Identifying Future Drinking Water Contaminants

1998 Workshop on Emerging Drinking Water Contaminants, National Research Council

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Board on Environmental Studies and Toxicology
Commission on Geosciences, Environment, and Resources
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Preface

With an increasing population, use of new and diverse chemicals that can enter the water supply, and emergence of new microbial pathogens, the U.S. federal government is faced with a regulatory dilemma: Where should it focus its attention and limited resources to ensure safe drinking water supplies for the future? The availability of increasingly powerful analytical methods for the detection and identification of smaller and smaller amounts of chemicals and microorganisms in the environment, many of them never before detected, complicates these decisions.

To help address these difficult issues, one of the major requirements of the Safe Drinking Water Act (SDWA) Amendments of 1996 is that the U.S. Environmental Protection Agency (EPA) publish a list of unregulated chemical and microbial contaminants and contaminant groups every five years that are known or anticipated to occur in public water systems and that may pose risks in drinking water. The first such list, called the Drinking Water Contaminant Candidate List (CCL), was published in March 1998. The CCL's primary function is to provide the basis for deciding whether to regulate at least five new contaminants from the CCL every five years. However, additional research and monitoring need to be conducted for many, if not most, of the contaminants on the current CCL. Thus, the CCL is also used to prioritize research activities.

At EPA's request, the Water Science and Technology Board (WSTB) and the Board on Environmental Studies and Toxicology (BEST) of the National Research Council (NRC) jointly formed the Committee on Drinking Water Contaminants to help the EPA develop and use the first and successive CCLs in a scientifically defensible manner. Specifically, EPA asked the committee for assistance in addressing three related tasks:

1. developing a scientifically sound approach for deciding whether or not to regulate contaminants on the current and future CCLs,
2. convening a workshop that focused on emerging drinking water contaminants and the database that should be created to support future decision-making on such contaminants, and
3. developing a scientifically sound approach for developing future CCLs.

While these tasks initially seemed closely related, one year, three meetings, and two reports have proved otherwise. The committee discovered through the presentations of several guest speakers, a review of relevant literature, and committee deliberations that the tasks were sufficiently different

and independent to demand additional time and meetings for each to be fully addressed. The committee gave thorough attention to the fast task in its fast report, *Setting Priorities for Drinking Water Contaminants*, which provides a phased decision process for determining which contaminants on a CCL are appropriate candidates for regulatory decisions and which will require research or monitoring. However, the committee had very little time to address the last two tasks, which are the subject of this report. Due to the short time available, the recommended approach for the development of future CCLs that is provided in this report is conceptual. The EPA would benefit from a more careful, detailed assessment of the CCL development process and how to identify critical contaminants for regulation from among tens of thousands of potential candidates.

This report is based on a series of presentations and subsequent committee deliberations that occurred at a December 2-4, 1998, workshop on emerging drinking water contaminants. The purpose of the workshop was to present and discuss a dozen papers on emerging microbiological and chemical drinking water contaminants, associated analytical and treatment methods, and existing and proposed environmental databases for their proactive identification and regulation. The presented papers are included in this volume. Following the open presentations, the committee met in closed session for the latter half of December 3 and all day on December 4 to develop a consensus-based approach and related recommendations for the creation of future CCLs. The approach and recommendations were developed exclusively from information gathered and discussed at the workshop, the committee's first report, and the expertise of committee members. The consensus report precedes the workshop papers.

I speak for the entire committee in thanking the workshop presenters and paper co-authors for their diligence and time in making the workshop a truly educational and enlightening experience for us all. I would also like to thank John Chelen of the Unison Institute and Jeanette Wiltse of the EPA for their remarks at the workshop. On behalf of the committee, I also wish to thank Jim Taft and Evelyn Washington of the EPA for supporting this important study throughout its development and fulfillment.

I also thank the very capable and professional assistance that the committee has received from the NRC staff. In particular, I want to acknowledge the outstanding efforts that we have received from Jacqueline MacDonald, study director and WSTB associate director; Mark Gibson, WSTB research associate; Carol Maczka, BEST director of toxicology and risk assessment programs; and Kimberly Swartz, WSTB project assistant. These staff members worked extraordinarily hard and effectively to help us produce this report in a very short period of time, in order to be of maximum utility to the EPA as it moves forward in using the current CCL and creating the next CCL.

This report has been reviewed, in accordance with NRC protocol, by individuals chosen for their expertise and broad perspectives on the issues addressed herein. The purpose of the external review is to provide independent, candid, and critical comments that will help ensure that the report is scientifically sound and meets NRC's standards for objectivity, evidence, and responsiveness to the study charge. The committee wishes to thank the

following people for their participation in this review and for their many constructive comments: Richard A. Conway, Union Carbide Corporation (retired); Joseph A. Cotruvo, NSF International; Gunther F. Craun, Gunther F. Craun & Associates, Staunton, Virginia; Joseph J. Delfino, University of Florida; Ann. N. P. Fisher, The Pennsylvania State University; and Eric D. Olson, Natural Resources Defense Council. The final content of this report is the responsibility of the Committee on Drinking Water Contaminants.

Lastly, I want to thank the diverse and talented members of the committee, who were once again able to bring together their different perspectives and extensive expertise to produce this report. I look forward to continue working with this wonderful group to help the EPA address other pressing drinking water issues and requirements mandated under the SDWA Amendments of 1996.

WARREN R. MUIR, PH.D.
CHAIR, COMMITTEE ON DRINKING WATER CONTAMINANTS

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Committee Report
A Conceptual Approach for the Development of Future Drinking Water Contaminant Candidate Lists

Americans drink billions of gallons of tap water each year, usually with little or no thought about its origins or safety. While this unquestioning faith has been largely justified in this century through advances in water treatment and source water protection efforts, chemical, microbiological, and other types of contaminants still occur in drinking water supplies. The presence of such contaminants, as well as more than two dozen documented outbreaks of waterborne disease that occur, on average, each year, constitute a reminder that unprotected and contaminated drinking water can still pose real health risks (NRC, 1997). Continuing public health vigilance is necessary to ensure that drinking water contaminants, especially new and emerging ones, are identified and that their health risks are appropriately addressed.

The Safe Drinking Water Act (SDWA) Amendments of 1996 substantially changed the way in which new drinking water contaminants are identified and regulated. Under these amendments, every five years the U.S. Environmental Protection Agency (EPA) must develop a list of currently unregulated priority contaminants that may pose risks in drinking water. Subsequently, EPA must decide whether or not to regulate at least five of those contaminants. In March 1998 (EPA, 1998a), EPA published the fast of these lists, known as the Drinking Water Contaminant Candidate List (CCL).

In support of these new requirements, EPA asked the National Research Council (NRC) for assistance with three of its tasks under the SDWA amendments:

1. developing a scientifically sound approach for deciding whether or not to regulate contaminants on the current and future CCLs,
2. identifying emerging drinking water contaminants and creating a database to support future decision-making on such contaminants, and
3. developing a scientifically sound approach for creating future CCLs.

In response to EPA's request, the NRC appointed the Committee on Drinking Water Contaminants in 1998. The committee consists of 14 volunteers with expertise in water treatment engineering, toxicology, public health, epidemiology, water and analytical chemistry, risk assessment, risk communication, public water system operations, and microbiology.

The committee's first report, *Setting Priorities for Drinking Water Contaminants* (NRC, 1999), addresses the first of the three topics above: it recommends a decision framework and related criteria for making decisions regarding regulation, research, and data collection for contaminants on current and future CCLs. This volume addresses the second and third topics. The individually-authored papers that follow this committee-authored report were presented at a December 1998 workshop focused on the most recent information available on new and emerging chemical and microbiological drinking water contaminants, treatment technologies, and related databases. This committee report recommends a conceptual process and related criteria for the development of future CCLs. Due to the limited time available for the committee to meet and prepare this report, the level of detail of the recommendations is limited.

LIMITATIONS OF THE FIRST CCL DEVELOPMENT PROCESS

In the *Federal Register* notice accompanying publication of the first draft CCL, EPA noted that the "first CCL is largely based on knowledge acquired over the last few years and other readily available information, but an enhanced, more robust approach to data collection and evaluation will be developed for future CCLs" (EPA, 1997a). Several public commenters on the aft CCL also noted the need for a more systematic and scientifically defensible approach for selecting contaminants for future CCLs (EPA, 1998b). Chapter 4 of the committee's first report (NRC, 1999) summarizes the development of the first CCL in detail. Based on this review, several limitations of the fast development process can be identified.

First, EPA used separate approaches to evaluate chemical and microbiological contaminants. All microbial contaminants included on the first CCL were identified by a group of experts that qualitatively evaluated a list of potential microbiological contaminants prepared by EPA, as well as other microorganisms identified during deliberations, according to a series of baseline criteria. The baseline criteria were: (1) the organism's public health significance, (2) known waterborne transmission of the organism, (3) occurrence of the organism in source water, (4) effectiveness of current water treatment methods in controlling the organism, and (5) adequacy of analytical methods for detecting the organism (NRC, 1999). In contrast, EPA relied extensively on culling existing lists of chemicals to identify potential chemical drinking water contaminants for inclusion on the first draft CCL.

Second, all potential chemical contaminants that were initially considered for inclusion on the CCL were taken directly from 10 (later reduced to 8) existing lists of chemicals produced by various regulatory programs within EPA and from stakeholder groups. This list of 391 chemicals was then narrowed to 50 chemicals and chemical groups using pre-defined screening criteria. This approach, while useful for developing a CCL in a short time period, is like "looking under the lamp post" because it overlooks potential chemical contaminants not previously identified through inclusion on one of the selected lists. For example, the first CCL development process did not collect and evaluate data on radionuclides, most degradation products of known contaminants, or even all classes of commercial chemicals (such as

pharmaceuticals). While the contaminants listed on the current CCL certainly merit consideration, a broader approach to CCL development potentially could identify higher risk contaminants.

Finally, in the selection of chemical contaminants for inclusion on the first CCL, EPA evaluated health effects and occurrence data on chemical contaminants sequentially rather than simultaneously. Specifically, EPA eliminated all contaminants from its list of 391 chemicals that did not meet either of two multi-component criteria specifying potential for occurrence in drinking water (see the committee's fast report). Any contaminant that met either of the occurrence criteria was subsequently evaluated for any evidence or suspicion that it may cause adverse health effects in exposed persons. An affirmative finding to any of eight health criteria resulted in the contaminant's inclusion on the CCL. By evaluating occurrence before any evaluation of health effects data could take place, EPA may have inadvertently excluded potential chemical contaminants associated with adverse health effects that are important even if known occurrence of the contaminant is limited.

Due to these limitations of the first CCL development process, the committee contends a new type of screening process should be used to identify and evaluate a broader universe of microbiological, chemical, and other types of potential drinking water contaminants in order to provide a more objective list of contaminants of concern.

