradiol (EE2) and diclofenac, respectively, at low environmentally relevant concentrations.

Many pharmaceuticals, hormones, and EDCs are highly polar—which necessitates the use of either LC/MS(/MS) or an efficient derivatization procedure combined with GC/MS (and GC/MS/MS) for their analysis. These mass spectrometry methods can typically measure pharmaceuticals at low-nanogram per liter levels in environmental samples. ESI and APCI are the most commonly used LC interfaces, but atmospheric pressure photoionization and sonic spray ionization are sometimes used. Increasingly, tandem-MS and MRM are being used with both LC/MS and GC/MS to provide added selectivity and sensitivity to these analyses. Innovations have also been made in rapid online extraction, microextraction, and online derivatization techniques used in combination with GC/MS/MS detection.

Pharmaceuticals. Fent et al. recently reviewed the ecotoxicology of human pharmaceuticals (*44*). While most pharmaceuticals have an acute or chronic effect on aquatic and other organisms, most of the lowest observed effect concentrations (LOECs) are substantially above the environmental concentrations that have been observed (ng/L to low μg/L). Those pharmaceuticals whose chronic toxicity LOECs approach levels observed in wastewater effluents include salicylic acid, diclofenac, propranolol, clofibric acid, carbamazepine, and fluoxetine. For example, for diclofenac, the LOEC for fish toxicity was in the range of wastewater concentrations, and the LOEC of propranolol and fluoxetine for zooplankton and benthic organisms was near the maximum measured in wastewater effluents. The contraceptive EE2 has the greatest potential for estrogenic effects of the pharmaceuticals studied, as it can induce estrogenic effects at extremely low concentrations (low and sub-ng/L). Effects include alteration of sex ratios and sexual characteristics and decreased egg fertilization in fish. Acute effects documented include fluoxetine, which has a LOEC concentration of 20 μg/L. Oetken et al. recently investigated the effects of the pharmaceutical carbamazepine on three aquatic invertebrate species (*45*). Carbamazepine did not cause any acute toxic effects up to 4 mg/L but did produce reproductive effects in an aquatic insect in chronic sediment exposure experiments. Ten percent effect concentrations ranged from 70 to 210 μg/kg, which is close to the range of previous reports of carbamazepine in sediments. So far, most data indicate that some pharmaceuticals may pose an ecological risk, but not a human health risk. For example, a recently published human health risk assessment for 26 active pharmaceutical ingredients and their metabolites (representing 14 different drug classes) predicts that there would be no appreciable human health risk from the presence of these 26 compounds at trace concentrations in surface water or drinking water (*46*). However, there is still a scarcity of human health assessments for environmental exposure to pharmaceuticals, so it is premature to draw firm conclusions at this time and to extrapolate this limited assessment to pharmaceuticals beyond the 26 investigated.

Veterinary pharmaceuticals have been gaining interest, and a recent review presented a global perspective on the use, sales, exposure pathways, occurrence, fate, and effects of veterinary antibiotics (*47*). Jones et al. reviewed the occurrence and behavior of human pharmaceuticals in wastewater treatment (*48*), and Petrovic et al. reviewed LC/MS/MS methods published for the analysis of pharmaceuticals in environmental samples (*49*). Pozo et al. wrote an excellent review detailing the achievements and pitfalls of LC/MS/MS for antibiotic and pesticide analysis (*50*). Pitfalls included the use of nonspecific MRM transitions (such as those involving the loss of water), which can result in false positive findings. On the other hand, false negatives are possible if coeluting isobaric interferences are present. The authors suggest that good chromatographic separations are essential for assuring accuracy in LC/MS/MS.

Fate and Transport Studies. Several excellent studies have been published in the last 2 years. Some of these involve fate in

the environment (in waters, sediments, wetlands), and others involve fate in wastewater treatment. Löffler et al. investigated the fate of 10 pharmaceuticals and pharmaceutical metabolites (diazepam, ibuprofen, iopromide, paracetamol, carbamazepine, clofibric acid, 10,11-dihydro-10,11-dihydroxycarbamazepine, 2-hydroxyibuprofen, ivermectin, oxazepam) in water−sediment systems (*51*). The first four pharmaceuticals were measured using their C-14 labeled standards (with radio-thin-layer chromatography analysis), and the others were measured with LC/MS/MS, using their nonlabeled standards. Sorption and transformation were the two competitive processes involved in their removal from water. Several pharmaceuticals were relatively persistent in the water, with the exception of paracetamol, which bound to the sediment. Buerge et al. investigated the occurrence and fate of the chemotherapy drugs, cyclophosphamide and ifosfamide, in wastewater and surface waters (*52*). These compounds were detected in untreated and treated wastewater at concentrations of <0.3−11 ng/L, and no significant degradation was observed in environmental samples. Concentrations were lower in surface waters (<50−170 pg/L) and were several orders of magnitude lower than levels that would cause acute ecotoxicological effects; however, a final risk assessment could not be made because of the lack of data on chronic effects on aquatic organisms. Fono et al. investigated the natural attenuation rates of a suite of wastewater-derived contaminants (including several pharmaceuticals) in a river during a period when wastewater effluent accounted for nearly the entire flow of the river (*53*). The X-ray contrast agent was constant over the 2-week travel time in the river, but concentrations of gemfibrozil, ibuprofen, metoprolol, and naproxen decreased significantly (60−90%) as the water flowed downstream. GC/MS/MS was used for their detection. Results indicated that natural attenuation can result in significant decreases in concentrations of wastewater-derived contaminants in large rivers. Gurr and Reinhard published a feature article describing how natural attenuation can be harnessed to remove pharmaceutical and hormone contaminants in rivers (*54*). Sorption, photolysis, biodegradation, dilution, and volatilization processes are discussed in this article.

Barbiturates were the focus of another occurrence and fate study by Peschka et al. (*55*). A GC/MS method was developed to measure butalbital, secobarbital, hexobarbital, aprobarbital, phenobarbital, and pentobarbital at a detection limit of 1 ng/L. SPE (using Oasis HLB cartridges) was used for extraction. These barbiturates were not detected in several rivers in Germany (Main, Rhine, Elbe) but were detected up to 5.4 μg/L in the River Mulde. Results indicated a point source contamination—potentially from an older landfill or from veterinary use of these substances.

Göbel et al. used LC/MS/MS to investigate the fate of sulfonamides, macrolides, and trimethoprim in different wastewater treatment plants (*56*). Primary treatment was ineffective for their removal, but membrane bioreactor treatment removed significant amounts of some of these pharmaceuticals. The behavior and fate of the antibiotic tetracycline was studied in rivers and wetlands in Canada (*57*). UV−vis irradiation and the type of water matrix were important in catalyzing the removal of tetracycline in the waters.

Jones-Lepp investigated the ability of the antibiotic azithromycin and the human waste marker urobilin to serve as chemical markers of human waste contamination (*58*). Source waters were collected from 21 sites in New England, Nevada, and Michigan, extracted using Oasis HLB SPE cartridges, and analyzed using LC/ESI-MS. Azithromycin, which is prescribed for human use only, was detected in many of those waters, up to 77 ng/L. It was suggested that azithromycin and urobilin could be used to track human waste contamination.

Occurrence Studies. Many good occurrence studies have been published in the last 2 years. Agricultural runoff from farms was the focus of one of these studies (*59*). In this study, several pharmaceuticals (carbamazepine, gemfibrozil, carisoprodol) were reported for the first time in runoff from agricultural fields that had been irrigated with wastewater. Wastewaters from European countries were the focus of a multiinvestigator study, which measured 36 polar pollutants (including pharmaceuticals) in 8 municipal wastewater treatment plants from 4 countries (*60*). Three of these plants were followed over 10 months. Some pharmaceuticals (e.g., diclofenac, carbamazepine) showed mean concentrations in the 1−10 μg/L range, and many of the polar compounds were not significantly removed in tertiary wastewater treatment. These authors proposed a water cycle spreading index (WCSI), which is calculated from a compound's effluent concentration and its normalized removal, to be used as an indicator for the potential of a polar pollutant to spread in an aquatic environment and for its expected concentration level. Of the polar analytes investigated, diclofenac and carbamazepine were the pharmaceuticals that would have the highest WCSI.

Veterinary Pharmaceuticals. Several new studies of veterinary pharmaceuticals have been recently published. Peru et al. developed a new method to measure spectinomycin and lincomycin in liquid hog manure supernatant and in runoff samples (*61*). SPE with a weak cation-exchange resin (Oasis WCX) or an Oasis HLB cartridge was used to extract spectinomycin and lincomycin, respectively. HILIC was used with APCI-MS/MS for separation and detection. When traditional C8 or C18 LC columns were used, there was little or no retention of spectinomycin, but the use of HILIC increased its retention and separation from other matrix interferences. A silica-based Altima HP hydrophilic interaction column was used for the LC separation. Lincomycin was detected at submicrogram per liter levels in runoff samples, and both were detected in high-microgram per liter levels in liquid hog manure. The impact of a concentrated animal feeding operation (CAFO) on well water was investigated by Batt et al., who measured veterinary sulfonamide antibiotics (*62*). A previously developed SPE-LC/MS/MS method was used for their measurement. Two veterinary antibiotics—sulfamethazine and sulfadimethoxine—were present in all samples collected at levels up to 0.22 and 0.068 μg/L, respectively. Ionophore antibiotics (monensin, salinomycin, narasin) were measured by Kim and Carlson in another study, using a SPE-LC/MS/MS method (*63*). These antibiotics are used to treat coccidiostats in poultry and as growth promoters in beef and dairy cattle. Low nanogram per liter levels (up to 38 ng/L) were found in river waters from the five sampling sites in Northern Colorado; higher levels were found in sediments.

Drinking water samples have been included in pharmaceutical studies, and new research is investigating illicit drugs and their metabolites. Hummel et al. used LC/ESI-MS/MS to measure

several psychoactive drugs and their metabolites in drinking water, surface water, groundwater, and wastewater in Germany (*64*). These drugs included opioids, tranquilizers, antiepileptics, the cocaine metabolite benzoylecgonine, and the antidepressant doxepin, as well as the calcium channel blocker verapamil. In drinking water, only carbamazepine, its metabolite 10,11-dihydroxy-10,11-dihydrocarbamazepine, and primidone were present (up to 0.020 μg/L). Most analytes (15 of 20) were found in raw and treated wastewater, as well as in surface water. The cocaine metabolite was found at a maximum of 78, 49, and 3 ng/L in wastewater influents, effluents, and surface water, respectively. Vanderford and Snyder measured 15 pharmaceuticals, 4 pharmaceutical metabolites, 3 EDCs, and 1 personal care product in drinking water, surface water, and wastewater (*65*). Only 2 of the 15 pharmaceuticals were detected in finished drinking water—meprobamate and dilantin—at levels of 5.9 and 1.3 ng/L, respectively. Other pharmaceuticals were found to degrade in drinking water treatment using ozone and chlorination. In the wastewater influents, seven pharmaceuticals were detected at levels above 1 μg/L (the highest being naproxen at 22.5 μg/L); levels were substantially lower in the wastewater effluents, with only one pharmaceutical above 1 μg/L (1.27 μg/L for meprobamate). In surface waters, atenolol was found at the highest level (0.86 μg/L) of the pharmaceuticals measured. Rabiet et al. measured 16 pharmaceuticals in drinking water, surface water, and wastewater in France using GC/MS (*66*). Seven of the pharmaceuticals were found in the drinking water (supplied by wells), with paracetamol and carbamazepine being found at the highest levels (211 and 43.2 ng/L, respectively). Higher levels were found in surface waters and wastewater effluents (up to 11 300 ng/L paracetamol). Loraine and Pettigrove used GC/MS to measure pharmaceuticals and personal care products in drinking water, surface waters, and reclaimed water (*67*). Ibuprofen, ibuprofen methyl ester, and triclosan were found with other analytes in finished drinking water, up to 1.35 μg/L (for ibuprofen). These pharmaceuticals were also present in raw source waters and reclaimed wastewater, up to 0.90 and 2.11 μg/L, respectively. Seasonal variations were observed, with higher levels being detected in the dry season when pollutants are generally more concentrated.

New Methods. Several new analytical methods have been reported for pharmaceutical measurements in environmental waters, including LC/MS/MS methods for antibiotics. A method by Pozo et al. utilizes on-line SPE-LC/ESI-MS/MS with Q-TOF-MS confirmation for 16 antibiotics (including quinolones) (*68*). Small water samples (9.8 mL) are injected directly onto the SPE-LC/MS/MS system, and 0.4−4.3 ng/L detection limits were achieved. Another method by Cha et al. uses offline SPE with LC/ESI-MS/MS for β-lactam antibiotics (amoxicillin, ampicillin, oxacillin, cloxacillin, cephapirin) (*69*). Detection limits ranged from 8 to 10 ng/L in surface water, 13 to 18 ng/L in wastewater influents, and 8 to 15 in wastewater effluents.