IDENTIFYING AND SELECTING CONTAMINANTS FOR FUTURE CCLS

If resources were unlimited and if information were perfect, an ideal CCL development process would include the following features:

- It would meet the statutory requirements of the SDWA Amendments of *1996*, including requirements for consultation with the scientific community and opportunities for public comment.
- It would start by identifying the entire universe of potential drinking water contaminants prior to any attempts to rank or sort them.
- It would consider risks from all potential routes of exposure to water supplies, including dermal contact and inhalation as well as ingestion.
- It would use the same identification and selection process for microbial, chemical, and all other types of potential drinking water contaminants.
- It would have mechanisms for identifying similarities among contaminants and contaminant classes that can be used to assess potential risks of individual contaminants.
- It would result in CCLs containing only contaminants that, when regulated, would reduce disease, disability, and death, and it would exclude contaminants that have few or no adverse effects on human health (e.g.,

contaminants entirely removed or detoxified through conventional drinking water treatment methods).

However, EPA's resources are constrained, no comprehensive list of potential drinking water contaminants exists, and there is a paucity of data on occurrence or health effects for the vast majority of potential contaminants. Thus, an ideal CCL selection process cannot be achieved at this time. However, there are practical steps that EPA can take to move in the direction of such an ideal. In this regard, the committee believes that EPA can and should develop and use a process that:

- starts broadly, using existing lists of potential drinking water contaminants, supplemented by readily available information;
- considers microbiological, chemical, and other types of potential contaminants in a common selection process;
- takes advantage of structure-activity relationships to help overcome deficiencies in health effects and occurrence data;
- expands the knowledge base over time;
- uses simple criteria, supplemented by expert judgment, to initially cull the candidates to a preliminary list; and
- employs a prioritization scheme, again supplemented by expert judgment, to identify final candidates for inclusion on a CCL.

The conceptual approach for developing future CCLs that the committee envisions for EPA is a two-step process, as shown in Figure 1. Under this two-step approach, the "universe" of potential contaminants, derived from a wide

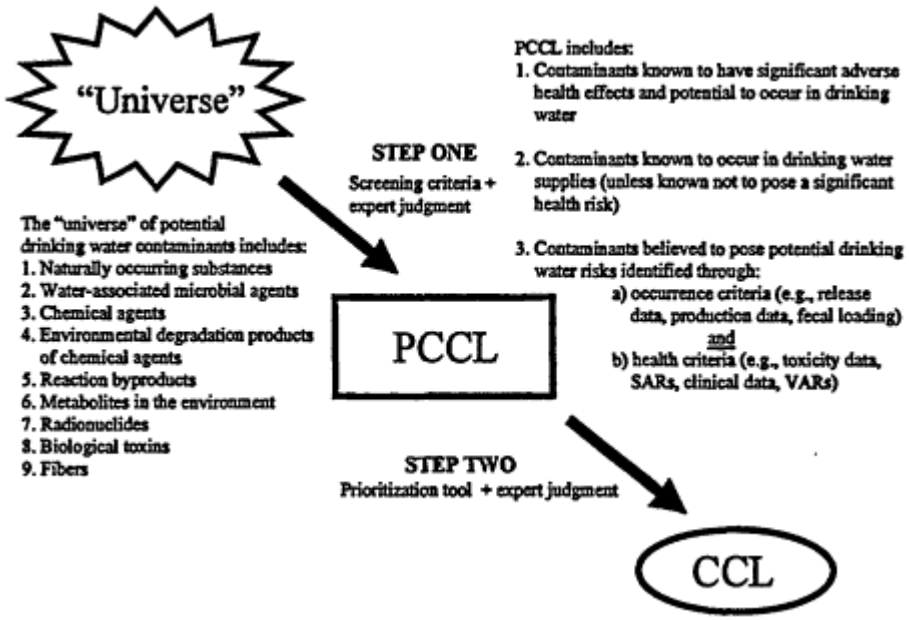

Figure 1
Conceptual two-step process for developing future CCLs.

variety of sources, would be combined and culled using simple criteria and expert judgment to prepare a "preliminary CCL" (PCCL). Next, the PCCL would be processed, using more information in conjunction with a quantitative screening tool and expert judgment, to prioritize which contaminants should be listed on the CCL to drive research and regulatory efforts equally. The process would be repeated for each CCL development cycle to account for new data and potential contaminants that inevitably arise over time. In addition, all contaminants that have not been regulated or removed from the existing CCL would be automatically retained on each subsequent CCL.

A Broad Approach

The committee identified 9 major drinking water contaminant categories (with 12 subcategories) that comprise the range of substances and microbes that should be evaluated for inclusion on future CCLs. These are listed in Table 1, along with examples of contaminants in each category. The total number of contaminants in this universe is likely to be close to 100,000, given that the Toxic Substances Control Act (TSCA) inventory of commercial chemicals alone includes about 72,000 substances.

Lists exist for some categories of potential drinking water contaminants; for others, no lists exist. The committee recommends that EPA consider the categories and subcategories of potential contaminants listed in Table 1, starting with lists that are available and information that is readily obtainable to supplement them. The committee also recommends that EPA develop a strategy for filling the gaps and updating the existing databases and lists of contaminants (e.g., through the National Drinking Water Advisory Council or panels of experts) for future CCLs. The strategy should be developed with public, stakeholder, and scientific community input.

Adherence to these recommendations would result in EPA considering expanded numbers and types of potential contaminants, in comparison to those considered for the first CCL (EPA, 1997a).

As an integral part of the CCL development process, the committee recommends that the lists be combined in a consolidated database that provides a consistent mechanism for recording and retrieving information on the contaminants under consideration. The chemicals database of the Interagency Testing Committee is an example of such a database. The database should be structured to accommodate microbial pathogens, mixtures of agents, and other types of potential contaminants that are not necessarily defined by a unique chemical formula. Such a database can function as a "master list" that contains a detailed record of how the PCCL and CCL were developed, as well as providing a powerful analytical tool for the development of future CCLs. The database should be prepared, maintained, and updated in open cooperation with the public, stakeholders, and the scientific community.

TABLE 1 Universe of Potential Drinking Water Contaminants

Category	Examples
Naturally occurring substances	Arsenic, hydrogen sulfide
Microbial agents	
Naturally occurring agents in water	*Legionella*, toxic algae
Agents associated with human feces	Enteric viruses, coxsackie B viruses, rotavirus
Agents associated with human and animal feces	Enteric protozoa and bacteria, *Cryptosporidium, Salmonella*
Agents associated with human and animal urine	Nanobacteria, microsporidia
Agents associated with water treatment and distribution systems	Biofilms, *Mycobacterium*
Chemical agents	
Commercial chemicals	Tetrachloroethene, liquid fuels
Pesticides	Atrazine, alachlor
Pharmaceuticals	Estrogen, diclofenac (antirheumatic), carbamazepine (antiepileptic), chloramphenicol (antibiotic)
Cosmetics	Musk xylenes, boron
Food additives	Propylene glycol, dyes
Water additives, including impurities	Aluminum
Water treatment and distribution system leachates and degradates	Vinyl chloride
Environmental degradation products of chemical agents	Dichlorodiphenyldichloroethylene, trichloroacetic acid
Reaction byproducts	Polycyclic aromatic hydrocarbons, 2,3,7,8-tetrachlorodibenzodioxin, trihalomethanes
Metabolites in the environment	Metabolites of pharmaceuticals (e.g., clofibric acid, fenofibric acid)
Radionuclides	Tritium, uranium, strontium-90
Biological toxins	Mycotoxins, aflatoxins
Fibers	Asbestos

As the database is expanded, estimates can be used to address important gaps in health effects and occurrence data, based on structure-activity relationship (SAR) models for chemical contaminants and virulence-activity

relationships (VARs) for microbial agents[1]. EPA regularly develops and uses SARs to review thousands of new chemical premanufacture notices each year.

Culling the Universe to Create a PCCL

As a starting point, the PCCL should automatically include all substances and microbes known to cause significant adverse health effects (regardless of exposure route) that could occur in drinking water, as well as those with demonstrated occurrence in drinking water supplies (unless they are known not to pose a significant health risk). A PCCL should also include all substances that may pose a drinking water risk based on their potential for occurrence and health effects. The committee leaves EPA to define and apply such terms as "known," "significant," and "demonstrated," taking into consideration that the PCCL is intended to be inclusive rather than exclusive.

Tables 2 and 3 list examples of existing and planned relevant sources of information for potential (primarily commercial) chemical contaminants with known health effects and demonstrated occurrence in drinking water, respectively. Table 4 summarizes this information for water-associated microbial pathogens. In this regard, the committee strongly urges EPA be proactive in identifying and regulating emerging microbiological drinking water contaminants; waiting until after major waterborne disease outbreaks occur is an inadequate and ineffective means to prevent future outbreaks and protect public health.

The databases for chemicals shown in Tables 2 and 3 will generate a large list of substances—too large to be included on the PCCL in its entirety. Therefore, EPA will need to develop methods to rapidly cull from these databases a shorter list of chemicals for inclusion on the PCCL. The committee envisions that the PCCL would contain on the order of thousands of substances.

The committee recommends that such culling be based upon simple objective criteria, supplemented by expert judgment. For example, because environmental occurrence data for the vast majority of these chemicals are lacking, and because collecting enough monitoring data to fill this void would be far too expensive and time consuming, the committee recommends that EPA consider a simple production cutoff approach to narrow the universe of commercial chemicals. A practical cutoff value to use might be 100,000 lbs. (45,350 kg) That is, any commercial chemical produced in quantities below 100,000 lbs./year (45,350 kg/year) should be dropped from consideration for the

[1] While such virulence-activity relationships have not yet been catalogued for microbes, EPA could develop such an approach for these contaminants in cooperation with the Centers for Disease Control and Prevention, National Institutes of Health, and other federal and state health organizations. Gene data banks, now used to search for commonalities in genes and evolutionary relationships associated with disease, virulence, toxin production, and health risks, should make this type of effort possible.

PCCL, unless otherwise included based upon health effects concern. Such a cutoff would produce a list of a few thousand chemicals, based on data currently

TABLE 2 Examples of Existing and Planned Information Sources for Chemicals Known to Cause Adverse Health Effects[a]

Name	Responsible Agency or Organization	Notes
Integrated Risk Information System	EPA	Official EPA summary of health effects information and reference doses or concentrations for approximately 600 compounds
Hazardous Substances Data Base	National Library of Medicine (NLM)	Summary of peer-reviewed health effect studies (about 2,000)
Registry of Toxic Effects of Chemical Substances	National Institutes of Occupational Safety and Health	Tabulation of effect levels for many substances reported in scientific literature
International Agency for Research on Cancer (IARC)	IARC	Expert group summaries of carcinogenic properties for a wide variety of substances and mixtures
National Research Council	NRC	Expert group publications summarizing health effects information, critical end points, and doses (e.g., arsenic, radon)
Toxic Substances Control Act Test Submissions-Health Effects	EPA	Information on unpublished health effects data for industrial chemicals
Peer-reviewed published literature		Individual studies about health effects and related information (e.g., metabolism)
TOXLINE	NLM	Abstracts of peer-reviewed toxicology-related studies
MEDLINE	NLM	Abstracts of peer-reviewed studies in medical literature

[a] Includes acute and chronic health effects, such as genotoxicity, developmental toxicity, reproductive toxicity, immunotoxicity, and carcinogenicity.
SOURCE: Adapted from EDSTAC, 1999.