UPLC-TOF-MS methods are gaining in popularity, as they produce narrow LC peaks (5−10 s wide) and dramatically shorten analysis times, often to 10 min or less. Petrovic et al. developed a new UPLC-Q-TOF-MS method for 29 pharmaceuticals in wastewater (*70*). Method detection limits ranged from 10 to 500 ng/L, and all compounds could be analyzed in 10 min.

Quintana et al. developed a new automated SPE-LC method for acidic pharmaceuticals (ketoprofen, naproxen, bezafibrate, diclofenac, ibuprofen) and one metabolite (salicylic acid) in surface waters (*71*). This method used a lab-on-valve approach with copolymeric beads (Oasis HLB) that can be renewed by automated packing and withdrawal after a single use. This approach overcomes band-broadening effects that are common with online SPE. Detection limits of 0.02−0.67 μg/L could be achieved. Sacher et al. developed a new IC−ICPMS method to measure X-ray contrast agents in water (*72*). Detection limits below 0.2 μg/L could be achieved.

Other methods reported involved the development of new sampling/concentration devices. Alvarez et al. reported a new passive sampler—POCIS—for measuring polar contaminants (including pharmaceuticals) in wastewater (*73*). This type of passive sampling allows for a time-weighted-average sampling, where transient contaminants can be detected that might have been missed in a grab sampling approach. Benito-Pena used a combination of SPE cartridges—Bond Elut C18 and Oasis MAX (a strong mixed-mode ion exchanger)—to clean up and concentrate β-lactam antibiotics prior to analysis by UV-diode array detection (*74*). Detection limits of 8−24 ng/L could be achieved in pure water, but were much higher in real wastewater (3−26 μg/L).

Endocrine Disrupting Compounds and Hormones. Certain synthetic and natural chemicals have the ability to mimic hormones and, thus, are able to interfere or disrupt normal hormonal functions. EDCs are of concern due to their ecotoxicological and toxicological potencies. A variety of natural compounds and anthropogenic chemicals are known or predicted to influence the endocrine system, such as natural estrogens (e.g., 17β-sitosterol, estrone), natural androgens (e.g., testosterone), phytosteroids (e.g., 17β-sitosterol), isoflavenoids (e.g., daidzeine), synthetic estrogens (e.g., 17β-ethinylestradiol), pesticides (e.g., atrazine), phthalates, alkylphenol ethoxylate surfactants, dioxins, coplanar polychlorinated biphenyls (PCBs), parabenes (hydroxybenzoate derivatives), bisphenol A, and organotins (*1*). Due to the large number of chemicals with different modes of action and different affinities to hormonal receptors, their EDC potencies differ substantially. 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 synthetic 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. GC/MS and GC/ion trap-MS/MS are still being used for EDC measurements, but increasingly, LC/MS and LC/MS/MS are being used. The main benefits of LC/MS/MS, in comparison to GC/MS, are lower statistical errors and no need for derivatization (*1*). However, when higher chromatographic resolution is needed to separate isomers or congeners (such as for PCBs, dioxins, or brominated flame retardants), GC/MS/MS systems are still the method of choice. Stuart recently published a nice review on recent GC/MS developments for measuring EDCs (*75*). Also discussed in this review are derivatizing agents, extraction techniques, and new

chromatographic methods (including 2 D-GC-TOF-MS) for analyzing EDCs.

CAFOs have recently been recognized as potentially important sources of estrogens in the environment. Hutchins et al. measured estrogens and estrogen conjugates in lagoons associated with swine, poultry, and cattle operations using GC/MS/MS and LC/MS/MS (*76*). Several estrogens were identified, and estrogen conjugates accounted for at least one-third of the total estrogen equivalents. Steroid estrogens were measured in wastewaters from a contraceptive-producing factory in a study by Cui et al. (*77*). These included estrone (E1), 17β-estradiol (E2), estriol (E3), and EE2. SPE-LC/MS/MS was used for analysis, which allowed 0.7−2.0 ng/L detection. Estrogens were present in the wastewater treatment plant effluents, but were significantly reduced (by 67−85%). Beck et al. used LC/MS/MS to measure estrogens in coastal waters from the Baltic Sea (*78*). Analyses showed the presence of five compounds between 0.10 (E1) and 17 ng/L (EE2) in these coastal waters. Swartz et al. used SPE-LC/MS to measure estrogens, nonylphenol ethoxylate metabolites, and other wastewater contaminants in groundwaters impacted by a residential septic system (*79*). E1, E2, and other contaminants were found in the groundwaters.

Several new methods have been developed for various hormones and EDCs. Trenholm et al. created a comprehensive method utilizing a single SPE step, along with GC/MS/MS and LC/MS/MS, to measure a broad range of EDCs and pharmaceuticals in water (*80*). Detection limits ranged from 1 to 10 ng/L, and recoveries from 50 to 112% for 58 EDCs. Basheer et al. reported a new polymer-coated hollow-fiber membrane microextraction method for measuring estrogens in water with GC/MS (*81*). Extremely low detection limits of 0.03−0.8 ng/L could be achieved. This method was demonstrated for reservoir and drinking water samples. Hintemann et al. used two immunoassays to measure E2 and EE2 in river water (*82*). Detection limits were 0.05 and 0.01 ng/L, respectively. Almeida and Nogueira used stir bar sorptive extraction and LC-diode array detection to measure E1, E2, E3, EE2, diethylstilbestrol, mestranol, progesterone, 19-norethisterone, and norgestrel in water and urine (*83*). A small sample size was used (30 mL), and detection limits ranged from 0.3 to 1.0 μg/L. The equilibrium time, ionic strength, and back extraction solvents were found to be the most important parameters to optimize in this method.

Alkylphenol Ethoxylate Surfactants. Alkylphenol ethoxylate surfactants continue to be investigated. Lara-Martin et al. developed a method using LC/MS (with the first part of the analysis in full-scan, negative-ion mode, and the second part in full-scan, positive-ion mode) to simultaneously measure anionic and nonionic surfactants and their carboxylated metabolites in environmental waters and sediment (*84*). Detection limits ranged from 0.05 to 0.5 μg/L in water. Loos et al. used SPE with LC/MS/MS to measure octyl- and nonylphenol ethoxylates, octyl- and nonylphenols, and their carboxylates in surface waters and wastewater plant effluents impacted by the textile industry (*85*). 4-Nonylphenoxy acetic acid (NPE1C) and 4-nonylphenol diethoxylate (NPE2O) showed the highest concentrations—up to 4.5 μg/L NPE1C in a wastewater effluent and up to 3.6 μg/L NPE2O in a river. The highest levels of nonylphenol were found in the receiving river samples (up to 2.5 μg/L). The predicted no-effect concentration for nonylphenol of 0.33 μg/L for aquatic species indicates that there could be potential adverse effects on the environment.

Fate in Drinking Water Treatment Plants. Because pharmaceuticals and EDCs can contaminate source waters used for drinking water, their removal by various drinking water oxidants has been investigated. In general, conventional drinking water and wastewater treatment plants do not completely remove pharmaceuticals and EDCs. However, oxidation with chlorine and ozone can result in transformation of some compounds (*1*). The identification of ozonation and chlorination products of pharmaceuticals, antibacterials, and EDCs was reported by several authors. McDowell et al. investigated the ozonation of carbamazepine in drinking water and identified three new oxidation products using a combination of MS and NMR (*86*). Concentrations of two of these byproducts were 0.48 and 0.15 μM for an ozone dose of 1.9 mg/L. In another study by Bedner and MacCrehan, chlorination of acetaminophen produced the oxidation products 1,4-benzoquinone and *N*-acetyl-*p*-benzoquinone imine, as well as two ring chlorination products (chloro-4-acetamidophenol and dichloro-4-acetamidophenol) (*87*). Rule et al. identified chlorination products of the antibacterial agent, triclosan, which formed chloroform, three chlorophenoxyphenols, and two chlorophenols under drinking water treatment conditions (*88*). Triclosan is used in many hand soaps, as well as other products, and the authors estimate that, under some conditions, the use of triclosan can increase a person's annual exposure to chloroform by as much as 40% above background levels from tap water. Vikesland's research group also investigated the reactivity of triclosan with monochloramine (*89*). The same DBPs (chloroform and 3 chlorinated phenols) that were formed by chlorination were also observed in chloraminated water, but the reaction rates were much slower, such that chloroform was only detected after 1 week. Finally, Shah et al. studied the kinetics and transformation of the veterinary antibacterial agent carbadox in chlorinated water (*90*). Carbadox and its metabolite were found to react rapidly with chlorine to form nonchlorinated, hydroxylated, and higher molecular weight byproducts. Because these byproducts retained their biologically active *N*-oxide groups, they are expected to remain as active antibacterial agents.

DRINKING WATER DISINFECTION BYPRODUCTS

In addition to new regulations and rules involving DBPs (e.g., the Stage 2 Disinfectants/DBP Rule and the UCMR-2, which requires monitoring of nitrosamines), there are also new, emerging issues with DBPs (*91*). New human exposure research is revealing that inhalation and dermal exposures (from showering, bathing, swimming, and other activities) can provide equivalent exposures or increased exposures to certain DBPs (*91*). Therefore, these exposure routes are now being recognized in new epidemiologic studies that are being conducted. And, epidemiology studies are beginning to focus more on reproductive and developmental effects—which recent studies have been shown to be important. A recent review article outlines these important routes of exposure, along with new, emerging DBPs (*91*).

Toxicologically Important DBPs. Toxicologically important DBPs include brominated, iodinated, and nitrogen-containing DBPs (so-called "N-DBPs"). Brominated DBPs are more carcinogenic than their chlorinated analogues (*91*), and new research

is indicating that iodinated compounds may be more toxic than their brominated analogues (*91*). Brominated and iodinated DBPs form due to 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 salt water 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 several other countries now live in coastal regions that are impacted by 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 iodo acids, bromonitromethanes, iodo-THMs, brominated forms of MX (MX is 3-chloro-4-(dichloromethyl)-5-hydroxy-2(*5H*)-furanone), haloaldehydes, haloamides, and NDMA, which is not brominated, but is classified as a probable carcinogen (*91*). Iodoacetic acid, one of five iodo acids identified for the first time in chloraminated drinking water, has recently been shown to be more genotoxic and cytotoxic to mammalian cells than all DBPs that have been studied, including the regulated HAAs and bromate (*91*). It is a factor of 2× more genotoxic than bromoacetic acid, which is the most genotoxic of the regulated HAAs. Other iodo acids identified—bromoiodoacetic acid, (*Z*)-3-bromo-3-iodopropenoic acid, (*E*)-3-bromo-3-iodopropenoic acid, and (*E*)-2-iodo-3-methylbutenedioic acid (*91*)—have been synthesized and are currently under investigation for genotoxic and cytotoxic effects. They were initially discovered in chloraminated drinking water extracts using methylation with GC/high-resolution-EI-MS. Analytical methods for the five iodo acids have been developed for a current occurrence study to determine their concentrations in chloraminated drinking water. These iodo acids are of concern not only for their potential health risks but also because early research indicates that they may be maximized (along with iodo-THMs) in waters treated with chloramines. Chloramination has become a popular alternative to chlorination for plants that have difficulty meeting the regulations with chlorine, and its use is expected to increase with the advent of the new Stage 2 D/DBP Rule. Chloramines are generated from the reaction of chlorine with ammonia, and it appears that the length of free chlorine contact time (before ammonia addition to form chloramines) is an important factor in the formation of iodo acids and iodo-THMs. Because of chlorine's competing reaction to form iodate as a sink for the natural iodide, it is likely that plants with significant free chlorine contact time before the addition of ammonia will not produce substantial levels of iodo acids or iodo-THMs.

The bromonitromethanes (including dibromonitromethane, tribromonitromethane, and bromonitromethane) are extremely cytotoxic and genotoxic to mammalian cells (*91*). 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 have been found to be DBPs formed by chlorination or chloramination and have been shown to increase in formation when preozonation is used before chlorine or chloramine treatment. Bromonitromethanes, iodo-THMs, and brominated forms of MX (so-called BMXs), as well as other priority DBPs were the focus of a U.S. Nationwide DBP Occurrence Study, which was recently published in *Environmental Science & Technology* (*92*). This Nationwide Occurrence Study focused on approximately 50 priority DBPs that were selected from an extensive prioritization effort (according to predicted cancer effects). In this study, haloacetaldehydes represented the third major class formed on a weight basis (behind THMs and HAAs). An important finding was that while the alternative disinfectants significantly lowered the formation of regulated DBPs (THMs and HAAs), other high-priority DBPs were increased in formation with alternative disinfectants. For example, iodinated DBPs (iodo-THMs and iodo acids) were increased in formation with chloramination, dichloroacetaldehyde was highest at a plant using chloramines and ozone, and preozonation was found to increase the formation of halonitromethanes. This has important implications for drinking water treatment, as many plants in the United States have switched or are switching to alternative disinfectants to meet the Stage 1 and 2 D/DBP Rule requirements. This study also reports the highest levels of MX analogues to-date, with MX analogues and brominated MX analogues frequently being found at levels above 100 ng/L, and in two plants the sum of these analogues was at low-ppb levels. Finally, 28 new, previously unidentified DBPs were reported, including brominated and iodinated acids, a brominated ketone, and chlorinated and iodinated aldehydes. Despite the fact that more than 90 DBPs were measured in this study, only about 30 and 39% of the total organic halide (TOX) and total organic bromine (TOBr) were accounted for, respectively, by the sum of the measured DBPs. This is consistent with earlier studies that have shown that there is more TOX accounted for in chlorinated drinking water, as compared to drinking water treated with alternative disinfectants.