TABLE 3 Examples of Existing and Planned Information Sources for Identifying Chemicals with a Demonstrated Occurrence in Drinking Water Supplies

Name	Responsible Agency or Organization	Notes
National Contaminant Occurrence Database	EPA	First operational version must be completed by August 6, 1999
Unregulated Contaminant Monitoring Rule	EPA	First list of ≤ 30 contaminants must be completed by August 6, 1999
National Ambient Water-Quality Assessment Program	U.S. Geological Survey (USGS)	Contaminant monitoring data for surface and ground water
Comprehensive Environmental Response, Compensation, and Liability Act Information System	EPA	Contaminant data for Superfund sites
Toxic Substances Control Act Inventory and Updates	EPA	Production volumes and sites for industrial chemicals
Permit Compliance System	EPA	Information on municipal and industrial wastewater discharge
Environmental Monitoring and Assessment Program	EPA	Monitoring information for air, ground water, surface water, biota, and soil contaminants
National Human Exposure Assessment Survey	EPA	Surveys designed to assess human exposure via multiple pathways (food, water, air, dust)

SOURCE: Adapted from EDSTAC, 1999.

TABLE 4 Examples of Existing and Planned Information Sources for Water-Associated Microbial Agents with Demonstrated Occurrence in Drinking Water Sources or Causing Adverse Health Effects

Name	Responsible Agency or Organization	Notes
National Waterborne Disease Outbreak Database	Centers for Disease Control and Prevention (CDC), EPA	Catalogs reported waterborne disease outbreaks since 1920
National Notifiable Diseases Surveillance System (NNDSS)	National Center for Health Statistics (NCHS) in the CDC	Compiles U.S. statistics on diseases. Reported cases are summarized by type of disease, reported month, state, age, and race in some cases. The data represent only clinically identified cases and case ratios (cases to total population) or incidence rates that are most often reported annually.
National Ambulatory Medical Care Survey	NCHS/CDC	Conducted in 1990, the survey provided data from office-based physicians through examination of patient records and gave an indication of the number of persons who seek a physician and are diagnosed
National Hospital Discharge Survey	NCHS	Begun in 1988, the survey assesses the number of patients treated in hospitals
National Mortality Followback Survey	NCHS	Represents about 1 percent of U.S. resident deaths
National Animal Health Reporting System	U.S. Department of Agriculture Animal and Plant Health Inspection Service, Veterinary Service, and Centers for Epidemiology and Animal and Animal Health	A pilot project begun in March, 1998, it will include all 50 states reporting on disease cases in commercial livestock (cattle, sheep, swine, poultry, fish)
State Department of Health Data	By state	Generally, state health departments report cases of disease by county

collected under TSCA (Carol Farris, EPA, personal communication, 1999).

Name	Responsible Agency or Organization	Notes
Land use data and mapping (e.g., sewage discharge, number of farms/heads of livestock, septic tanks, storm water drains)	USGS, states	
FoodNet data	CDC	Provides data on incidence of diseases associated with key enteric bacteria
Gen Bank	Indiana University and others	Internet-based database with information on gene sequences for key microorganisms

One key database that can provide such chemical production information is the TSCA chemical inventory. This database of more than 72,000 commercial chemicals in commerce is updated every four years with production data on nonpolymeric organic chemicals produced or imported by facilities in greater than 10,000 lbs./year (4,535 kg/year) quantities. Such data are invaluable for identifying commercial (nonpesticide, nonpharmaceutical, nonfood-additive) organic chemicals in production above 100,000 lbs. (45,350 kg). If EPA expands these updates to include inorganic chemicals or to include information on chemical uses, as it has been considering, such data could be the basis for refined criteria for culling the list of potential contaminants for inclusion on the PCCL.

A second way to cull the list of potential contaminants would be possible if EPA expands the reporting requirements for the Toxics Release Inventory (TRI—the best database available on releases and transfers of toxic chemicals from manufacturing facilities). EPA has expanded this list frequently, and expanded TRI data can be used as part of an improved basis for culling the list.

A third mechanism for EPA to use in shortening the list of potential chemical drinking water contaminants for inclusion on the PCCL could use a screen based on health effects data, when available, and SAP scores, when not. As previously noted, EPA has developed and used SAR scores for thousands of chemicals as part of its TSCA program. The development and use of microbial VARs would also greatly assist the evaluation of microbial pathogens with little or no occurrence data for inclusion on a PCCL.

As a fourth mechanism for culling the list, the committee envisions exclusion criteria for the PCCL based upon knowledge or reasonable expectation that there is little or no chance of a particular substance or microbe occurring in drinking water supplies.

In applying any or all of these criteria, the committee again urges EPA, when in doubt, to err on the side of safety and include the contaminant on the PCCL. However, the committee emphasizes that the development of a PCCL should not require extensive data collection and analysis or drive monitoring or research activities.

The committee recommends that all aspects of the PCCL development process should be made accessible to the public (e.g., posted on the Internet and published in the *Federal Register*) and should include the review and input of the scientific community. Further, whatever form EPA's future CCL development process takes, it must continue to comply with the relevant statutory requirements of the SDWA Amendments of 1996. For example, EPA must still consider, but not be limited to, certain substances referred to under the Comprehensive Environmental Response, Compensation, and Liability Act and substances registered under the Federal Insecticide, Fungicide, and Rodenticide Act (EPA, 1997).

Generating the CCL from the PCCL

To help narrow the PCCL to a manageable number of contaminants that can be considered for regulation, EPA should develop a single, quantitative tool that can be used to evaluate and prioritize all types of potential drinking water contaminants. However, the committee emphasizes that no tool can completely replace the critical role of expert judgment in the contaminant selection process for the CCL, particularly for contaminants that lack health effects and occurrence data. Thus, the committee recommends that EPA reserve a number or percentage of slots on the CCL for contaminants that are listed on the CCL based solely or primarily on expert judgment.

While the main purpose of the CCL is to identify contaminants that in the future may require regulation in public drinking water supplies, the CCL also should help to drive the research required for future regulatory decisions. Future CCLs should be designed to include a significant portion of contaminants that drive research on health effects, analytical detection and identification methods, water treatment methods, and occurrence monitoring, as well as contaminants that are nearly ready for regulatory decisions. Although the precise number of contaminants included primarily for research purposes is a policy decision that EPA must make, the committee suggests a roughly equal division on the CCL between contaminants that are ready for regulatory determination and those for which additional research and monitoring need to be conducted. This recommendation is consistent with EPA's partitioning of the first CCL into equivalent future action ("next step") categories (EPA, 1998a). The prioritization tool that EPA develops to help prepare the CCL should be able to help identify contaminants that are ready for regulatory decisions and those requiring additional research and monitoring.

Characteristics of an Ideal Prioritization Tool

Any quantitative prioritization tool for the development of a CCL should be as simple as possible. The committee strongly recommends that no factors or components (e.g., measures of occurrence or health effects) of the tool should be weighted in any way (even through expert judgment). In its previous review of hazard ranking schemes (NRC, 1999), the committee found that most weighting factors were qualitatively, or at best semi-quantitatively, derived and applied. Further, they were usually used without adequate justification or rationalization and acted to obscure the overall ranking scheme. Thus, even if thoroughly documented, the use of weighting measures at this stage of the CCL process may be considered as arbitrary. In contrast, simplicity in tool design and use lends itself to transparency and helps to improve public and other stakeholder understanding of the development process. Adherence to this basic guideline should help dispel or minimize any perception or accusations of "black box" decision-making.

The prioritization tool should not only be able to function quickly, properly, and consistently when addressing contaminants with data gaps, it should also help identify data gaps. The tool should not be static and unchanging. Rather, it should be continually updated and improved as more experience is gained in its use.

The committee further recommends that any prioritization tool should be subjected to validation and scientific review prior to use. For example, the tool's performance could be benchmarked by evaluating regulated contaminants with extensive occurrence and health effects data and whose drinking water risks are well established.

No matter what type of tool is developed, its results will be associated with some amount of (probably unquantified) uncertainty. For this reason, the committee emphasizes that the use of any such tool should err on the side of being inclusive.

Review of Existing Hazard Ranking Approaches

The committee re-examined the 10 existing chemical contaminant prioritization schemes reviewed in the previous report (NRC, 1999) with regard to their suitability for identifying and selecting contaminants for the development of future CCLs; these are listed in Table 5. (Refer to the previous report for further information concerning the development, characteristics, and uses of these ranking schemes.) As noted in the previous report, there are no formal schemes for ranking water-associated microbial agents. Therefore, all of these approaches are severely limited in their ability to evaluate nonchemical potential drinking water contaminants.

TABLE 5 Re-examined Contaminant Prioritization Schemes and Sources

Contaminant Prioritization Schemes	Source[a]	Contaminant Prioritization Function
Cadmus Risk Index Approach	Cadmus Group (Cadmus Group, 1992)	Drinking water contaminants
American Water Works Association (AWWA) Screening Process	AWWA (RCG et al., 1993)	Drinking water contaminants
Proposed Regulation Development Process	AWWA, National Association of Water Companies, Association of Metropolitan Water Agencies, and Association of State Drinking Water Administrators (Cook, 1998)	Drinking water contaminants
Waste Minimization Prioritization Tool	EPA Office of Solid Waste and Emergency Response and Office of Pollution Prevention and Toxics (EPA, 1997)	All potential environmental contaminants
Section 4(e) of Toxics Substances Control Act	Interagency Testing Committee (Walker and Brink, 1989; Walker, 1991, 1995	All potential environmental contaminants
State of California Safe Drinking Water and Toxic Enforcement Act of 1986 (Proposition 65)	California Environmental Protection Agency (OEHHA, 1997)	All potential environmental contaminants
Hazard Ranking System	EPA (CFR, 1997)	Hazardous waste sites
Comprehensive Environmental Response, Compensation, and Liability Act Priority List of Hazardous Substances	Agency for Toxic Substances and Disease Registry and EPA (ATSDR, 1996)	Hazardous materials
Sediment Contaminant Inventory Hazard Analysis of Releases Inventory	EPA Office of Science and Technology (EPA, 1996)	Sediment contaminants
Pesticide Leaching Potential	EPA Office of Pesticide Programs (Wolf, 1996)	Pesticides

[a] Agency, industry, or act responsible for the development of the specific ranking scheme.
SOURCE: Adapted from NRC, 1999.

In the first report, the committee stated that while none of these schemes was appropriate for making decisions about regulating contaminants already on the CCL, they might be appropriate for use in generating future CCLs. In re-examining the 10 schemes for potential use in CCL development, the committee considered four issues:

1. Can the tool evaluate the full range of drinking water contaminants?
2. Does its method for determining exposure potential include indicators of occurrence (e.g., reported releases under TRI) in drinking water sources?
3. Does it determine toxicity potential based on human, not ecosystem, effects?
4. Does it account for and integrate exposure and toxicity potential?

Seven schemes were quickly removed from further consideration because they did not meet these four criteria. The Hazard Analysis of Releases and Pesticide Leaching Potential schemes were eliminated because they are limited to sediment contaminants and pesticides, respectively. The Hazard Ranking System was eliminated because it ranks hazardous waste sites and not individual contaminants. The California Safe Drinking Water and Toxic Enforcement Act of 1986 (Proposition 65) process was eliminated because it is a largely qualitative approach and relies on extensive expert judgment throughout the entire process. The screening process prepared for the American Water Works Association (AWWA) was eliminated because it is extensively dependent on subjective judgment and is not appropriate for screening large numbers of contaminants. The Regulation Development Process was eliminated because it is an unpublished position paper that does not prioritize drinking water contaminants. The Comprehensive Environmental Response, Compensation, and Liability Act approach for hazardous substances was eliminated due to its complexity and unconventional methods for characterizing exposure and toxicity potential.

The committee further re-evaluated the Cadmus Risk Index, the Interagency Testing Committee (ITC), and the Waste Minimization Prioritization Tool (WMPT) approaches due to their design qualities and their greater level of applicability to prioritizing drinking water contaminants.

Cadmus Risk Index Approach.

The Cadmus approach was developed as a health-risk-based methodology for ranking a candidate list of drinking water contaminants (Cadmus Group, 1992). In this approach, a risk index is derived to identify and prioritize chemicals that pose a potential threat in drinking water. The risk index is based on the following chemical parameters: quantity produced, quantity released to water, persistence in water, frequency of detection in water, and toxicity to human health. Thus, this scheme incorporates both toxicity and exposure criteria.

In brief, an overall risk index for each chemical is computed by multiplying all the chemical parameters in conjunction with weights assigned to each parameter. This sum is then multiplied by a human health risk value and another weighting factor. This scheme is generally easy to use and integrates both exposure and health risks into an overall risk index. However, many factors (e.g., weighting values) of the scheme are determined qualitatively. In addition, the ranked list of chemicals at the back of the Cadmus report indicates that many of the chemicals originally compiled for prioritization were not evaluated by this scheme because they were missing a critical data element.

Conceivably, this approach could be modified for future use in evaluating and prioritizing potential contaminants from a future PCCL to create a CCL. However, it would need to be adapted to enable it to evaluate and prioritize all types of drinking water contaminants (microbial as well as chemical) and to identify and address data gaps. The use of qualitative weighting factors would need to be eliminated.

Interagency Testing Committee Approach.

The ITC was established in 1976 under TSCA to screen and recommend commercial chemicals and chemical groups for priority testing and potential rulemaking to control their use in the United States. The ITC has developed and used three chemical selection processes to screen and identify chemicals for priority testing consideration (Walker and Brink, 1989; Walker, 1991, 1995). For the purpose of this report, the committee focused on the current approach.

At present, the ITC uses a system, the Substructure-Based Computerized Chemical Selection Expert System, that relies on computerized processes to simultaneously integrate effects and exposure information. In brief, chemicals from sources of environmental monitoring data and with substructures with the potential to cause adverse health (or ecological) effects are assigned codes, and these values are used to select chemicals with environmental exposure and adverse effects potential. Those chemicals with no or low effects potential or low or no exposure potential are removed from the list and may be reconsidered as new effects and exposure potential data become available. This list of chemicals is then screened using a minimum production-importation ceiling to select chemicals for further evaluation. A quantitative algorithm is then applied for scoring chemicals for potential adverse effects, potential exposure, and production volume. Information profiles are developed on those chemicals with high scores that are subsequently reviewed at an ITC chemical selection workshop. At the workshop, chemicals are selected for in-depth review based on consensus decisions.

The ITC approach of combining quantitative, automated sorting of chemicals (often with little or no effects or occurrence data) with expert input is advantageous in that it allows a large number of chemicals to be considered while still allowing for use of expert judgment. While this approach is well established and demonstrably useful for evaluating large numbers of commercial chemicals, it would have to be extensively modified to include types of potential drinking water contaminants other than commercially produced chemicals. Its transparency and simplicity of design and use would also need to be improved.

Waste Minimization Prioritization Tool.

WMPT was developed as a priority-setting tool in response to the Waste Minimization National Plan (a program that focuses on reducing the generation and subsequent release to the environment of the most persistent, bioaccumulative, and toxic chemicals in hazardous wastes) by the EPA's Office of Solid Waste and Office of Pollution Prevention and Toxics (EPA, 1997b). The contaminant pool considered is the TSCA inventory list, which includes many but not all contaminants of concern in drinking water. The determination of exposure potential is based on the contaminant's bioaccumulation potential and persistence or production and release data. While persistence, production, and release data are relevant for assessment of exposure potential for drinking water contaminants, bioaccumulation potential is not because it applies to animals other than humans. The determination of toxicity potential includes indicators of both human and ecosystem toxicity, the latter of which is not relevant for drinking water contaminants. The prioritization scheme is based on a score that combines toxicity and exposure severity scores.

WMPT is not directly applicable to drinking water contaminants because some elements of its prioritization scheme (bioaccumulation potential and ecosystem toxicity) are irrelevant for drinking water contaminants. Furthermore, because it is not intended solely for water contaminants, it contains no measures of mobility and retention in water. Nonetheless, the committee was positively disposed to WMPT because of its simplicity, transparency, careful justification and documentation, and use of a "binning" approach. A binning or "fence line" scoring approach involves comparing the quantitative value for a given chemical data element against predefined high and low threshold values, termed fence lines. A major advantage of a binning approach is that it groups data into similar bins and avoids the false sense that such data are highly precise.

This scheme could conceivably be used as a tool for prioritizing PCCL drinking water contaminants for future CCLs if modified to be specifically applicable to all types of potential drinking water contaminants. It also would have to specifically evaluate and prioritize contaminants according to appropriate indicators of exposure and toxicity, such as measures of mobility and retention in water, but not ecosystem toxicity or bioaccumulation potential.

In summary, by modifying the Cadmus Risk Index, ITC approach, or WMPT, EPA could create a quantitative or semi-quantitative tool to help narrow the list of contaminants for inclusion on the CCL. The committee recommends that EPA analyze these tools carefully, using the guidelines set forth above, to determine which could be most easily adapted for this purpose.

CONCLUSIONS AND RECOMMENDATIONS

EPA's first CCL was prepared in a short time period to meet the statutory requirements and mandated time line of the SDWA Amendments of 1996. For chemicals, the approach used ad hoc contaminant Occurrence and health effects criteria suggested by the National Drinking Water Advisory Council Working Group on Contaminant Identification and Selection and readily available sources of potential contaminant information. For microbiological contaminants, the approach relied on the recommendations of a panel of experts who qualitatively evaluated individual microorganisms according to a series of five baseline criteria. In short, the overall approach was limited by "looking under the lamp post" for relatively few types and numbers of drinking water contaminants compared to the universe of potential contaminants. The contaminants included on the first CCL merit consideration, but a broader approach to contaminant selection could identify higher-risk contaminants. The first CCL is nonetheless a very useful list of contaminants that should help EPA set priorities for future drinking water research, monitoring, and guidance development, especially if evaluated in accordance with the decision framework that was recommended in the committee's first report (NRC, 1999).

To improve the process for developing future CCLs, the committee recommends the following conceptual approach and related steps:

- EPA should develop a two-step process for creating future CCLs. In this process, a broad universe of potential drinking water contaminants (see Table 1) is examined and then narrowed to a preliminary drinking water contaminant candidate list (PCCL) using simple screening criteria and expert judgment. Then, the PCCL is narrowed to a CCL using a quantitative screening tool in conjunction with expert judgment.
- EPA should be as inclusive as possible in narrowing the universe of contaminants (perhaps on the order of 100,000 substances) down to a PCCL. The committee envisions that a PCCL would contain on the order of thousands of potential drinking water contaminants of all types for subsequent evaluation, prioritization, and culling to a CCL.
- As a start, a PCCL should contain all substances and microbes that are known to cause significant adverse health effects (regardless of exposure route) and have the potential to occur in drinking water and those demonstrated to occur in drinking water supplies (unless they are known not to pose a significant health risk). A PCCL should also include all substances that may pose a drinking water risk based on their potential for occurrence and health effects.
- Preparation of a PCCL should not involve extensive collection or analysis of data, nor should it drive research or monitoring activities. However, the committee recognizes that it will be necessary to develop and use screening criteria (e.g., production values of commercial chemicals) to shorten the list of contaminants for a PCCL.
- Development of a PCCL should begin as soon as possible to support the development of the next CCL; the PCCL should be available for public and other stakeholder input (especially through the Internet) and should undergo scientific review.

- A new PCCL should be generated for each CCL development cycle to account for new data and potential contaminants.
- As an integral part of the CCL development process, the committee recommends the use of a comprehensive database that provides a consistent mechanism for recording and retrieving information on all the contaminants under consideration. A well-designed relational database can function as a "master list" that contains a detailed record of how the PCCL and CCL were developed, as well as providing a powerful analytical tool for the development of future CCLs.
- To help identify commercial chemicals that might pose risks in drinking water, EPA should consider exercising its authority under TSCA to collect production and import data on both organic and inorganic chemicals by use category.
- To assist in the evaluation of microbial pathogens, it also may be useful to identify common mechanisms of pathogenicity among contaminants in order to include them on future CCLs. An approach analogous to chemical SARs for microorganisms does not currently exist, but EPA should develop such a prioritization tool for microbial contaminants through use of gene data banks and with the cooperation and support of other federal and state health organizations.
- Preparation of a CCL from a PCCL will require collection and evaluation of all available health effects and occurrence data for each substance on the PCCL. To cull a list of thousands of potential drinking water contaminants of all types to approximately a hundred for inclusion on the CCL, EPA must combine expert judgment equally with a single prioritization tool that can be used to evaluate any type of PCCL contaminant.
- EPA should develop a prioritization tool to help narrow the PCCL to a CCL. The tool should be kept as simple as possible and be developed with regular public and other stakeholder input. Ensuring transparency throughout its development and avoiding "black-box" decision-making are critical steps. The tool should be validated using contaminants with extensive health effects and occurrence data and well-established risks. The tool must be able to identify and effectively address data gaps for each contaminant. Following a re-examination of 10 existing chemical hazard ranking schemes, the committee concluded that none was directly suitable for developing a CCL from a PCCL. However, 3 of the schemes (Cadmus, ITC, and WMPT) contain features that would be suitable for CCL development and could conceivably be adapted for this purpose.
- EPA should reserve a number of contaminants or a percentage of the CCL for contaminants that are listed based solely or primarily due to expert judgment. EPA must also retain the ability to remove contaminants from inclusion on a CCL based on expert judgment.
- The CCL should consist of roughly equal numbers of contaminants ready for regulatory decisions and those requiring further research to drive such efforts equally. This recommendation is consistent with EPA's partitioning of the first CCL into equivalent future action categories.