GC/MS continues to be an important tool for measuring DBPs and identifying new DBPs. However, LC/MS is being increasingly used for highly polar DBPs and high molecular weight DBPs. In fact, this was the focus of a recent review article by Zwiener and Richardson (*93*). Useful derivatization techniques, as well as related MS techniques, such as ESI-high field asymmetric waveform ion mobility spectrometry (FAIMS)-MS, IC-ESI-MS, and membrane introduction MS (MIMS), are also discussed. This review covered not only traditional DBPs that are formed by the reaction of the disinfectant (oxidant) with NOM but also newly identified DBPs that are formed by the reaction of the disinfectant with contaminants. Examples of those include reaction products with estrogens, alkylphenol ethoxylates, pesticides, and algal toxins.

Brominated and iodinated DBPs have been the focus of several new studies. In an innovative study, Becalski et al. investigated the potential formation of iodoacetic acids during cooking (*94*). In this study, municipal chlorinated tap water (containing NOM) was allowed to react with iodized table salt (containing potassium iodide) and with potassium iodide itself in boiling water. Samples were extracted with TAME and methylated prior to analysis with GC/MS. Iodoacetic acid and chloroiodoacetic acid were identified as byproducts, and iodoacetic acid was formed at 1.5 μg/L levels when the water was boiled with 2 g/L iodized table salt. The concentration of chloroiodoacetic acid was estimated to be 3−5×

lower. Hua et al. examined the effect of bromide and iodide on the formation of DBPs during chlorination (*95*). TOBr, total organic iodine (TOI), and total organic chlorine (TOCl) were measured in this study, as well as THMs, HAAs, and TOX. At higher levels of bromide, there was a decreasing level of unknown TOX and unknown TOCl, but an increasing level of unknown TOBr. The extent of iodine substitution was much lower than bromine substitution because a substantial amount of iodide was oxidized by chlorine to iodate. The tendency toward iodate formation resulted in the unusual situation where higher chlorine doses actually reduced levels of iodinated DBPs. However, this is not the case with chloramination, where iodo-DBPs preferentially form instead of iodate (*92*). The method for TOCl, TOBr, and TOI analysis is described in a separate paper by Hua and Reckhow (*96*). After investigating different pyrolysis-IC procedures, the optimum method included a pyrolytic analyzer that uses pure O_2 and offline IC combined with a standard TOX carbon (coconut-based). This procedure allowed the most complete recovery of TOCl, TOBr, and TOI. Brominated and chlorinated acetaldehydes were the focus of another study by Koudjonou and Lebel (*97*). These DBPs were measured in Canadian drinking water with GC/electron capture detection (ECD), and their stability was investigated. Most of the haloacetaldehydes were found in the drinking waters, with chloral hydrate (trichloroacetaldehyde) comprising 7−51% of the total haloacetaldehydes measured, as well as a substantial portion of the total DBPs (as in the U.S. Nationwide Study). Mixed results were obtained for their stability in drinking water—the trihaloacetaldehydes degraded somewhat over time to the corresponding THMs at increasing pH and temperature.

New DBPs continue to be identified. Often, low- and high-resolution EI-MS is used, and sometimes combinations of GC/MS or LC/MS with Fourier transform (FT)-infrared (IR) spectroscopy or NMR are used. In addition, derivatizing agents continue to be developed to aid in the identification of highly polar DBPs, which are largely unaccounted for. Gong et al. used FT-IR spectroscopy, EI-MS, ^{1}H and ^{13}C NMR spectroscopy, and single-crystal X-ray diffraction to identify a new DBP in chlorinated drinking water (*98*). This DBP was identified as 2,2,4-trichloro-5-methoxycyclopent-4-ene-1,3-dione. Ames test results showed it to be highly mutagenic. Vincenti et al. tested four newly developed fluorinated chloroformate derivatizing agents for identifying highly polar alcohol, carboxylic acid, and amine DBPs in drinking water with GC/negative chemical ionization (NCI)-MS (also referred to as electron capture negative ionization) (*99*). 2,2,3,3,4,4,5,5-Octafluoro-1-pentyl chloroformate performed the best, with good reaction efficiency, good chromatographic and spectroscopic properties, low detection limits (10−100 fmol), and a linear response over more than 2 orders of magnitude. The entire procedure from raw aqueous sample to ready-to-inject hexane solutions of the derivatives required less than 10 min. This method was used to identify three highly polar ozonation byproducts: malic acid, tricarballylic acid, and 1,2,3-benzenetricarboxylic acid.

Other Occurrence Studies. Huang et al. used GC/high-resolution-EI-MS to comprehensively identify DBPs formed by the ozonation of polluted source waters (*100*). Fifty-nine different organic compounds were identified, including low molecular weight carboxylic acids, benzoic compounds, aldehydes, bromoform, bromoacetic acid, dibromoacetic acid, 2,4-dibromophenol, and dibromoacetonitrile. When the NOM was fractionated from the source water into humic acid and hydrophilic neutral fractions, different distributions of DBPs were observed in the fractions. Malliarou et al. recently carried out a large survey of HAAs in UK drinking waters (*101*). Means ranged from 35 to 95 μg/L, and a maximum of 244 μg/L was observed. In two out of the three regions investigated, there was a high correlation between total THMs and total HAAs, and the ratio of total THMs to total HAAs was significantly correlated with temperature, pH, and free and total chlorine. This study is particularly important because HAAs are rarely measured in Europe, and most epidemiologic studies relate effects back to THMs only. Another large survey was carried out in Athens, Greece, over a 2-year period (*102*). DBPs measured (by GC/MS) included THMs, haloacetonitriles, haloketones, chloral hydrate, chloropicrin, and nine HAAs. All DBPs were identified in prechlorinated drinking water samples. The most commonly detected DBPs were chloroform, trichloroacetic acid, dichloroacetic acid, and chloroacetic acid. Annual mean concentrations ranged from 1.1 to 61.8 μg/L.

Discovery Research for High Molecular Weight DBPs. More than 50% of the TOX formed in chlorinated drinking water remains unidentified, and much higher percentages of TOX are unaccounted for when alternative disinfectants are used (ozone, chloramine, chlorine dioxide). Earlier ultrafiltration studies indicate that >50% of the TOX in chlorinated drinking water is >500 in molecular weight, which would be missed with traditional GC/MS approaches. ESI-MS/MS is allowing researchers to investigate these high molecular weight DBPs. Most of this work is very preliminary, due to the complexity of the mass spectra obtained ("a peak at every mass" situation). Minear's group at the University of Illinois has carried out much of the pioneering work in this area. In a follow-up study to their earlier work, Zhang and Minear used radiolabeled chlorine (^{36}Cl) to further probe high molecular weight DBPs formed upon chlorination of drinking water (*103*). Results of this study showed that oxidation was the dominant reaction compared to halogenation and that high molecular weight DBPs decreased when the chlorine contact time was increased. High molecular weight DBPs could not be separated into discrete LC peaks.

NDMA and Nitrosamines. NDMA is a probable human carcinogen, and NDMA and other nitrosamines were recently discovered to be DBPs in drinking water. NDMA can form in chloraminated or chlorinated water. ^{15}N-Labeling studies have shown that the nitrogen present in monochloramine becomes incorporated into the structure of NDMA. And, as with iodo-DBP formation, the length of free chlorine contact time prior to ammonia addition to form chloramines can be an important factor in the formation of NDMA. Charrois and Hrudey published a recent study showing that a free chlorine contact time of 2 h (before ammonia addition) resulted in significant reductions (up to 93%) in NDMA formation (*104*). Chlorination can also form NDMA, when nitrogen precursors are present (e.g., natural ammonia in the source water or nitrogen-containing coagulants, such as diallyldimethylammonium chloride, used in water treatment). NDMA was initially discovered in chlorinated drinking waters from Ontario, Canada, and has since been found in other locations. The detection of NDMA in U.S. waters is largely due

to improved analytical techniques that have allowed its determination at low-nanogram per liter concentrations. NDMA is generally present at low nanograms per liter in chloraminated/chlorinated drinking water, but it can be formed at much higher levels in wastewater treated with chlorine. 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 (www.dhs.ca.gov/ps/ddwem/chemicals/NDMA). NDMA is not currently regulated in the United States for drinking water, but is now included on the UCMR-2, where occurrence data are being collected on a national scale for NDMA and other nitrosamines. Ontario has issued an interim maximum acceptable concentration for NDMA at 9 ng/L (www.ene.gov.on.ca/envision/gp/4449e.pdf). Andrzejewski et al. published a nice review on NDMA in 2005, where its toxicological issues, mechanisms of formation in drinking water treatment, and physiochemical properties are discussed (*105*). This review also cites the possibility of NDMA being formed with chlorine dioxide disinfection.

To-date, all methods to measure NDMA have been GC/MS-(/MS) or GC/ECD methods, including the EPA method created to measure nitrosamines (EPA Method 521). Zhao et al. created the first LC/MS/MS method to measure nitrosamines and, in doing so, identified two new nitrosamine DBPs in drinking water—nitrosopiperidine and nitrosodiphenylamine (*106*). LC/MS/MS was essential for detecting nitrosodiphenylamine, as it is thermally unstable and cannot be measured by GC/MS. An isotopically labeled NDMA standard was used as the surrogate standard for determining recovery, and isotopically labeled *N*-nitrosodi-*n*-propylamine was used as an internal standard for quantification. Detection limits ranged from 0.1 to 10.6 ng/L. Measurements in a drinking water distribution system revealed that nitrosamine concentrations increased with increasing distance from the water treatment plant, indicating that the amount of formation was greater than the amount of decomposition. Cheng et al. expanded and refined three previously existing GC/MS/MS methods for measuring nitrosamines in drinking water, wastewater, and recycled water (*107*). Detection limits for two SPE-GC/MS/MS methods ranged from 0.3 to 1.4 ng/L, and detection limits for a micro-liquid−liquid extraction-GC/MS/MS method ranged from 2 to 4 ng/L. These methods were used to measure NDMA and several other nitrosamines in drinking water, wastewater, and recycled water in California. In drinking water, NDMA was the only nitrosamine detected, but other nitrosamines were present in recycled water and wastewater. Cha et al. reported a new LC-fluorescence method for measuring NDMA in water (*108*). Samples were denitrosated and derivatized with dansyl chloride for fluorescence detection. Detection limits of 10 ng/L could be achieved. This method did not suffer interferences even in complex wastewater samples. Grebel et al. developed a new SPME method for extracting seven nitrosamines from water (*109*). SPME could be used with nitrogen chemiluminescence detection, nitrogen−phosphorus detection, or chemical ionization (CI)-MS. Detection limits for NDMA ranged from 30 to 890 ng/L.

Mechanistic Studies. Researchers continue to explore the mechanism of formation of nitrosamines. Schreiber and Mitch examined the importance of chloramine speciation and dissolved oxygen on the formation of nitrosamines (*110*). Dichloramine and dissolved oxygen were found to be critical in their formation, and a new nitrosamine formation pathway was proposed, in which dichloramine reacts with secondary amine precursors to form chlorinated dialkylhydrazine intermediates. Oxidation of these intermediates by dissolved oxygen to form nitrosamines competes with their oxidation by chloramines. This new model was able to explain the formation of nearly all nitrosamine species. Chen and Valentine developed a kinetic model to validate proposed reactions and predict NDMA formation in chloraminated drinking water (*111*). Inputs to this model include chloramine demand, a coefficient relating the amount of NDMA produced to the amount of NOM oxidized, and other kinetic parameters describing NOM oxidation. NOM oxidation was determined to be the rate-limiting step governing NDMA formation.