- Regardless of what process is adopted by EPA to develop future CCLs, the committee strongly recommends that all contaminants that have not been regulated or removed from the existing CCL (and future CCLs) should be automatically retained on each subsequent CCL for reevaluation.

As in the previous report, the committee recognizes that the need for policy judgments by EPA cannot and should not be removed from any CCL development process. In making these decisions, EPA should use common sense as a guide and err on the side of public health protection.

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Historical Overview of Drinking Water Contaminants and Public Water Utilities

Daniel A. Okun

A recent editorial in *Science* expressed a need for a more credible scientific basis for environmental regulations (Madia, 1998). The editorial goes on to point out that government regulators must rely on the research performed in their own laboratories as well as in private laboratories and universities in all of the agencies of government and not the U.S. Environmental Protection Agency (EPA) alone. It concludes that, "now is the time for science to close the gap."

My contention is that, under current circumstances, it may not be feasible to even begin to close the gap and that waiting for scientific evidence before adopting regulations is not adequate if protection of public health is the goal. History may help us understand what measures in the past, in the absence of scientific evidence, have been successful in helping reduce the risks to public health from assaults on the environment.

LONDON, NINETEENTH CENTURY

In 1832 annual deaths from cholera in London ranged from 10 to 110 per 10,000 population. The introduction of tap water to the wealthier homes and the consequent introduction of the flush toilet led to the discharge of human wastewaters to the Thames River via the storm sewers that had been built to permit London's commercial center to remain active during rainy periods. By 1849 the death rates had increased to more than 200 per 10,000 for those taking water from the Thames in the center of the city.

At that time, decades before the germ theory of disease had been hypothesized and proven, the spread of cholera was attributed to poisons in the air emanating from the miasmas rising from the Thames during the occasional hot summers that frequented London. During such periods, the people of London avoided using London Bridge, the only crossing of the Thames in the city, obliging them to go far upstream to make the crossing.

John Snow, physician to Queen Victoria, hypothesized that the drinking water in London, which was drawn from the Thames by water companies and from private wells in the city, was responsible for the cholera outbreaks. The epidemic of 1854 helped demonstrate, if not prove, his theory. He mapped deaths in London's West End (see Figure 1-1) and identified a well on Broad Street as the focus for the

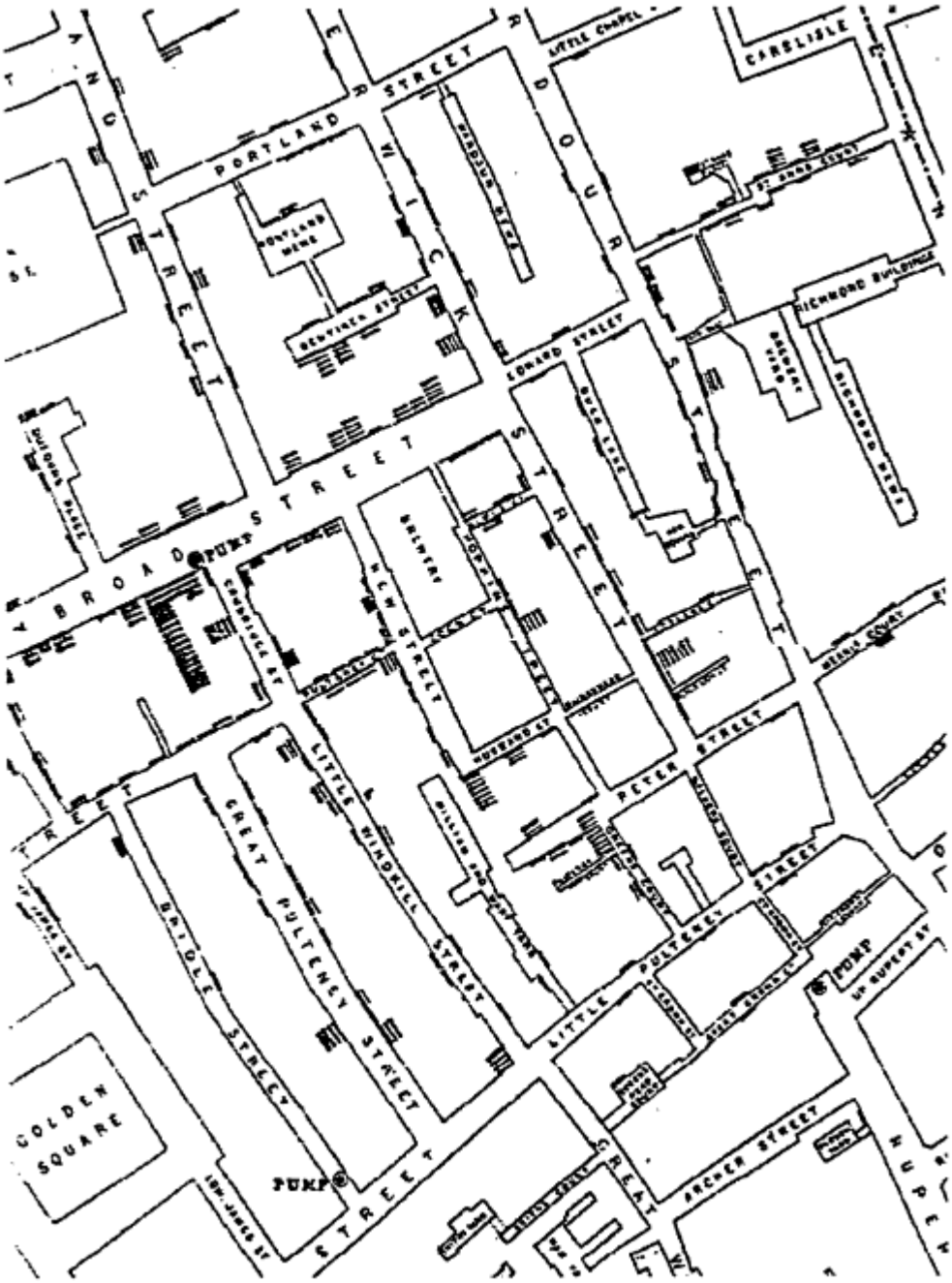

Figure 1-1
Deaths from Cholera in Broad Street, Golden Square, London, and the neighborhood, 19 August to 30 September 1854 (NCGIA, 1994).

fatalities. The water had been clear and apparently very attractive as people sent carts to carry water from the well to homes even miles away. A "shoe leather" epidemiologist, Dr. Snow interviewed individuals in their homes and ascertained the presence of disease and deaths and concluded that the well was the common source of exposure for those affected (Snow, 1936).

Two private water companies (all water distribution services were then private) were in competition to serve the south bank of the Thames with piped water drawn from the Thames in the center of the city. These supplies had been characterized as being among the worst of the water supplies of London. In 1852 the Lambeth Company, in an attempt to attract more customers by improving the aesthetic quality of its product, moved its intake upstream above the wastewater and storm water discharges from London. Dr. Snow seized the opportunity this offered to compare the impact on those taking water from the Lambeth Company with their neighbors who continued to subscribe to their larger competitor, the Southwark and Vauxhall Company. Table 1-1 shows the significance of the move of the intake in the Thames—an almost 90 percent decrease in the rate of fatalities. The relatively few deaths that occurred among customers of the Lambeth Company might be attributed to exposures of the residents elsewhere in London in connection with their employment.

The affirmation of Dr. Snow's hypothesis provided a basis for water management for decades before there was scientific proof of causality—namely, the identification of the agent responsible for the disease, nor had he met many of the requirements of a modem epidemiological study. Nevertheless, a principle, which is valid today, emerged from that early work: that water should be taken from the highest-quality source available and be protected from contamination.

UNITED STATES, TWENTIETH CENTURY

Typhoid fever death rates in the United States during the early years of this century, before widespread acceptance of filtration and the introduction of chlorination, indicated that the death rates from typhoid were a function of the quality of the source, as shown in Table 1-2. Groundwater and upland watersheds showed the lowest rates of typhoid with a threefold higher rate in waters drawn from rivers (Kober, 1908). The introduction of filtration reduced the incidence of enteric disease generally and typhoid specifically, the latter dropping in rate by more than 55 percent (Ellms, 1928).

Introduction of chlorine in the early years of this century, which combined with filtration virtually eliminated waterborne enteric disease in the United States, had one unfortunate consequence: filtration and chlorination appeared to make the quality of the source unimportant, and the principle of using the best source succumbed to the expedience of developing lower-cost polluted river sources and providing filtration and chlorination. Some large cities located on major rivers opted to take their water supply from these rivers despite the fact that upstream other cities, industries, and agricultural enterprises were discharging wastewaters into their water sources. Among these cities were Philadelphia, New Orleans, Cincinnati, and London, all of which had better-quality options that were more difficult to pursue and perhaps marginally more

costly. The more costly options were rejected because filtration and chlorination gave assurance that the treated water would "meet the drinking water standards." (Unfortunately, today, most cities in Asia, Africa, and Latin America draw their water supplies from large rivers and do not provide filtration and chlorination effectively and have made few efforts at protecting their sources, with the result that infant mortality rates in these countries are more than 10-fold higher than in industrialized countries.)

TABLE 1-1 Data of John Snow on Cholera in London, 1854

Water Service and Source	Number of Houses Served	Deaths from Cholera	Deaths per 10,000 Households
Southwark & Vauxhall Co.: from Thames River at London	40,046	1,263	315
Lambeth Co.: from Thames River above London	26,107	98	37
Rest of London: wells and surface sources	256,423	1,422	59

SOURCE: Adapted from Snow, 1936.

TABLE 1-2 Mean Typhoid Death Rates in U.S., 1902-06

Source	Number of Cities	Death Rate per 100,000
Ground water	4	18.1
Impoundments and protected watersheds	18	18.5
Small lakes	8	19.3
Great lakes	7	33.1
Mixed surface and groundwater	5	45.7
Run-of-river supplies	19	61.6

SOURCE: Adapted from Kober, 1908.

An interesting characterization of the status of drinking water in the United States in the first half of the twentieth century can be found in the book *The Quest for Pure Water*, published by the American Water Works Association

(Baker, 1948). The 27-page index to this 527-page book does not include the words "typhoid," "cholera," "bacteria," "health," "standards," or "regulations." A brief epilogue states:

> In the last 60 years (from about 1880), with advances in the arts and sciences, including the acceptance of the germ theory of disease and of water as one of the chief means of spreading cholera and typhoid, standards for the quality of water have been raised.

The standards then were directed almost exclusively at the prevention of transmission of enteric pathogens, with *E. coli* serving as a useful surrogate for the waterborne diseases prevalent during that period. As we are now aware, this surrogate is no longer useful and the search is on for some other approach to ensuring microbial safety without having to test for every likely pathogen.

THE CHEMICAL REVOLUTION

The chemical revolution that accompanied the increasingly technical sophistication of the major combatants of World War II led to the creation of thousands of synthetic organic chemicals (SOCs). They were designed for the most part to be toxic to biota and to be long lasting to achieve economy in their application. That these compounds would reach the environment and drinking water sources was slow to be recognized. Among the first to draw attention to the potential was W.C. Hueper of the National Cancer Institute who wrote:

> It is obvious that with the rapidly increasing urbanization and industrialization of the country and the greatly increased demand placed on the present resource of water from lakes, rivers, and underground water reservoirs, the danger of cancer hazards from the consumption of contaminated drinking water will grow considerably within the foreseeable future. (Hueper, 1960)

Only two years later, Rachel Carson's *Silent Spring* (1962) raised the issue throughout the nation and the industrialized world.

The U.S. Public Health Service recognized the issue with its 1962 Drinking Water Standards, the first to include mention of organic compounds with a limit for chloroform extractables. This test measured the total of all organic compounds, both natural and synthetic, toxic and nontoxic, that would be adsorbed by passing the water through a granular activated carbon (GAC) column and desorbed with chloroform. (It should have been no surprise that GAC filters would show up well in studies for the treatment of water for the removal of these organics.)

It was not until the early 1970s that the EPA recognized there were hundreds of SOCs in drinking water sources, particularly in the Mississippi River at New Orleans near its mouth. A large number of these compounds were believed to be carcinogenic, teratogenic, and/or mutagenic in animals and possibly in humans. These findings, together with epidemiological studies comparing populations in New Orleans who drank treated Mississippi River

water with nearby populations using untreated groundwater, revealed somewhat higher rates of some forms of cancer in those using the Mississippi River water, led to passage of the Safe Drinking Water Act (SDWA) in 1974. EPA's Interim Primary Drinking Water Regulations included, for the first time in federal regulations, six widely used pesticides (EPA, 1976).

The EPA also contracted with the National Research Council (NRC) to prepare a series of volumes, ultimately nine over a 13-year period, entitled *Drinking Water and Health* to provide guidance on methodologies for selecting contaminants and establishing maximum contaminant levels (MCLs) for contaminants known to be in drinking water (NRC, 1977-1989). One quote from Volume 2 is of interest:

> Over 700 volatile organic compounds have been identified in drinking water ... These compounds make up only a small fraction of the total organic matter ... Approximately 90% of the volatile organic compounds that can be analyzed by gas chromatography have been analyzed, but this represents no more than 10% by weight of the total organic material. Only 5-10% of the non-volatile organic compounds that comprise the remaining 90% of the total organic matter have been identified. (NRC, 1980)

Two problems were largely ignored in assessing the problems with organics in drinking water and regulations for their control:

1. MCLs were established for each contaminant individually, with no account taken of the impact of several compounds being present in a sample and no consideration of the possible synergistic effects of one of the contaminants with another. This problem still faces us.
2. No attention was given to the impact of using chlorine for disinfection. Being a strong oxidant, chlorine reacts with other organic compounds in the water being treated to create what are now termed disinfection byproducts (DBPs). This problem was addressed by the addition of trihalomethanes to the regulations in 1979.

Amendments to the SDWA in 1986 obliged EPA to establish MCLs and MCL goals for many more contaminants, including primarily SOCs. A requirement was that every three years 25 new contaminants would be added to the drinking water regulations. Figure 1-2 shows the rate at which contaminants have been added to the regulations since early in this century. The unreasonableness of this approach was addressed with the SDWA amendments of 1996, which established new protocols for incorporating contaminants in the regulations. The World Health Organization and the European Community, as well as other industrialized countries, have been incorporating contaminants either as guidelines or regulations in about the same numbers over the past several decades.

EPA's focus on the problems of SOCs and DBPs arose from their potential for causing cancer. The selection of compounds of concern and setting their acceptable MCLs were difficult because the onset of cancer requires decades-long exposure and the epidemiology to date had not been sufficiently

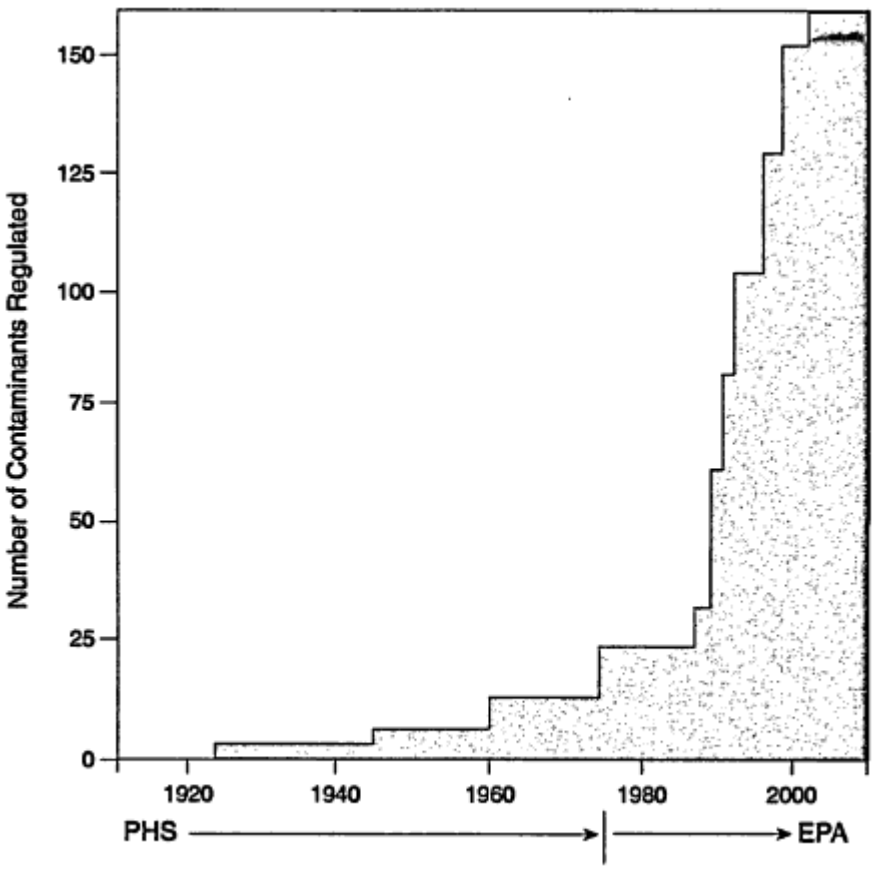

Figure 1-2
Number of drinking water contaminants regulated by the U.S. government. The large increase in regulated contaminants that begins after 1976 is due to regulations issued under the Safe Drinking Water Act and its subsequent amendments. SOURCE: Reprinted, with permission, from Okun (1996).
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robust to distinguish the significance of any single contaminant if ingested for 70 years, the exposure period adopted in establishing risk. Several epidemiological studies by the National Cancer Institute were contradictory (Cantor et al., 1978, 1998). A controversial metanalysis on the significance of chlorine consumption on cancer rates, which combined 10 previously published epidemiology studies, reported increased relative risk for bladder and rectal cancers in proportion to the exposure to chlorinated water (Morris et al., 1992).

EPA's concern for the formation of DBPs and its belief that they might be responsible for cancers after long-term exposures led to one unfortunate side effect, illuminated by the cholera epidemic that surfaced in Peru in 1991 and rapidly spread throughout much of Latin America. Some of the blame for the spread was attributed by Peruvian officials to the EPA because its considerable concern for the deleterious effects of chlorine had been responsible for Peru reducing and even ceasing chlorination of its water supplies. With the high infant mortality rates in developing countries, most of which are attributable to waterborne infectious diarrheal diseases such as typhoid and cholera that have largely been eliminated in the industrialized world, disinfection of water is absolutely essential. Chlorine is the disinfectant of choice in the developing countries because it is by far the lowest in cost and easiest to apply. Yet the ubiquity of radio and television throughout the world and the spread of news that EPA is urging reduced chlorination because chlorine is said to contribute to cancer have induced many authorities in developing countries to reduce or even abandon the use of chlorine.

THE MICROBIAL REVIVAL

EPA's focus on DBPs and SOCs led the *Milwaukee Journal* to adopt the title "Fatal Neglect" for a special reprint following the devastating April 1993 cryptosporidiosis outbreak (Rowen and Behm, 1993). The newspaper asserted that EPA had sufficient knowledge about *Cryptosporidium* and its effects because of six earlier outbreaks in the United States and several in England but that this knowledge had not been translated into any type of meaningful response. The Surface Water Treatment Rule, promulgated in 1989, did focus on giardiasis, which is a far less serious disease than cryptosporidiosis and one for which there is adequate therapy. More importantly, *Cryptosporidium* oocysts, as was the case with the cysts of amoebic dysentery, a serious waterborne pathogen that flourished a half a century earlier, are not inactivated by conventional chlorination and, being smaller in size than *Giardia* cysts, would more easily pass through conventional filters. A particularly serious problem is that fecal coliform is not an appropriate surrogate for the oocysts of *Cryptosporidium*. Moreover, while the oocysts are relatively large, determination of their presence has been very difficult. A problem that arises with diarrheal diseases is that their endemicity is not easily recognized as the symptoms do not generally require medical attention and, even if a physician becomes involved, seldom is the stool sent off for examination.

The International Life Sciences Institute held a conference in August 1992 entitled "Balancing the Risk" (Craun, 1993). One day was devoted to microbial risk and another to chemical risk. An informal poll among the conferees indicated that, at the time, microbial risks were more important and

should not, in effect, be neglected under the assumption that they were well under control. In fact, considerably more attention has begun to be given to microbial risks of all types. New pathogens are continually appearing on the scene, and the search for a suitable surrogate for determining microbial safety enjoys a high priority.

RETURN OF TRACE CHEMICAL CONTAMINANTS

This was pretty much the situation when I prepared a paper entitled "From Cholera to Cancer to Cryptosporidiosis" (Okun, 1996). In the few years since, new problems with SOCs have begun to take center stage. Uncertainties remain about the roles of SOCs and DBPs in connection with reproductive anomalies which, if shown to be a problem, will change our assessment of DBPs (Bove et al., 1995; Savitz et al., 1995; Swan et al., 1998). Currently, our concern is with long-term exposures, so that averaging concentrations of DBPs is adequate for monitoring water quality. With reproductive effects, a three-month period of exposure would become significant, which would require more frequent monitoring and a concern for seasonal variations in DBP concentrations.