Mechanistic studies have also been carried out for other DBPs, including cyanogen chloride, *N*-chloroaldimines, and ozonation DBPs. Lee et al. examined 17 amino acids as potential precursors for CNCl in chlorinated drinking water (*112*). Among these amino acids, only glycine was found to produce detectable CNCl, and the glycine nitrogen was stoichiometrically converted to CNCl at pH <6. From examinations of river water, it was estimated that glycine may account for 42−45% of the CNCl formed (at pH 8.2). In another study by Freuze et al., amino acids were investigated as precursors to DBPs involved in an odor episode in Paris (*113*). The reaction of several amino acids with chlorine was investigated to solve the odor mystery. *N*-Chloroaldimines were identified in these amino acid−chlorine reactions by GC/MS, and they were suspected of being the DBPs responsible for the odor episode. Finally, These and Reemtsma used size exclusion chromatography with Q-TOF-MS to examine ozone DBP formation of different NOM fractions (*114*). A preferential reaction with fulvic acids at a low oxidation state (low O/C ratio) and a high degree of unsaturation (low H/C ratio) was observed, and the data suggested that molecules with a more extended carbon skeleton and fewer carboxylate substituents are more reactive with ozone.

Other New DBP Methods. Several new methods have been developed for the measurement of DBPs (beyond nitrosamines mentioned earlier). Khan et al. reported a new aqueous-phase aminolysis method to measure epoxides in water (*115*). This method also uses SPE, silylation, and GC/MS analysis. With this method, 1,2-epoxybutane, epichlorohydrin, and epifluorohydrin could be measured at 5−10 ng/L detection limits. Onstad and Weinberg created a refined method using liquid−liquid extraction, methylation, and GC with micro-ECD or ion trap-MS detection for measuring halogenated furanones (MX analogues) in drinking water (*116*). A preconcentration factor of 1000:1 allowed low-nanogram per liter detection limits. This method was used to measure the 12 halogenated furanone species in the U.S. Nationwide Study discussed earlier. Yang and Shang created a new MIMS method to quantify CNCl and cyanogen bromide in water (*117*). A linear response over 3 orders of magnitude was achieved, and CNCl and CNBr could be measured down to limits of 1.2 and 3.8 μg/L, respectively. Recoveries were >93%. A new SPME-GC/ECD method to measure 2,4,6-trichloroanisole in chlorinated drinking water was also developed (*118*). Detection limits and quantification limits of 0.7 and 2.5 ng/L, respectively, were achieved. THMs could also be measured with this method. De

Borba et al. created a new IC method to measure bromate in municipal and bottled drinking waters (*119*). This method utilized an electrolytically generated hydroxide eluent combined with a hydroxide-selective anion-exchange column and was able to provide significant noise reduction, along with 0.5 μg/L detection limits.

Several new continuous, online methods have also been recently developed, and these have the promise of being used in water treatment plants to allow real-time determination of DBPs. Wang et al. developed a new continuous hollow-fiber, liquid−liquid membrane extraction-LC/UV method to measure HAAs in drinking water (*120*). Method detection limits were at sub-ppb levels. Simone et al. developed an online IC method for HAAs that uses a postcolumn reaction with nicotinamide and fluorescence detection (*121*). Detection limits of 0.5−5 μg/L were achieved, and this on-line method was compared to EPA Method 552.3. Finally, Brown and Emmert developed a new on-line method for THMs, using capillary membrane sampling and GC/ECD detection (*122*). Method detection limits were in the 0.5 μg/L range. This method was compared to EPA Method 502.2, and it offers advantages for monitoring a drinking water distribution system because it is a near real-time method and can be used at remote locations in the distribution system.

New Human Exposure Studies. Researchers have been investigating other routes of exposure, besides ingestion, in new human exposure studies of drinking water DBPs. And, in many cases, inhalation and dermal exposures that would result from bathing or showering offer greater exposures to particular DBPs than ingesting 2 L of water per day. Exhaled breath is often a convenient, noninvasive way to assess a person's exposure, either dermally or through inhalation. Once a DBP has been absorbed either through the lungs or through the skin, it is transported to the blood stream, where it can be released in exhaled breath from the lungs. Blood measurements are more invasive, but can be more precise measures of exposure. It is of particular interest to epidemiologic studies to know the entire dose of specific DBPs being investigated for effects. Xu and Weisel investigated the dermal absorption of 1,1-dichloropropanone, 1,1,1-trichloropropanone, and chloroform in human volunteers (in their exhaled breath) following a 30-min bath (*123*). The maximum haloketone breath concentration ranged from 0.1 to 0.9 ug/m^3, which were approximately 2 orders of magnitude lower than the maximum chloroform breath concentrations. The permeability of chloroform was found to be much higher than the permeability of the haloketones. Gordon et al. carried out a human exposure study that investigated breath and blood THM levels from 12 common household water-use activities (*124*). Water, indoor air, blood, and exhaled breath samples were collected during each exposure activity. Although showering (10 min), bathing (14 min), machine washing of clothes, and opening dishwashers at the end of the cycle resulted in significant increases in indoor air chloroform levels, only showering and bathing caused significant increases in breath chloroform levels. For bromodichloromethane, only bathing produced significantly higher concentrations. For chloroform from showering, strong correlations were observed for indoor air and exhaled breath, blood and exhaled breath, indoor air and blood, and tap water and blood. Evidence of the importance of dermal and inhalation routes for DBPs, a new epidemiologic study by Villanueva et al. revealed a higher risk of bladder cancer from showering, bathing, and swimming in pools (*125*). Long-term THM exposure was associated with a 2-fold bladder cancer risk (odds ratio of 2.10) for average household THM levels of >49 μg/L. The odds ratio for ingestion was 1.35 (compared to people who did not drink tap water), and the odds ratio from showering and bathing was 1.83.

New Swimming Pool Research. Related to other research involving alternate exposures to ingesting drinking water, swimming pool studies have shown a marked increase in the last 2 years. The Villanueva et al. epidemiologic study mentioned earlier showed an odds ratio of 1.57 for swimming in pools and developing bladder cancer (*125*). Zwiener et al. published a review article on swimming pool waters, detailing the adverse health effects (including asthma, bladder cancer, and endocrine effects), the formation of DBPs in swimming pool water, and precursor chemicals that give rise to them (*126*). Details on swimming pool operation and treatment are also given. Glauner et al. investigated the elimination of swimming pool DBPs using ozonation and advanced oxidation processes (ozone/UV and ozone/hydrogen peroxide) (*127*). Advanced oxidation processes (AOPs) substantially reduced the levels of TOC, adsorbable organic halogen, and THMs. A contact time of 3 min between the pool water and the oxidants was found to be sufficient for lowering DBP levels. Ozonation showed a small advantage to AOPs in removing THMs, and the combination of membrane filtration and AOPs resulted in the elimination of 10−90% of the DBPs and their precursors. The ozone/hydrogen peroxide process was recommended for pool water treatment because of higher elimination rates compared to ozonation alone and lower costs as compared to ozone/UV treatment.

DBPs of Pollutants. DBPs are going beyond the "classic" DBPs formed by the reaction of NOM with disinfectants, such that reactions of pollutant material with disinfectants are now being studied. The last 2 years have produced studies of disinfectant reactions with pharmaceuticals, antibacterial agents, and pesticides. Most of this research has been conducted in order to find ways to degrade and remove these contaminants from wastewater effluents and drinking water sources. It is not surprising that DBPs can form from these contaminants, as many of them have activated aromatic rings that can readily react with oxidants like chlorine and ozone. However, until recently, these types of DBPs have not been investigated. Due to the growth in this area and the potential toxicological significance of these new types of byproducts (by increasing or decreasing the toxicity/biological effect relative to the parent compound), this research area is being included in this review. Some of these references are also cited in the section on Pharmaceuticals, Hormones, and EDCs.

The ozonation of the pharmaceutical carbamazepine produced three new oxidation products: 1-(2-benzaldehyde)-4-hydro-(1*H*,3*H*)-quinazoline-2-one (BQM), 1-(2-benzaldehyde)-(1*H*,3*H*)-quinazoline-2,4-dione (BQD), and 1-(2-benzoic acid)-(1*H*,3*H*)-quinazoline-2,4-dione (BaQD) (*86*). These were identified using a combination of MS and NMR techniques. Concentrations of BQM and BQD were 0.48 and 0.15 μM, respectively, for Lake Zurich water spiked with 1 μM carbamazepine and treated with an ozone dose of 1.9 mg/L. In another study, the chlorination of acetaminophen produced 1,4-benzoquinone and *N*-acetyl-*p*-benzoquinone imine

(*87*). Two other ring chlorination products (chloro-4-acetamidophenol, dichloro-4-acetamidophenol) were also identified. Chloroform, 5,6-dichloro-2-(2,4-dichlorophenoxy)phenol, 4,5-dichloro-2-(2,4-dichlorophenoxy)phenol, and 4,5,6-trichloro-2-(2,4-dichlorophenoxy)phenol were formed as byproducts from the chlorination of the antibacterial agent, triclosan under drinking water treatment conditions (*88*). Triclosan—which is 5-chloro-2-(2,4-dichlorophenoxy)phenol—is used in many hand soaps, as well as other products, and the authors estimate that the use of triclosan can increase a person's annual exposure to chloroform by as much as 40% above background levels in tap water. Vikesland's research group also investigated the reactivity of triclosan with monochloramine (*89*). The same DBPs (chloroform and 3 chlorinated phenols) that were formed by chlorination were also observed in these chloraminated waters, but the reaction rates were much slower, such that chloroform was detected only after 1 week of reaction. The veterinary antibacterial agent, carbadox, was also found to form byproducts in chlorinated water (*90*). Five nonchlorinated byproducts were observed, but each retained its biologically active *N*-oxide group, suggesting the byproducts may still be active antibacterial agents.

Pesticide DBPs were the focus of other research. Duirk and Collette investigated the reaction of the organophosphate pesticide chlorpyrifos with chlorine (*128*). Under drinking water treatment conditions, chlorpyrifos rapidly oxidized to chlorpyrifos oxon by HOCl. The oxon reaction product is of concern because it is more toxic than the parent pesticide. At elevated pH, both chlorpyrifos and chlorpyrifos oxon were susceptible to alkaline hydrolysis and chlorine-assisted (OCl^-) hydrolysis, resulting in 3,5,6-trichloro-2-pyridinol, which is not as toxic. In another study, the herbicide, clethodim, was found to react with chlorine under drinking water treatment conditions to form clethodim sulfoxide and a sulfone (*129*). LC/MS was used to identify these reaction products. Other minor products were also observed but were not identified. Hladik et al. reacted 4 chloroacetamide herbicides (acetochlor, alachlor, metolachlor, dimethenamid) and 20 of their environmental degradates with chlorine or ozone under simulated drinking water conditions (*130*). All of the compounds reacted with ozone, and most reacted with chlorine. Several DBPs were detected by GC/MS and LC/UV; two DBPs were identified (for dimethenamid and deschlorodimethenamid), both of which had a chlorine in their structures. Shemer and Linden investigated the reaction of the organophosphorus pesticide diazinon during UV and UV/hydrogen peroxide treatment (*131*). Using a medium-pressure UV lamp, 2-isopropyl-6-methyl-pyrimidin-4-ol was the major byproduct (at pH 4−10), and trace levels of diethyl-2-isopropyl-6-methylpyrimidin-4-yl phosphate (diazoxon) were detected during the UV/hydrogen peroxide reaction. Decay of both products was observed, but mineralization was not achieved. Diazinon is currently on the U.S. EPA's CCL, and UV disinfection is increasingly being explored as a new disinfectant option at drinking water treatment plants. Chlorination of the herbicide, glyphosate (*N*-(phosphonomethyl)glycine), was examined in another study (*132*). The C1 carboxylic acid carbon quantitatively converted to CO_2 upon chlorination, and the C2 methylene carbon converted to CO_2 and methanediol. Phosphoric acid also formed as a DBP. The structure of glyphosate contains a glycine moiety, and its reactions were similar to those observed for glycine.

Finally, Oliveira et al. investigated DBPs formed by the chlorination of disperse azo dyes (*133*). This study was carried out because the local water treatment plant in Sao Paulo, Brazil, had repeated detections of mutagenic materials that could not be explained by traditional DBPs, and source waters had been contaminated by a dye processing plant. In this study, solutions of a commercial black dye, which contained Disperse Blue 373, Disperse Orange 37, Disperse Violet 93, and chemically reduced dye, were chlorinated in a manner similar to the drinking water treatment plant, and this chlorinated solution was compared to a drinking water sample collected from the local water treatment plant. LC/MS was used to identify the byproducts. A reduced chlorinated byproduct was detected, along with the parent dye components, in both samples, and the mutagenicity of these products suggested that the byproduct and dye components accounted for much of the mutagenic activity in the drinking water.

SUNSCREENS/UV FILTERS

UV filters used in sunscreens, cosmetics, and other personal care products have increased in interest due to their presence in environmental waters and their endocrine and developmental toxicity (*1*). Levels observed in environmental waters are not far below the doses that cause toxic effects in animals (*1*). There are two types of UV filters—organic UV filters, which work by absorbing UV light, and inorganic UV filters (TiO_2, ZnO), which work by reflecting and scattering UV light. Organic UV filters are increasingly used in personal care products, such as sunscreens, cosmetics, beauty creams, skin lotions, lipsticks, hair sprays, hair dyes, and shampoos (*1*). Examples include benzophenone-3 (BP-3), 4-hydroxybenzophenone (HBP), 2-hydroxy-4-methoxybenzophenone (HMB), 2,4-dihydroxybenzophenone (DHB), 2,2′dihydroxy-4-methoxybenzophenone (DHMB), 2,3,4-trihydroxybenzophenone (THB), octyl-dimethyl-*p*-aminobenzoic acid, 4-methylbenzylidene camphor (4-MBC), ethylhexyl methoxycinnamate, octyl methoxycinnamate (OMC), octocrylene, butyl methoxydibenzoylmethane, terephthalylidine dicamphor sulfonic acid, ethylhexyl triazone, phenylbenzimidazole sulfonic acid (PBSA), ethylhexyl salicylate, benzhydrol (BH), and 1-(4-*tert*-butylphenyl)-3-(4-methoxyphenyl)-1,3-propanedione (BPMP). The majority of these are lipophilic compounds (low water solubility) with conjugated aromatic systems that absorb UV light in the wavelength range of 280−315 (UVB) or 315−400 nm (UVA) (*1*). Most sunscreen products contain several UV filters, often in combination with inorganic micropigments. Because of their use in a wide variety of personal care products, these compounds can enter the aquatic environment indirectly from showering, washing off, washing clothes, etc., via wastewater treatment plants and also directly from recreational activities, such as swimming and sunbathing in lakes and rivers.

Both GC/MS and LC/diode array detection (DAD) methods have been used for the measurement of UV filter compounds. Giokas et al. reported a preconcentration method using a nonionic surfactant to capture UV filter compounds (PBSA, HMB, BP-3, MBC, OMC, BPMP) in micelles (*134*). The analytes are then back-extracted into an organic solvent and analyzed by GC/MS or LC/DAD. Using this method, recoveries of 95−102% could be achieved, with detection limits of 2.2−30.0 ng/L and 0.14−1.27

μg/L for GC/MS and LC/DAD detection, respectively. Kawaguchi et al. developed a method using stir bar sorptive extraction and thermal desorption-GC/MS for analyzing benzophenone, BP-3, and 2-hydroxy-4-methoxy-4′-methylbenzophenone (BP-10) in water (*135*). A 10-mL water sample was extracted, and 0.5−1 pg/mL (ng/L) detection limits were obtained. Jeon et al. developed a new GC/MS method for seven UV filters using derivatization with *N*-methyl-*N*-(trimethylsilyl)trifluoroacetamide (*136*). BP-3, BH, HBP, HMB, DHB, DHMB, and THB could be measured in 23 min with detection limits ranging from 5 to 100 ng/L. Using this method, water samples from Korea were measured and were found to contain 27−204 ng/L levels of the UV filters. Other occurrence/fate studies include one by Buser et al., who investigated the stereoisomer composition of the chiral UV filter 4-MBC in the aquatic environment (*137*). 4-MBC exists as (*E*)- and (*Z*)-isomers (like cis/trans isomers), both of which are chiral. Chiral-GC/MS was used to determine the stereoisomers. Technical material and a commercial sunscreen lotion contained mostly the (*E*)-isomer, with a racemic composition of the enantiomers ($R/S = 1.00$). Untreated wastewater showed a nearly racemic composition, suggesting that most if not all commercial 4-MBC is racemic. Treated wastewater showed a slight excess of (*R*)- or (*S*)-stereoisomers, indicating that some enantioselective biodegradation is occurring. A slight enantiomeric excess was also observed in Swiss lakes, rivers, and fish.

BROMINATED FLAME RETARDANTS

Brominated flame retardants have been used for many years in a variety of commercial products including children's sleepwear, foam cushions in chairs, computers, plastics, textile coatings, and electronic appliances. Of the 175 different types of flame retardants, the brominated ones dominate the market due to their low cost and high performance (*1*). Brominated flame retardants work by releasing bromine free radicals when heated, and these free radicals scavenge other free radicals that are part of the flame propagation process (*138*). The use of these flame retardants is believed to have successfully reduced fire-related deaths, injuries, and property damage. However, there is recent concern regarding these emerging contaminants because of their widespread presence in the environment and in human and wildlife samples and their presence in locations far from where they were produced or used. There is also strong evidence that levels of some of these flame retardants are increasing, doubling every 3−5 years (*138*). Worldwide, more than 200 000 metric tons of brominated flame retardants are produced each year. PBDEs have been a popular ingredient in flame retardants since the polybrominated biphenyls were banned about 30 years ago. Approximately 70 000 metric tons of PBDEs are produced per year, with most being used in the United States and Canada. This explains the higher levels observed in humans and wildlife from North America (*138*). Penta-, octa-, and deca-BDEs (and congeners of these) are commercially available (*138*). The most commonly observed isomer is the 2,2′,4,4′tetrabromodiphenyl ether (BDE-47). The greatest health concern for potential health effects comes from recent reports of developmental neurotoxicity in mice (*1*), but there are also concerns regarding the potential for hormonal disruption and, in some cases, cancer. Due to these concerns, a European Union Directive was established to control emissions of these compounds in Europe. In addition, the major U.S. manufacturer of PBDE-based flame retardants (Great Lakes Chemical) has voluntarily stopped producing the penta- and octa-brominated diphenyl ethers. However, the deca-BDE is still being manufactured.

Hites gave an excellent summary of brominated flame retardants in the environment and discussed PBDEs, polybrominated biphenyls, hexabromocyclododecanes, and other brominated flame retardants (*138*). Most previous PBDE studies have focused on their measurement in biological samples, including human blood, milk, and tissues, as well as marine mammals and other wildlife. However, there are now increasing measurements in environmental waters. Because PBDEs are hydrophobic, GC with EI-MS and NCI-MS can be used for their measurement. Some methods also use high-resolution EI-MS with isotope dilution and GC/MS/MS.

Streets et al. used GC/NCI-MS to measure PBDEs and PCBs in water and fish from Lake Michigan (*139*). PBDE congeners ranged from 0.2 to 10 pg/L and were similar to dissolved-phase PCB congener concentrations. Partitioning between the particulate and dissolved phases was also similar. Wurl et al. measured the occurrence and distribution of PBDEs in the dissolved and suspended phases of sea-surface microlayers and seawater in Hong Kong (*140*). Concentrations were generally low (pg/L range in the water) and were highest in the harbor waters, which was likely due to discharge of untreated wastewaters.

Most new analytical methods involve the use of recently developed extraction techniques, such as stir bar sorptive extraction, hollow-fiber membrane liquid−liquid extraction, carbon nanotubes, and SPME. Llorca-Porcel et al. developed a new stir bar sorptive extraction method for measuring nine PBDEs in water (*141*). Recoveries were near 100% with 100-mL water samples. Detection limits ranged from 0.4 to 9.4 ng/L. Fontanals et al. reported a new hollow-fiber microporous membrane liquid−liquid extraction-GC/MS method for measuring PBDEs in water (*142*). Enrichment factors of 5200× could be achieved, along with recoveries of 85−110%, and detection limits of 1.1 ng/L. Wang et al. developed a method using multiwalled carbon nanotubes for solid-phase microextraction of PBDEs in water and milk samples, followed by GC/ECD analysis (*143*). These carbon nanotube coatings gave improved enrichment factors over the more common poly(dibenzenedimethylsiloxane) coatings, and a 30-min extraction of a 10-mL sample provided 3.6−8.6 ng/L detection limits. Recoveries were 90−119%. Polo et al. reported a new SPME method for measuring another type of flame retardant—3,5,3′,5′tetrabromobisphenol A—in water (*144*). GC/MS was used for analysis, along with in situ acetylation, and sampling with a carboxen−poly(dimethylsiloxane) fiber. Detection limits were low picograms per milliliter (ng/L).

BENZOTRIAZOLES

Interest in benzotriazoles is emerging, and this class of emerging contaminant is included in this review for the first time. Benzotriazoles are complexing agents that are widely used as anticorrosives (e.g., in engine coolants, aircraft deicers, or antifreezing liquids) and for silver protection in dish washing liquids. The two common forms, benzotriazole and tolyltriazole, are soluble in water, resistant to biodegradation, and are only partially

removed in wastewater treatment (*5*). Because of their water solubility, LC/MS and LC/MS/MS methods have been recently developed for their measurement in environmental waters. While reports of benzotriazoles in environmental samples have just occurred in the last 2−3 years, early studies indicate that they are likely ubiquitous environmental contaminants.

Recent studies have included the measurement of benzotriazoles in surface waters and wastewater. Weiss and Reemtsma developed a LC/ESI-MS/MS method for measuring benzotriazole and two isomers of tolyltriazole (5- and 4-tolyltriazole) in environmental waters (*145*). Using SPE for extraction, their method could achieve detection limits of 10 ng/L (for groundwater) and 25 μg/L (for untreated wastewater). Microgram per liter levels were found in municipal wastewater, and removal in wastewater treatment was poor, which allowed these compounds to be cycled back to surface water and to drinking water source waters. Of the two tolyltriazole isomers, the 4-tolyltriazole isomer was more stable in the environment. Giger et al. measured benzotriazole and tolyltriazole in rivers and wastewaters in Switzerland using a SPE-LC/MS/MS method (*146*). Benzotriazole was found at a maximum of 6.3 μg/L in the Glatt River, and a mass flow of 277 kg per week was observed in the Rhine River. Tolyltriazole was generally found at 5−10× lower concentrations. During the winter of 2003−2004, benzotriazole mass flows indicated input from the Zurich airport, where benzotriazole was used as an anticorrosive in deicing fluid. Lake waters showed 0.1−1.2 μg/L levels. Voutsa et al. used LC/MS/MS to measure benzotriazoles, alkylphenols, and bisphenol A in municipal wastewaters and in river water in Switzerland (*147*). Benzotriazole and tolyltriazole levels varied from below 10 to 100 μg/L in wastewater effluents, and from 0.12 to 3.7 μg/L in river water.

Weiss et al. investigated the discharge of three benzotriazoles in municipal wastewater (*148*). Mean concentrations of 12, 2.1, and 1.3 μg/L were observed for benzotriazole, 4-tolyltriazole, and 5-tolyltriazole, respectively, and they were removed differently in wastewater treatment and with biodegradation. Removal in sludge was 37% for benzotriazole, but almost no removal of 4-tolyltriazole was observed. In controlled laboratory biodegradation experiments, 5-tolyltriazole was mineralized completely, but 4-tolyltriazole was only mineralized to 25%. A membrane bioreactor was found to improve their removals in wastewater treatment, and the use of ozonation provided almost complete removal at a dose of 1 mg of O_3/mg of dissolved organic carbon. Corsi et al. measured aircraft deicer and anti-icer compounds in airport snowbanks and snowmelt runoff (*149*). 4-Methyl-1*H*-benzotriazole and 5-methyl-1*H*-benzotriazole were found, along with alkylphenol ethoxylates, in the snowbank and airport snowmelt samples. Toxicity (as measured in the Microtox assay) remained in the snowbanks for a long time, after most glycol had been removed during melt periods. The benzotriazoles and alkylphenol ethoxylates found in the aircraft deicing solutions were indicated to be the source of the toxicity.

DIOXANE

Interest is increasing in 1,4-dioxane, which has been discovered to be a widespread contaminant in groundwater (often exceeding water quality criteria and guidelines) and is a probable human carcinogen (*150*). As a result, it is included in this review for the first time. Dioxane is a high production chemical and is used as a solvent stabilizer, especially for 1,1,1-trichloroethane (TCA), which is a popular vapor degreasing solvent. In 2002, more than 500 metric tons of dioxane were produced or imported to the United States (*150*). Dioxane is problematic to extract and measure because it is highly water soluble.

Isaacson et al. developed a SPE method based on activated carbon disks and used GC/MS for the analysis of dioxane in groundwater (*150*). Recovery was 98%, with quantification limits of 0.31 μg/L for an 80-mL water sample. This method was used to measure dioxane at a TCA-impacted site. Dioxane levels ranged from below detection to 2800 μg/L and were higher than TCA levels observed (maximum of 980 μg/L). Jochmann et al. developed a new method using headspace solid-phase dynamic extraction (SPDE) with GC/MS to measure dioxane and other contaminants in water (*151*). SPDE is a SPME technique where the inside of a syringe needle is coated with an extraction phase, and the needle is moved up and down in the sample or headspace (as in this study) several times, after which the needle is injected into the GC injection port, and the analytes are thermally desorbed. SPDE typically has 4−6× larger extraction-phase volumes than 100-μm SPME fibers. With this method, detection limits of 0.8 μg/L were achieved.