Another manifestation of the role of anthropogenic impacts on our water supply emerged from Europe, where it was found that all the drinking waters withdrawn from sources that had received human wastewaters were showing trace concentrations of the pharmaceutical compounds commonly used by people with a wide range of ailments—heart disease to mental stress to control of conception (Stan and Heberer, 1997; Buser and Muller, 1998).

More recently, evidence from England indicates that waters impacted by human wastes were responsible for "feminizing fish" (Jobling et al., 1998). This last observation may have special significance in that fish may be a better source of information about trace contaminants in water than samples of water themselves.

In studies related to the safety of San Francisco delta water for drinking, analyses failed to show the presence of trace concentrations of SOCs in the water. However, the fish did reveal their presence, which had been inferred from the sanitary survey conducted on the watershed. This revealed that hundreds of thousands of tons of pesticides were being applied annually to lands draining into the rivers feeding the delta but had not shown up in analyses of water samples (Okun et al., 1985). The more important concern exhibited by the fish is that the impact on them might well be a signal for us to be concerned about impacts on humans drinking these waters for long periods of time. The fish may be our canaries.

THE CHALLENGE

Is science now able to identify all of the trace chemical contaminants and microbials in water, let alone determine their concentration? Can science establish methods for their reduction or removal and characterize their health significance?

A currently appropriate metaphor, football talent, might give us a clue as to the difficulties that face science today if it is to provide the basis for regulations. In football, if a team were to spend 100-fold more on its offensive players than its opponents did on their defensive players, the likelihood of the defense containing the offense would be small indeed. Football teams, if they are to contend, recognize that they must invest as much in defense as in offense. But this imbalance between offense and defense is precisely the situation facing environmental sciences today in the protection of the public health.

Billions of dollars are invested annually by industry in inventing new chemical compounds—all potential contaminants and parents of daughter contaminants born of reactions of these compounds with other compounds in the aquatic environment. How much money is available to support the scientists who have the responsibility to identify these chemical compounds that are developed in secrecy? The offensive is carried out in secret to protect patents and licenses. Regulatory agencies only learn about them when they are cleared for marketing and the water utilities much later. Only then can their scientists begin to determine their presence and concentrations and establish the significance and fate of these chemical compounds in the aquatic environment. The regulators are handicapped because there is little literature describing the birth and development of these compounds. (While the literature may be replete with papers that address methods for identifying, characterizing, and determining the health effects of these chemicals.)

This is not to imply that these developments of industry are not valuable. They have been seized on and perceived as improving the quality of life. In fact, it is the great value placed on these very important developments, such as pesticides for agriculture, chemicals for plastics and pharmaceuticals, radiation, and myriad new breakthroughs that result in the very heavy assault on water quality. The offense will continue to be strong. Our role is to create a defense that has the potential to contain the offense. This may oblige some to communicate not only with our science colleagues but also with those who have the power to support the defense.

In the meantime, as scientists provide the data for regulators and public officials who are responsible for the initiatives of the defense, they might consider introducing the "precautionary principle" (Hileman, 1998) onto the playing field. Application of the principle would reduce the power of the offense by placing the burden of demonstrating the harmlessness of a new product or technology on its proponents rather than on the general public.

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2

Emerging Drinking Water Contaminants: Overview and Role of the National Water-Quality Assessment Program

Timothy L. Miller and William G. Wilber

Several programs and initiatives of the U.S. Geological Survey (USGS) contribute information useful in identifying emerging drinking water contaminants. These programs include the National Water-Quality Assessment (NAWQA) program, the Toxic Substances Hydrology Program, and the Drinking Water Initiative. The goals of the NAWQA Program, the largest of these efforts, are to assess the status of, and trends in, the quality of the nation's surface- and groundwater resources and to link the status and trends with an understanding of the natural and human factors that affect water quality (Hirsch et al., 1988; Leahy et al., 1990; Gilliom et al., 1995). The purpose of this paper is to provide an overview of the design of the NAWQA Pro ram, especially those aspects of the program that contribute information relevant to identifying emerging contaminants of concern to drinking water. Selected findings from the program are also highlighted, along with suggested enhancements to existing monitoring programs that would greatly increase the utility of these data for identifying emerging drinking water contaminants.

NAWQA DESIGN

The NAWQA program attempts to balance the unique assessment requirements of individual hydrological systems with a nationally consistent design structure that incorporates a multiscale interdisciplinary approach. The building blocks of the national assessment are investigations in major hydrological basins of the nation, referred to as "study units." The goal for the first phase of investigation in each study unit is to characterize, in a nationally consistent manner, the broad-scale geographic and seasonal distributions of water quality conditions in relation to the most significant contaminant sources and background conditions.

The NAWQA study units cover about 40 percent of the conterminous United States, encompass 60 to 70 percent of both national water use and the population served by public water supplies, and include diverse hydrological systems that differ widely in the natural and human factors that affect water quality. The study units are divided into three groups, which are studied on a

rotational schedule of three-year periods of intensive data collection. About one-third of the study units are in the intensive data collection phase at any given time, and the nine-year cycle is designed to be repeated perennially. The first complete cycle of intensive data collection in the study units began during 1992 and is scheduled to be completed in 2002.

The national assessment goals of NAWQA are being accomplished in two main ways. First, the accumulation of consistent and comparable water quality assessments for some of the largest and most important hydrological systems of the nation will stand alone as a major contribution to our knowledge of regional and national water quality conditions. Second, the NAWQA national synthesis builds on and expands the findings from individual study units by combining and interpreting results from multiple study units together with historical information reported by the USGS and other agencies and researchers. National synthesis analyses produce regional and national assessments for priority water quality topics by comparative analysis of study unit findings. National synthesis efforts focused on pesticides and nutrients began in 1991; synthesis of data on volatile organic compounds began in 1994. Draft plans for synthesis of data on trace elements and stream ecology were developed in 1998 and are currently in peer review.

External coordination at all levels is an integral component of the NAWQA Program. Information exchange and coordination occur through several mechanisms. First, study unit liaison committees help ensure that the water quality information produced by the program is relevant to regional and local interests. The liaison committees are comprised of non-USGS members who represent a balance of technical and management interests. Represented organizations include, as appropriate, federal, state, interstate, and local agencies; Indian nations, and universities. At the national level, the NAWQA Advisory Committee, a subcommittee of the National Water-Quality Monitoring Council, helps ensure that federal and nonfederal interests and needs at the regional and national levels are met. Finally, the USGS and NAWQA have established liaison positions with the U.S. Environmental Protection Agency's (EPA) Offices of Pesticide Programs and Ground Water and Drinking Water to provide a stronger and more timely linkage with the information needs of these two groups.

Overview of Study-Unit Investigations

Study unit investigations are designed to meet national synthesis requirements for consistent and integrated information and study unit requirements for assessing water quality with sufficient flexibility to adapt to local conditions. Each study unit investigation consists of four interrelated components: (1) retrospective analysis; (2) occurrence and distribution assessment; (3) trend and change assessment; and (4) case studies of sources, transport, fate, and effects. The retrospective analysis consists of a review and analysis of existing water quality data. It forms the basis for addressing what is already known and what needs to be further investigated with respect to current water quality conditions, trends and changes, and understanding causes and effects. The occurrence and distribution assessment builds on findings of the retrospective analysis to complete a broad-scale geographic and seasonal

characterization of the distribution of current water quality Conditions in relation to major point and nonpoint sources and natural and background conditions. A key objective is to fill gaps in existing data for each study unit. Design features, such as physical, chemical, and biological measurements, media sampled, and spatial and temporal resolution, are consistent among the study units.

The occurrence and distribution assessment is the largest and most important component of the first three-year intensive study phase in each study unit because it provides the foundation of data and information needed for other components. Periodic repetition of selected parts of the occurrence and distribution assessment during future intensive study phases is a key part of the trend and change assessment. Results of the occurrence and distribution assessment also are used to identify the most important questions about sources, transport, fate, and effects to be addressed by the case studies. The trend and change assessment focuses on documenting long-term trends and changes, results in new questions about causes and effects, and identifies changes that need to be made in the periodic intensive study phases. Case studies are used to improve understanding of selected questions about sources, transport, fate, and effects that arise from all aspects of NAWQA investigations and often lead to changes in assessment approaches over time.

Sampling Design for Surface Water and Groundwater

Rivers and Streams

The national study design for surface water and groundwater has been described by Gilliom et al. (1995, 1998), and only a brief outline is provided here. The surface water design focuses on water quality conditions in rivers and streams using the following interrelated components:

- Water-column studies assess physical and chemical characteristics, which include suspended sediment, major ions, nutrients, organic carbon, and dissolved pesticides.
- Bed sediment and tissue studies assess trace elements and organic contaminants that are hydrophobic (tend to associate with particles and accumulate in biological tissues rather than be dissolved in water).
- Ecological studies evaluate characteristics of benthic algae, macroinvertebrate, and fish communities and physical habitat in streams.

Sampling designs for all three components rely on coordinated sampling of varying intensity and scope at integrator sites, which are chosen to represent water quality conditions of rivers in large basins that are commonly affected by complex combinations of land-use settings, and at indicator sites, which are chosen to represent water quality conditions of streams and smaller rivers associated with specific environmental settings. The most complete data collection for the three components is at a selected core of three to five integrator sites and four to eight indicator sites in each study unit, which constitute the

fixed-site monitoring network for regular collection of samples over time. A subset of two to five sites in each study unit, usually one integrator site and two to four indicator sites, is sampled more intensively than the rest, and these are the only sites for which water samples are routinely analyzed for pesticides. Samples at these sites are analyzed for 76 pesticides and 7 degradation products, accounting for about 75 percent of agricultural pesticide use in the United States and substantial commercial, garden, and home use. Low-level analyses of 87 volatile organic compounds (VOCs) are completed for samples collected at urban indicator sites only.

The 226 surface water sampling sites in the first 20 study units include a wide range of stream sizes, types, and land-use settings in major regions of the nation, but the sites were not selected to be a statistically representative sample of the nation's streams. NAWQA sites with relatively small basins (17 to 1,243 km^2), include a greater prevalence of basins with large proportions of agricultural and urban land compared with all similarly sized basins in the United States, particularly the subset of sites sampled for pesticides. NAWQA sites with large basins (1,244 to 221,497 km^2), which are mainly integrator sites, also have a greater prevalence of agricultural land compared with similarly sized basins in the United States, although the pattern is less clear than for the smaller basins. This bias toward agricultural and urban land is the expected consequence of the NAWQA design. Most of the streams sampled are not directly used as sources of drinking water. The agricultural and urban indicator sites can generally be viewed as extreme examples of what drinking water sources would be like in highly developed watersheds in the region. Some of the sites sampled on major rivers are close enough to water-supply withdrawals that they are reasonably representative of the source water used for drinking water, while others are in regions where groundwater or remote surface water sources are used for drinking water.