NAPHTHENIC ACIDS

Naphthenic acids are becoming important emerging environmental contaminants, so they are included in this review for the first time. Current research is focusing on naphthenic acids in the oil sands region in Alberta, Canada, one of the highest producers of crude oil in the world. Caustic hot water is used in the extraction of crude oil from oil sands, which results in a residual tailing water that contains clay, sand, and organic compounds of high polarity and molecular weight (*5*). The tailing water is known to be toxic, and the primary toxic components have been identified as oil sand naphthenic acids (a complex mixture of alkyl-substituted acyclic and cycloaliphatic carboxylic acids that dissolve in water at neutral or alkaline pH and have surfactant-like properties). Naphthenic acids are toxic to aquatic organisms, including phytoplankton, daphnia, fish, and mammals, and are also endocrine disrupting (*5*). High levels of naphthenic acids are released in the extraction process, with 80−120 mg/L levels common, and 0.1−0.2 m^3 of tailings per ton of oil sands processed (*5*). The total volume of tailing ponds is projected to exceed 10^9 m by the year 2020 (*5*). Clemente and Fedorak published a review on the occurrence, analysis, toxicity, and biodegradation of naphthenic acids (*152*).

Naphthenic acids are challenging to measure because they are present as a complex mixture of isomers and homologues. Two-dimensional (2-D)-GC (also called GC × GC) and TOF-MS are currently enabling researchers to better separate the complex mixture of naphthenic acids (through greater chromatographic peak capacity and fast scanning of the TOF-MS instrument) and to identify the individual compounds (through the use of exact mass data provided by TOF-MS). Hao et al. used a 2-D-GC/TOF-MS method to investigate pattern recognition for naphthenic acids in tailing waters (*153*). Contour plots of different homologous series were constructed using fragment ions that were characteristic of the naphthenic acids' structures. Well-ordered patterns

were found, and specific zones could allow the origin of the naphthenic acids to be determined. Lo et al. tested a new APCI-MS method and analyzed fractions of naphthenic acids collected from tailing ponds (*154*). When APCI-MS analysis was compared to previously published ESI-MS analyses, APCI-MS had a wider range of quantification, but with higher detection limits.

PESTICIDE DEGRADATION PRODUCTS AND NEW PESTICIDES

Herbicides and pesticides continue to be studied more than any other environmental contaminant. Recent studies have focused more on their degradation products, with the recognition that the degradation products (often hydrolysis products) can be present at greater levels in the environment than the parent pesticide itself, and sometimes the degradation product is as toxic or more toxic than the parent pesticide (*155*). New pesticides have also come on the market (such as glyphosate and organophosphorus pesticides), and studies are being conducted to understand their fate and transport in the environment.

Pesticide Degradation Products. Two sets of pesticide degradation products are currently on the U.S. EPA's CCL: alachlor ESA and other acetanilide pesticide degradation products, and triazine degradation products (including, but not limited to cyanazine and atrazine-desethyl) (www.epa.gov/safewater/ccl). LC/MS and LC/MS/MS are now commonplace for measuring pesticide degradates, which are generally more polar than the parent pesticides, making LC/MS ideal for their detection. Several reviews published in the last 2 years have focused on the use of LC/MS and LC/MS/MS for analyzing pesticides and their degradates (*155*−*158*). One of these reviews compares LC/MS/MS to GC/MS for measuring 500 high-priority pesticides (*158*). For nearly all of the pesticides, LC/MS/MS was a better choice, offering better sensitivity (ng/L vs μg/L) and the ability to analyze a greater number of pesticides within one analysis. The ability to measure more pesticides in a single analysis by LC/MS/MS stems from the broader peak width of LC versus GC. Assuming a cycle time in GC/MS of 1 s or shorter and a dwell time of 40 ms, not more than 25 characteristic ions can be recorded in one time window. And, assuming 10 time windows in a typical GC/MS run, 250 ions, or 83 pesticides with 3 characteristic ions can be analyzed during a single analysis. In contrast, typical LC/MS/MS measurements would be able to monitor 625 MRM transitions with one injection. As a result, 312 pesticides versus 83 pesticides can be analyzed by LC/MS/MS versus GC/MS. Of the pesticides investigated, GC/MS performance was superior for one class—the organochlorine pesticides—where the GC/MS response was better than LC/MS.

As in studies of other emerging contaminants, TOF-MS (and Q-TOF-MS) is increasingly being used to identify new pesticide transformation products. Sancho et al. reviewed the potential of LC/TOF-MS for determining pesticides and their transformation products in water (*159*). Advantages of LC/TOF-MS include the high sensitivity available in full-scan acquisitions and high resolution (10 000−12 000) as compared to other MS analyzers, such as triple quadrupole mass spectrometers. LC/TOF-MS also reduces the chance of false positives, but it can be less sensitive than triple quadrupole mass spectrometers in quantification, when specific MRM transitions are monitored. A nice example of the use of LC/Q-TOF-MS is provided in a study by Ibanez et al., where LC/Q-TOF-MS was used to identify transformation products and metabolites of various pesticides (*160*). In this study, photodegradation products and in vivo and in vitro metabolism products were identified for the insecticide, diazinon. Accurate mass measurements and MS/MS capability were essential for identifying these transformation products.

Other LC/MS/MS methods include two online SPE-LC/ESI-MS/MS methods by Marin et al. for rapidly determining 18 polar pesticides and 9 transformation products (mostly from triazine herbicides) in water (*161*). Injection of only 2 mL of a water sample produced detection limits of <5 ng/L. Two MS/MS transitions allowed reliable confirmation of positive detections. Using this method, groundwater and surface waters were analyzed, and several samples had transformation products at higher levels than the parent pesticides. Glyphosate (*N*-phosphonomethyl glycine) was the focus of several papers. Glyphosate is the active ingredient in the broad spectrum herbicide, Roundup, and is currently the most widely used herbicide in the world (*162*). Because glyphosate is highly polar, LC/MS methods are ideal. Kolpin et al. determined urban contributions of glyphosate and its degradate, aminomethyl phosphonic acid (AMPA), in streams in the United States (*162*). A precolumn derivatization with 9-fluorenylmethyl chloroformate was used, followed by LC/MS analysis. Stream samples collected upstream and downstream of wastewater treatment plants showed a 2-fold increase in the downstream samples, indicating an urban contribution. Overall, AMPA was detected much more frequently (67.5%) compared to glyphosate (17.5%). Kjaer et al. investigated the leaching of glyphosate and AMPA from farms in Denmark (*163*). Differences were observed, depending on the type of soil. One loamy site showed substantial leaching into the runoff water, with average concentrations exceeding 0.1 μg/L, the European threshold value for drinking water. Further, AMPA was frequently detected more than 1.5 yr after application. Ibanez et al. used a SPE-LC/ESI-MS/MS method to measure glyphosate and AMPA in water (*164*). Despite the use of isotopically labeled glyphosate, its recovery in groundwater was low (15%) initially. However, when the water was acidified to pH 1, neutralized and derivatized with 9-fluorenylmethyl chloroformate before LC/MS/MS measurement, recoveries improved to 98%.

Ma et al. used GC/ion trap-MS to measure atrazine and its deethylated degradation product (deethylatrazine) in environmental waters and sediments (*165*). Method detection limits were subnanograms per liter. Atrazine was then measured in a reservoir from Beijing, where levels of 35.9−217.3 ng/L were observed. Levels of deethylatrazine in sediment were 5−20 times lower than the atrazine measurements in the water. Mills et al. carried out a large occurrence study of 16 herbicides and 13 herbicide degradates in samples from 55 wells in shallow aquifers underlying grain producing regions of Illinois (*166*). Fifty-six percent of the samples contained compounds above 0.05 μg/L, and the six most frequently detected were degradates.

Finally, enzyme immunoassay methods are also popular as rapid screening methods for pesticides and pesticide degradation products, and Morozova et al. reviewed these techniques (*167*).

False positives can be obtained with ELISAs, and often LC/MS-(/MS) analysis is provided as a follow-up to initial detection by ELISAs to eliminate false positives.

PERCHLORATE

Perchlorate became an important environmental issue following its discovery in a number of water supplies in the western United States. It has also recently been found in water supplies across the United States at microgram per liter levels. High quantities of perchlorate have been disposed of since the 1950s in Nevada, California, and Utah, which is believed to have contributed to much of the contamination in the western United States. However, new analyses have revealed that perchlorate contamination is not limited to the western United States; even areas such as Washington DC have reported perchlorate contamination, possibly caused by buried munitions. Ammonium perchlorate has been used as an oxygenate in solid propellants used for rockets, missiles, and fireworks, as well as highway flares, and there is also potential contamination from fertilizers (that contain Chilean nitrate). In addition, surprising results from a new study published in 2005 indicate that perchlorate contamination can also come from natural sources, arising from atmospheric processes (*168*). Perchlorate is an anion that is very water soluble and environmentally stable. It can accumulate in plants (including lettuce, wheat, and alfalfa), which can contribute to exposure in humans and animals. In addition, perchlorate is not removed by conventional water treatment processes, so human exposure could also come through drinking water. Health concerns arise from perchlorate's ability to displace iodide in the thyroid gland, which can affect metabolism, growth, and development. Perchlorate has also been found in cow's milk, human breast milk, and human urine. Due to these concerns, the U.S. EPA placed perchlorate on the U.S. EPA's CCL and the UCMR. The U.S. EPA also set a reference dose for perchlorate at 0.0007 mg kg^{-1} day^{-1}, which translates to a drinking water equivalent level of 24.5 μg/L (www.councilonwaterquality.org/issue/regulation.html). In 2004, the State of California became the first state to set a drinking water public health goal (6 μg/L) (*169, 170*), and at least seven other states have issued advisory levels ranging from 1 to 18 μg/L (*168*). California is close to finalizing a new regulation for perchlorate in drinking water (*169*), where an MCL of 6 μg/L has been proposed (www.dhs.ca.gov/ps/ddwem/chemicals/perchl/default.htm).

Because perchlorate is listed on the CCL and the UCMR, new EPA methods have been developed, including two drinking water methods, EPA Method 314.1 (an IC method; www.epa.gov/safewater/methods/sourcalt.html) and EPA Method 331.0 (a LC/ESI-MS/MS method; www.epa.gov/safewater/methods/sourcalt.html). These methods were created to overcome matrix interferences in high ionic strength waters and also to lower detection limits to levels that are of human health concern. Journal articles were recently published describing the performance of these methods (*16, 17*). New EPA methods were also developed for measuring perchlorate in wastewater using LC/ESI-MS (EPA Methods 6850 and 6860; www.epa.gov/epaoswer/hazwaste/test/new-meth.htm). Further details on these four methods are provided in the section on New Regulations/Regulatory Methods.

As mentioned earlier, there was a new discovery by Dasgupta et al. that perchlorate contamination can arise from natural sources. This was a surprising discovery and came from the observation of high perchlorate levels in groundwater from the Texas Panhandle region, where there is no historical or current evidence of the presence of rocket fuel or Chilean fertilizer sources (*168*). This perchlorate contamination is spread over 60 000 square miles, and levels of 20 μg/L are consistently found, with some measurements as high as 60 μg/L. While there were no known anthropogenic sources for the perchlorate contamination, the land had been irrigated since the 1940s, and this led the researchers to investigate potential natural sources. To this end, Dasgupta et al. demonstrated for the first time that perchlorate can readily form by a variety of simulated atmospheric processes, including by electrical discharge of chloride aerosols (with lightning) and by exposing aqueous chloride to high concentrations of ozone, which may occur in the atmosphere. Large-volume preconcentration with IC/ESI-MS was used to measure perchlorate in rain and snow samples collected from this region. Perchlorate was found in 70% of these samples at concentrations ranging from 0.02 to 1.6 μg/L. These results strongly suggest that some perchlorate is formed in the atmosphere and that a natural perchlorate background of atmospheric origin exists.

Besides the new EPA methods, other methods for perchlorate have also been published in the last 2 years. Mathew et al. developed an IC/ESI-MS method that used a suppression column to lower matrix backgrounds (*171*). Submicrogram ler liter levels could be measured, and this method was tested on groundwater and wastewater samples. Lamb et al. developed a new IC method that uses a 18-crown-6 mobile phase with an underivatized reversed-phase, mobile-phase IC column to measure perchlorate in water (*172*). To enable measurements in high ionic strength waters, the authors used a Cryptand C1 concentrator column (Dionex Corp.) to reduce background ion concentrations. This method enabled the measurement of perchlorate at 5 μg/L levels.

Jackson et al. carried out a large occurrence study for perchlorate in groundwaters in Texas (*173*). A total of 254 wells were sampled, 179 wells (70%) had detectable perchlorate levels (>0.5 μg/L), and 88 wells (35%) had perchlorate levels of ≥4 μg/L. The highest perchlorate level was found at a private well (58.8 μg/L). Stetson et al. conducted a study to investigate the stability of perchlorate in various water samples, to determine holding times for samples (*174*). IC was used for the measurements, and concentrations of 0.5, 1.0, 100, and 1000 μg/L were found. Results showed that groundwater samples were stable for at least 300 days and surface water samples were stable for at least 90 days. Finally, Sturchio et al. investigated stable-isotope ratios of oxygen and chlorine in perchlorate under biodegradation conditions to determine whether isotope ratio analysis would be useful for determining the source of perchlorate (*175*). Negligible isotope exchange was observed between perchlorate and water in these experiments, indicating that isotope ratio analysis could reliably be used to determine the source of the perchlorate.

GASOLINE ADDITIVES: MTBE AND EDB

MTBE contamination is a concern, due to its introduction to 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 as an octane enhancer during the organolead phase-out. It was also used to improve combustion and to reduce emissions of ground-level ozone and other toxic pollutants; by 1998, MTBE was added to approximately 30% of all gasoline sold in the United States. But, by late 2006, its usage has been largely eliminated in U.S. gasolines. In the United States, the 1990 Amendments to the Clean Air Act required a minimum oxygen content of 2.7 (w/w) and 2.0% (w/w) for gasolines sold in areas of the country where carbon monoxide and ozone air standards are exceeded, respectively. In Europe, there are no minimum oxygen content requirements for gasoline, but the addition of up to 15% (v/v) is allowed, and it is estimated that approximately 2 million tons of MTBE has been added to gasoline in Europe each year. MTBE was the most common oxygenate added to gasoline because of its low cost, availability, and high octane rating. Ethanol, ETBE, TAME, DIPE, and TBA are also sometimes used as gasoline oxygenates, but were not as popular as MTBE.

MTBE has been responsible for taste and odor problems in drinking water, and there are also concerns about possible adverse health effects. There are strategies to remove MTBE from source waters or drinking water, including air stripping, granular activated carbon, advanced oxidation, and home treatment units (www.epa.gov/safewater/mtbe.html). The U.S. EPA recommends monitoring of oxygenate compounds in groundwater at leaking underground storage tank sites, and MTBE was included in the first UCMR (www.epa.gov/safewater/ucmr/ucmr1), which required large public drinking water systems to measure MTBE. MTBE is not currently included in the UCMR-2. The U.S. EPA is continuing to study both the potential health effects and the occurrence of MTBE, and it is currently on the U.S. EPA's CCL. While there are not U.S. federal bans or MCLs, several states have developed their own standards for MTBE in drinking water, and 26 states have banned the use of MTBE in gasolines (although de minimus levels of 0.3−1.0% have been allowed) (www.epa.gov/athens/research/regsupport/ust.html). In addition, the Energy Policy Act of 2005 removed the 2.0% requirement for ozone nonattainment areas and mandated increased usage of renewable fuels (e.g., ethanol and biodiesel). The U.S. refining industry has responded by removing the majority of ether additives to gasoline. California and a few others states have also set limits on the use of other oxygenates that might be used as alternatives to MTBE: ETBE, TAME, DIPE, methanol, 2-propanol, 1-propanol, 1-butanol, isobutanol, *sec*-butanol, *tert*-butanol, or *tert*-pentanol (*tert*-amyl alcohol).

GC/MS is probably the most common analytical technique used to measure MTBE. SPE, headspace-SPME, and purge-and-trap are popular extraction techniques. Direct aqueous injection and direct headspace analysis have also been used. Methods can generally detect MTBE in the low-microgram per liter range. In water, MTBE can degrade to TBA and *tert*-butyl formate, so these degradates are sometimes analyzed along with MTBE. Atienza et al. published a review on the state of the art in the determination of MTBE in water and soils (*176*). This review includes sample preparation methods, sample concentration and injection techniques (including direct injection, headspace analysis, purge-and-trap, SPME), and detection methods, including GC/MS, and stable-isotope analysis. Nakamura and Daishima published a new headspace SPME-GC/MS method to measure MTBE, 1,4-dioxane, and 20 other volatile organic compounds in water (*177*). The detection limit for MTBE was 0.01 μg/L, and excellent recoveries were obtained for all analytes (94−104%). Borsdorf and Rammler reported a new continuous online method for measuring MTBE in water using ion mobility spectrometry (*178*). This method required no sample preparation and involved continuous extraction using a membrane extraction unit. Detection limits were quite high (100 μg/L) compared to other methods, so this method might be limited to in situ monitoring of highly contaminated waters.

While most of the attention has focused on MTBE, another gasoline additive that is much more toxic has been widely overlooked. EDB was used from the 1920s to the late 1980s as a gasoline additive, as a lead scavenger in leaded gasolines (*179*). Leaded gasoline was phased out in the United States in the early 1970s, and many other countries reduced it during the 1980s−1990s. However, EDB, which is classified as a probable human carcinogen, has persisted at high levels in groundwater despite the phase-out. In fact, EDB is among the most commonly detected contaminants in U.S. public drinking water systems that use groundwater. And, recent research in South Carolina has revealed that about half of the state's underground gasoline storage tank sites and groundwater is contaminated at levels above the MCL of 0.05 μg/L (*179*). EDB is highly water soluble (4300 mg/L) and can readily dissolve out of free-phase gasoline and mobilize in groundwater. Moreover, despite the leaded gasoline phase-out, EDB concentrations are not declining with time—in South Carolina, EDB has increased in concentration in about 40% of the wells monitored. This is believed to be due to regional water levels rising following a 4-yr drought, which facilitated groundwater contact with the free-phase gasoline at some sites. South Carolina is one of only 11 states that require testing for EDB in groundwater at sites contaminated by gasoline. EDB contamination is only recently being recognized as a widespread environmental problem, and it is included in this review for the first time. Because the MCL is quite low (0.05 μg/L), analytical methods must be able to detect nanogram per liter levels. EPA Method 8011 (which uses liquid−liquid extraction and GC/ECD) is currently the only EPA method that can achieve sufficient detection limits (0.01 μg/L) (www.epa.gov/epaoswer/hazwaste/test/pdfs/8011.pdf).

ALGAL TOXINS

Algal toxins (mostly cyanobacterial toxins produced from blue-green algae) continue to be of increasing interest in the United States and in other countries around the world. Increased discharges of nutrients (from agricultural runoff and from wastewater discharges) have led to increased algal blooms and an accompanying increased incidence of shellfish poisoning, 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. The most commonly occurring algal toxins are microcystins, nodularins, anatoxins, cylindrospermopsin, and saxitoxins. "Red tide" toxins are also often found in coastal waters. Microcystins and nodularins have high molecular weight, cyclic peptide structures and are hepatotoxic. Anatoxins, cylindrospermopsin, and saxitoxins have heterocyclic alkaloid structures; anatoxins and saxitoxins are neurotoxic, cylindrosper-

mopsin is hepatotoxic. Red tide toxins include brevetoxins, which have heterocyclic polyether structures and are neurotoxic. Microcystins (of which, there have been more than 70 different variants isolated and characterized) are the most frequently reported of the algal toxins. The most common microcystins are cyclic heptapeptides that contain the amino acids leucine (L) and arginine (R) in their structures. Nearly every part of the world that uses surface water as a drinking water source has encountered problems with cyanobacteria and their toxins (*180*). Algal toxins are currently on the U.S. EPA's CCL (www.epa.gov/safewater/ccl). Several countries, including Australia, Brazil, Canada, France, and New Zealand, have guideline values for microcystins, anatoxin-a, and cylindrospermopsin, set between 1.0 and 1.5 μg/L (*180*). The World Health Organization (WHO) also has issued a provisional guideline of 1.0 μg of microcystin-LR in drinking water (www.who.int/water_sanitation_health/dwq/en/gdwq3_12.pdf), and the European Drinking Water Directive has a guideline of 0.1 μg/L. Many of these toxins have relatively high molecular weights, and are highly polar. Methods for algal toxins include LC/MS, LC/MS/MS, matrix-assisted laser desorption/ionization-MS, ESI-FAIMS-MS, LC, and ELISAs. Using these methods, detection limits ranging from low nanograms per liter to low micrograms per liter can be achieved.

Several reviews have been published in the last 2 years on algal toxins. Hawkins et al. reviewed analytical methods for microcystins and their corresponding cyanobacteria (*181*). Perez and Aga reviewed recent developments for analyzing microcystins, including new extraction methods (e.g., immunosorbents) and new LC/MS/MS developments for measuring and identifying new transformation products (*182*). Advanced oxidation and other removal processes are also discussed. Msagati et al. reviewed extraction methods (including ELISAs) and detection methods (including LC and LC/MS) for measuring microcystins and nodularins (*183*). Diehnelt et al. published a review on the use of LC/MS/MS and exact mass measurements with FT-ion cyclotron resonance-MS for measuring microcystins and for identifying new microcystins (*184*).

New methods have also been reported in the last 2 years. Zhao et al. developed a SPME-microbore-LC/Q-TOF-MS method for measuring microcystins in water (*185*). Detection limits of 0.6 and 1.6 pg were possible for microcystin-RR and microcystin-LR, respectively. Recoveries were >86 and >70%, respectively. This technique also required small sample volumes (12 mL) and provides sensitive and information-rich analysis of unknown toxins. Li et al. developed a new LC/MS/MS method for measuring microcystin-LR in drinking water (*186*). Enhanced sensitivity (1-pg detection limit) was achieved by using the doubly charged microcystin-LR as a precursor ion for MRM analysis.

Cong et al. created a LC/ESI-MS/MS method for measuring microcystin-RR, -LR, -LW, and -LF in water (*187*). Recoveries ranged from 95 to 105%, and quantification limits of 0.04−1.0 μg/L could be achieved. Bogialli et al. developed a LC/MS/MS method for measuring anatoxin-a in lake water and fish muscle (*188*). After filtration, anatoxin-a could be analyzed directly by injecting 0.5 mL of the water sample onto the LC column. The limit of quantification in water was 13 ng/L. Derivatization with 2-[4-(2-hydroxyethyl)-1-piperazinyl]ethanesulfonic acid (HEPES) and analysis by LC/ESI-MS/MS was the focus of a new method for cylindrospermopsin (*189*). The quantification limit was 0.16 ng. Surface-enhanced laser desorption/ionization-TOF-MS was used in another method to measure microcystins in water (*190*). An innovative extraction/sample enrichment technique was used in this method: a protein chip coated with a microcystin antibody. Unlike conventional immunoassays, individual microcystin congeners could be resolved from mixtures, and this method allowed levels as low as 0.025 μg/L to be measured.

Several nice occurrence studies have been conducted in the last 2 years. In a large occurrence study in New Zealand, Wood et al. used ELISAs, LC/MS, LC, and neuroblastoma assays to measure microcystins and nodularins in 227 different water bodies between 2001 and 2004 (*191*). Microcystins were identified in 54 different water bodies; concentrations as high as 36.5 mg/L were found in the algal mass. Anatoxin-a was found in three water bodies, and saxitoxins were found in 41 water bodies, but at lower levels than the other algal toxins. The detection of anatoxin-a was the first definitive report for New Zealand. Bogialli et al. developed a SPE-LC/MS/MS method to measure five microcystins (microcystin-RR, -YR, -LR, -LA, and -LW) and cylindrospermopsin in water (*192*). Limits of quantification of 2−9 and 300 ng/L were achieved, respectively. Using this method, a lake in Italy was monitored in different regions and depths for 4 months. Cylindrospermopsin was the most abundant algal toxin found, reaching as high as 16.0 μg/L. Of the five microcystins measured, microcystin-YR reached the highest level at 9.2 μg/L. In addition, two desmethyl-microcystin-RR isomers were found in the lake water, and their levels reached 2.2 μg/L. Demethylated microcystin-RR variants are characteristic toxic markers of the algal species, *Planktothrix rubescens*. Hoeger et al. used an ELISA-LC method to investigate the occurrence and removal of microcystin-LR in two drinking water treatment plants in Germany and Switzerland (*180*). The authors also give a nice summary of cyanobacteria and their toxins in drinking water treatment plants worldwide. Microcystin-LR concentrations ranged from below 1.0 μg/L to greater than 8 μg/L in raw source waters, but were below 1.0 μg/L after treatment with ozonation and filtration. Ozonation was found to be much more effective than chlorination for removing this microcystin.

New microcystins have also been identified in recent work. For example, Frias et al. identified a new microcystin variant, microcystin-hRhR, for the first time in a reservoir in Brazil (*193*). LC/ESI-MS/MS was used to elucidate its structure, which had two homoarginines in positions 2 and 4. Dos Anjos identified gonyautoxin-2, -3, and neosaxitoxin for the first time in a reservoir in Brazil (*194*). LC/ESI-MS/MS was used to determine the structures of these toxins during a cyanobacterial bloom event.

Finally, new studies have investigated the elimination of microcystins by chlorination and ozonation. Xagoraraki et al. found that extracellular microcystin-LR was inactivated by free chlorine, and the highest inactivation rates were achieved at pH 6.0, the lowest at pH 9.0 (*195*). Brooke et al. found a loss of microcystin-LA and -LR, along with a complete loss of toxicity with ozonation. Therefore, results indicate that the microcystins are not transformed into toxic byproducts with ozonation (*196*).

ARSENIC

Unlike many other contaminants that are anthropogenic, arsenic contamination of waters generally comes from natural

sources. Arsenic contamination of drinking water in Bangladesh and India has become a highly recognized problem, but natural arsenic contamination also affects several regions of the United States and other parts of the world. In 2002, the U.S. EPA lowered the MCL for arsenic in drinking water from 50 to 10 μg/L (www.epa.gov/safewater/arsenic). Drinking water systems had to comply with this new standard by January 23, 2006. The WHO also has this same standard of 10 μg/L in drinking water. 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 addition, there are recent reports of excess risk of spontaneous abortion, stillbirth, and neonatal death.

Different arsenic species have different toxicities and chemical behavior in aquatic systems, so it is important to be able to identify and quantify them. More than 20 arsenic species are present in the natural environment and in biological systems. These include arsenite, arsenate, monomethylarsonic acid, monomethylarsonous acid, dimethylarsinic acid, dimethylarsinous acid, trimethylarsine oxide, trimethylarsine, arsenobetaine, arsenocholine, tetramethylarsonium ion, dimethylarsinoyl ethanol, and arsenosugars (5).

A puzzling observation about arsenic has been the drastic difference in metabolism, disposition, and carcinogenicity between humans and rats. In particular, rats show a longer retention time in the blood for arsenic, whereas arsenic is rapidly cleared from human blood (half-life of 1 h). These biological differences have not been understood and can limit the use of animal models for understanding human health effects. Lu et al. made an important new discovery that may explain these differences (*197*). In characterizing arsenic species in rats that were treated with inorganic arsenate, monomethylarsonic acid, and dimethylarsinic acid, they found that arsenic significantly accumulated in the red blood cells of rats in the form of hemoglobin complexed with dimethylarsinous acid, regardless of the species of arsenic the rat was exposed to. This suggests a rapid methylation of arsenic species, followed by strong binding of dimethylarsinous acid to rat hemoglobin. The binding site was found to be cysteine-13 in the α chain of rat hemoglobin, with a stoichiometry of 1:1. More than 99% of the total arsenic in rat blood cells was bound to hemoglobin. The lack of cysteine-13-α in human hemoglobin may be responsible for the shorter retention of arsenic in human blood, and these differences in disposition of arsenic species may contribute to the differences in susceptibility of carcinogenicity.

Munoz and Palmero published a review on the analysis and speciation of arsenic by stripping potentiometry (*198*). Advantages of stripping potentiometry compared to other electrochemical methods is discussed. New methods for arsenic species have also been published. Ronkart et al. developed a LC/ICPMS method to measure arsenite, arsenate, monomethylarsonic acid, dimethylarsinic acid, and arsenobetaine in water (*199*). Detection limits were approximately 0.4 pg. This method was used to measure arsenic species in surface and well waters in Belgium. Arsenite and arsenate were the major species found in surface and well waters, but arsenobetaine and dimethylarsinic acid were also found in surface waters. In other natural mineral waters near a volcanic region, arsenic levels exceeded the maximum admissible arsenic content. Niedzielski developed a new method using LC/hydride generation-fast sequential-atomic adsorption spectrometry to simultaneously measure arsenic(III), arsenic(V), selenium(IV), and selenium(VI) (*200*). Detection limits were 7.6 ng/mL (μg/L) for As(III) and 12.0 ng/mL for As(V). Anthemidis and Martavaltzoglou created a flow injection-SPE-on-line hydride generation-atomic absorption spectrometry method for measuring arsenic(III) in water (*201*). Poly(tetrafluoroethylene) turnings were used to extract and concentrate the arsenic on a microcolumn. The method involves a 60-s preconcentration time for a 10.4-mL sample, a sampling frequency of 25 samples/h, and a detection limit of 20 ng/L. Morita and Kaneko reported a new spectrophotometric method for measuring arsenic in water (*202*). This method involved the use of nanoparticles of ethyl violet with a molybdate−iodine tetrachloride complex as a probe for molybdoarsenate. When arsenic is present in a water sample, the reaction gives a purple color, with an intensity proportional to the amount of arsenic present. Detection limits of 0.5 μg/L were achieved. Measurements with this method compared favorably with hydride generation atomic absorption spectrometry.

Finally, Pellizzari and Clayton measured total arsenic and arsenic species (arsenate, arsenite, dimethylarsenic acid, monomethylarsonic acid, arsenobetaine, arsenocholine) in archived samples from the National Human Exposure Assessment Survey (NHEXAS) and in a Children's Study in Minnesota (*203*). Samples included drinking water, urine, hair, dust, and food. Except for arsenobetaine and arsenic(V), the levels found in drinking water and food were low or nondetectable. However, additional arsenic species were present in the samples (likely organic forms of arsenic), as judged by total arsenic measurements. Exposures to total arsenic in food were about twice as high as in the general population (17.5 vs 7.72 μg/L). The predominant form of arsenic in drinking water was As(V).

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. Several microorganisms are included on the U.S. EPA's CCL (Table 7). The U.S. EPA's National Exposure Research Laboratory in Cincinnati has developed several methods for measuring microorganisms in water (www.epa.gov/nerlcwww). These include methods for *Cryptosporidium*, *Giardia*, *E. coli*, *Aeromonas*, coliphages, viruses, total coliforms, and enterococci.

Several important microorganisms were recently included in a special issue on Emerging Contaminants in the journal *Environmental Science & Technology*. *E. coli* O157:H7 is currently capturing a lot of attention because it has caused a number of outbreaks and deaths around the world. Muniesa et al. reviewed the occurrence of *E. coli* O157:H7 and other enterohemorrhagic *E. coli* in the environment (*204*). The authors also summarize methods for measuring *E. coli* O157:H7, which include culture and immunological methods and nucleic acid-based methods (including polymerase chain reaction, PCR), While outbreaks of *E. coli* O157:H7 are often tracked to food contamination, 15% of all outbreaks in the United States were drinking water related, and many outbreaks were due to swimming in lakes and rivers

(*204*). Water is the third highest known route of transmission after food-borne and person-to-person transmission. Humans and animals are the source of *E. coli* O157:H7, which release shiga toxins to induce hemorrhagic colitis. Abulreesh et al. reviewed the occurrence of *Campylobacter* in the aquatic environment and summarized methods for their detection, including culture methods, PCR, and DNA sequencing (*205*). Filtration methods for recovering *Campylobacter* from water are also discussed. Wild birds, especially waterfowl, have been recognized as sources for *Campylobacter*, and outbreaks of gastroenteritis have been linked to contaminated food and drinking water. Jiang reviewed the occurrence and health implications of human adenoviruses (*206*). Adenoviruses are one of nine microorganisms on the U.S. EPA's CCL for drinking water because their survival in drinking water is not fully understood. Viruses are much smaller than other commonly measured microorganisms (including *E. coli*), and can escape filtration barriers designed to remove them. Adenoviruses are also more resistant to treatment (including UV treatment) and to environmental degradation (*206*). A challenge in measuring adenoviruses in environmental waters is the generally low level in environmental waters, which necessitates amplification methods, such as PCR. The development of PCR techniques has dramatically increased the reports of adenoviruses in river and coastal waters. Adenoviruses come from humans and a variety of animals, but only human adenoviruses infect humans. Adenoviruses have been implicated in enteric illnesses, as well as respiratory and eye infections, and some of the first detections of human adenoviruses were made in swimming pool water, where low chlorine residuals were associated with disease outbreaks (*206*).

Several new occurrence studies have been published in the last 2 years for emerging microorganisms. Albinana-Gimenez et al. measured human polyomaviruses, adenoviruses, and hepatitis E virus in environmental samples and in drinking water (*207*). In this study, water samples were centrifuged and filtered, and nested-PCR was used for amplification. Human adenoviruses and JC polyomavirus (JCPyV) were detected in river water, and 99% removal was obtained with granular activated carbon filtration in drinking water treatment. However, low concentrations of the viruses were still detected in the prechlorinated drinking water. A risk assessment for noroviruses in drinking water was conducted by Masago et al. (*208*). Noroviruses have been estimated to be responsible for as many as 23 million cases of gastroenteritis a year in the United States. Most cases occur in closed settings, such as hospitals and nursing homes, but some waterborne outbreaks have been documented (*208*). The annual risk in this study was determined to be higher than the U.S. EPA's acceptable risk level (10^{-4} infection per person per year). Cooling towers were the focus of another occurrence study by Berk et al. (*209*). Amoebae pathogens that are similar to *Legionella*, but have been ignored in previous studies, were measured in this study. Centrifugation and PCR were used to measure these infected amoebae, and their occurrence in cooling towers was compared to environmental waters to determine whether cooling towers were "breeding grounds" for these pathogens. In fact, 22 of the 40 cooling tower samples were positive for the infected amoebae, but only 3 of the 40 environmental waters sampled were positive, suggesting the importance of cooling towers in the transmission of these emerging pathogens. The majority of the infecting bacteria appeared to be something other than *Legionella pneumophila*, strengthening the idea that many pneumonia-like infections in humans may be due to novel amoeba-associated microorganisms that are difficult to culture and are not typically measured.

Finally, Heinemann et al. discussed the use of a new concept, called an environment array, for identifying emerging waterborne threats (*210*). The environment arrays would use a genomics-based approach, but would not depend on a priori knowledge of virulence genes. These environment arrays would be assembled from molecular profiles of the infectious elements that transfer between bacteria (called integrons). With this system, a wide range of bacteria could be measured, without having to culture the organisms.

NANOMATERIALS AND OTHER CONTAMINANTS ON THE HORIZON

Two emerging contaminants on the horizon are worthy of mentioning here: nanomaterials and siloxanes. Both are important emerging areas that are in their infancy, but for which rapid growth is expected in the next few years. Nanomaterials are the focus of a new initiative at the U.S. EPA, where research on their ecologic fate, transport, and health effects will be investigated. In addition, universities are forming new departments built around the study of nanomaterials, and government investment in nanotechnology has dramatically increased in the last 5 years. Nanomaterials are 1−100 nm in size and can have unique properties, including high strength, thermal stability, low permeability, and high conductivity. Nanomaterials are already being manufactured and used in many products, including cosmetics, sunscreens, clothing, automobiles, and electronics. In the near future, nanomaterials are projected to be used in areas such as chemotherapy, drug delivery, removal of pollutants from contaminated groundwater, and labeling of food pathogens ("nano bar codes"). However, there is significant concern about their potential human and ecological effects (*211*) that could result from distribution of these substances in the environment. Early efforts to assess environmental exposure to manufactured nanomaterials have been initiated (*212*). Siloxanes are also becoming an intense area of research. These include octamethylcyclotetrasiloxane (D4), decamethylcyclopentasiloxane (D5), and dodecamethylcyclohexasiloxane (D6), which are used in a number of products, such as cosmetics, deodorants, soaps, hair conditioners, hair dyes, car waxes, and water-repellent windshield coatings. There is concern about potential toxicity and transport into the environment.

MISCELLANENOUS TECHNIQUES AND APPLICATIONS

A couple of recently developed analytical techniques were reviewed in the last 2 years, and they are included here. The recent combination of 2-D GC with TOF-MS is revolutionizing the identification and measurement of trace contaminants in complex environmental samples. TOF-MS as a detector allows the collection of many mass spectra per second and is an ideal detector for 2-D GC, which produces many more separated GC peaks than traditional GC. 2-D GC works by separating compounds on two different GC columns, which provide independent separation mechanisms. Data are plotted in 2-D plots of retention time in

dimension 2 versus retention time in dimension 1. Panic and Gorecki published a review summarizing 2-D GC and discusses recent applications in environmental monitoring (*213*). The development of Q-TOF-MS has also revolutionized the elucidation of unknown environmental contaminants by LC/MS. Traditional LC/MS is generally carried out a single quadrupole or triple quadrupole mass spectrometer, which are good instruments for carrying out quantitative analyses of known pollutants. However, these instruments generally only allow unit mass resolution and are often insufficient for elucidating the structures of unknown chemical contaminants. Because Q-TOF mass spectrometers can achieve 10 000−12 000 resolution, they provide exact mass data and allow empirical formulas to be obtained for unknown contaminants. Many recent studies have used them for this purpose (e.g., for the identification of pesticide and pharmaceutical degradation products) and are included in previous sections in this review. Ibanez et al. discussed the use of Q-TOF-MS in the elucidation of unknown contaminants in environmental waters in a recent paper (*214*). Finally, Ferrer and Thurman published a paper that is particularly relevant to the use of higher resolution techniques in LC/MS analyses (e.g., TOF-MS, Q-TOF-MS, and FT-MS) (*215*). They discussed the observation of "twin ions" in negative ion and positive ion-ESI-TOF-MS, which had the same nominal mass, but a different exact mass. The difference was due to the mass of an electron that can only be observed with higher resolution techniques, such as TOF-MS, Q-TOF-MS, or FT-MS. The mass of an electron (0.000 55 Da) can be important to include in exact mass measurements.

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