Groundwater

The national study design for groundwater focuses on water quality conditions in major aquifers and in recently recharged shallow groundwater associated with current and recent land uses:

- Aquifer or "study unit" surveys assess the quality of water in the major aquifer systems of each study unit. All samples collected for the aquifer surveys are analyzed for the same field characteristics and dissolved constituents that are analyzed samples from surface water sites plus VOCs. Depending on study unit priorities, trace elements were determined in samples from some of the aquifer surveys in the first 20 study unit investigations.
- Land-use studies assess the quality of recently recharged shallow ground water (generally less than 10 years old) associated with specific combinations of land uses and hydrogeological conditions. In general, the same national target constituents are analyzed in samples from the land-use studies as for the aquifer surveys. The addition of other constituents varies among land-use studies as in the aquifer surveys.

Generally, each aquifer survey and land-use study consists of sampling about 30 randomly selected sites (wells or springs) in the geographic area and aquifer zone targeted for the specific study. One sample was collected from most of the sites. Thirty-six aquifer surveys and 56 land-use studies were completed in the first 20 study units. The 36 aquifer surveys have mixed land-use influences. Of the 56 land-use studies, 41 targeted agricultural settings, 14 targeted urban settings, and 1 targeted forested setting. Although suitable geographic delineation of aquifer boundaries throughout the United States is not available to enable comparison of NAWQA groundwater study areas to groundwater resources of the entire United States (as it was for stream drainage basins), the focus of the NAWQA groundwater design on agricultural and urban settings is similar to surface water. For purposes of evaluating water quality characteristics and comparing constituent concentrations to established water quality criteria, aquifer surveys and land-use studies were reclassified according to two categories of groundwater resources:

- Drinking-water aquifers, which are currently used as sources of drinking water (though wells sampled by NAWQA were not necessarily drinking water supply wells).
- Shallow groundwater, which is recently recharged groundwater, that may or may not be currently used as a source of drinking water. Because of the nature of their design, some land-use studies were reclassified as both drinking water aquifers and shallow groundwater.

Selection of Target Analytes

The NAWQA program has selected a wide range of physical, chemical, and biological measurements to monitor in a nationally consistent manner. Selection of these target analytes was based on their relevance to important water quality issues and on the existence of appropriate analytical methodologies. Water measurements include field measurements of stream flow, temperature, pH, dissolved oxygen, and specific conductance, and laboratory analyses of major ions, nutrients, trace elements, organic carbon, pesticides, and VOCs. Lists of analytes and, where appropriate, associated reporting limits are presented in Gilliom et al. (1995, 1998) and for pesticides and VOCs through the World Wide Web at: http://water.wr.usgs.gov/pnsp.anstrat and http://wwwsd.cr.usgs.gov/nawqa/vocns/targets91.html.

For some water quality issues the choice of target analytes is a relatively simple task. For example, there are a small number of analytes relevant to the issues of nutrient enrichment, acidification, salinity, and sedimentation, and their chemical analysis is relatively inexpensive. In contrast, for the issue of chemical contamination, selection of target analytes is much more difficult because of the large number of substances to consider and their relatively high cost of measurement.

The process used to select target VOC analytes for the groundwater component of the NAWQA Program serves as an example of how this design

element has been addressed. Fifty-five of the 87 VOCs routinely analyzed in groundwater samples by the NAWQA Program are targeted for emphasis. These compounds were selected from an initial list of 130 compounds using an eight-step screening process that considered available information about the compounds: (1) physical properties; (2) human cancer rating; (3) noncancer human-health risk; (4) toxicity to freshwater aquatic organisms; (5) occurrence data for VOCs in groundwater, surface water, and drinking water; (6) potential for atmospheric ozone depletion and bioconcentration in aquatic organisms; (7) use or potential use as a fuel oxygenate, and (8) feasibility of analysis using purge-and-trap gas chromatography/mass spectrometry (Zogorski et al., in press).

Of the initial 130 compounds, 124 were from one or more regulatory lists associated with the Safe Drinking Water Act and Clean Water Act. Six additional compounds were included on the basis of: (1) listing as a carcinogen in the EPA's Toxics Release Inventory (chloromethyl methyl ether and bis-2-chloroethyl sulfide); (2) potential for ozone depletion (1,1,2-trichloroethane, 1,2,2-trifluoroethane); and (3) use or potential use as a gasoline oxygenate (diisopropyl ether, ethyl *tert*-butyl ether, and *tert*-amyl methyl ether). Of the 55 VOC target analytes, 29 have a national enforceable drinking water regulation; 28 are classified as known, probable, or possible human carcinogens; 35 have noncancer human health effects; and 33 are known to impart taste and odor to water. For the protection of freshwater biota, 33 of the 55 target analytes have water quality guidelines established by the EPA, and 17 have water quality guidelines established by Environment Canada.

Identification of Emerging Contaminants

NAWQA samples for pesticides and VOCs are routinely analyzed at the USGS National Water-Quality Laboratory by several broad-spectrum methods usually involving gas chromatography/mass spectrometry. Each method is capable of detecting a number of target pesticides and/or VOC analytes. In an ideal world, modifications to target analyte lists would consider changes in chemical-use patterns and many of the other characteristics described above for screening candidate VOCs. In some situations, however, the above information may not exist. Furthermore, in addition to parent compounds, there is growing interest and concern over contaminant degradates—particularly for pesticides. In the NAWQA Program, nontarget analytes are tentatively identified using computerized searches of libraries of mass spectra. For those nontarget compounds that are frequently detected, efforts are made to obtain standards for the compound and, where appropriate, include it as a target analyte. in 1991 methyl *tert*-butyl ether (MTBE), a fuel oxygenate, was added to the USGS's VOC analyte list using just such an approach.

SELECTED FINDINGS

Individual Study Units

Major findings for individual study units and national synthesis teams are published in reports, many of which are available on the Internet via the World Wide Web. The NAWQA Program's home page is http://water.usgs.gov/lookup/get?nawqa.

At the end of the initial assessment, each study unit published a report summarizing major findings for the period 1992 to 1995. Included in each of these reports is a series of tables summarizing concentrations of individual contaminants detected in groundwater, surface water, bed sediment, and tissue for the study unit in relation to the national range observed across all 20 NAWQA study units and in relation to existing environmental standards and guidelines.

National Synthesis: Pesticides in Surface Water and Groundwater

Results from the first 20 study units during 1992 to 1996 include analyses of 76 pesticides and seven pesticide degradates in more than 8,000 samples of water from rivers, streams, and wells. The 76 pesticides account for about 75 percent of national agricultural use Coy weight) and a substantial portion of urban and suburban use. More than 95 percent of all samples collected from streams and rivers contained at least one pesticide compared to about 50 percent for groundwater. Seventy-four of the 83 pesticide compounds were detected at least once in streams and ground water. Most detections in streams were greater than 0.01 µ/L and more than haft were greater than 0.05 µ/L. Agricultural and urban streams, as well as major rivers, had relatively similar high frequencies of detection, although the highest concentrations generally occurred in the smaller streams. Detection frequencies in ground water were highest in shallow groundwater in agricultural areas, somewhat lower in shallow groundwater in urban areas, and lowest in major aquifers. The shallow groundwater is generally derived from relatively recent recharge within the land-use area of interest. The major aquifers are generally deeper, have variable land use influences, and were sampled using existing production wells.

Concentrations of the 21 most commonly detected pesticides exceeded 0.05 µ/L in more than 10 percent of the stream samples or in more than 1 percent of groundwater samples at least one of the land-use categories. The most frequently detected pesticides in agricultural areas were the major herbicides: atrazine and its degradation product deethylatrazine, metolachlor, cyanazine, and alachlor, which rank first, second, fourth, and fifth, respectively, in national herbicide use for agriculture. These most heavily used herbicides also account for most of the detections in larger rivers and major aquifers and many detections in urban streams and groundwater. The herbicides that were generally found most often in urban streams are simazine, prometon, 2,4-D, diuron, and tebuthiuron, with simazine and prometon accounting for most detections in

streams and shallow groundwater. 2,4-D and prometon rank first and fourteenth among herbicides in frequency of home and garden use, and 2,4-D, simazine, and diuron rank third, eighteenth, and twenty-third, respectively, in national herbicide use for agriculture. Prometon and tebuthiuron have no reported agricultural use. Insecticides were detected much more frequently in urban streams than in agricultural streams and were seldom detected in groundwater in any setting. Most detections were accounted for by diazinon, carbaryl, malathion, and chlorpyrifos, which nationally rank first, eighth, thirteenth, and fourth, respectively, among insecticides in frequency of home use.

Low-level mixtures are the most common form of pesticide occurrence in streams and groundwater. More than 50 percent of all stream samples contained five or more pesticides, and about 25 percent of groundwater samples had two or more pesticides. In accordance with use patterns, the composition of the most common mixtures differs between urban and agricultural areas and among agricultural areas with different crops and pests. For example, simazine and prometon were present in the most commonly occurring mixtures of two or more compounds in urban areas, whereas atrazine, deethylatrazine (DEA), and metolachlor were the most common compounds in mixtures found in agricultural areas. The most common pair of compounds found in groundwater in agricultural areas was atrazine and DEA. A distinctive feature of urban streams was the common occurrence of mixtures with both herbicides and insecticides. More than 10 percent of urban stream samples contained a mixture of at least. four herbicides plus diazinon and chlorpyrifos.

Drinking water standards for individual pesticides were rarely exceeded in streams or groundwater, but aquatic life criteria were commonly exceeded in some streams. Most of the major aquifers and about half of the shallow groundwater zones sampled are sources of drinking water. Most concentrations are substantially below EPA drinking water standards, which were exceeded in less than 1 percent of the wells sampled. In streams, peak concentrations of several herbicides frequently occurred above EPA drinking water standards in some agricultural areas, but annual average concentrations, which are used for regulation, rarely exceeded standards. For drinking water, NAWQA results are generally good news regarding individual pesticides and current regulations. This conclusion is tempered, however, by the fact that criteria are not established for many pesticides and mixtures and degradation products are not considered. Furthermore, a limited range of potential effects have been assessed.

VOCs in Ground Water

Preliminary results from the first cycle of 20 NAWQA study units are summarized and available on the Internet via the World Wide Web at: http://wwwsd.cr.usgs.gov/nawqa/vocns/datasum91.html. The summary represents analyses of VOCs in 1,600 groundwater samples collected in 1993 to 1995. For most VOCs, the minimum reporting level was 0.2 µ/L. Forty-six VOCs were detected in groundwater. VOCs were most frequently detected in shallow groundwater in urban areas, in comparison to shallow groundwater in agricultural areas and major aquifers. About 54 percent of the samples of shallow ground water in urban areas contained one or more VOCs. Frequently detected VOCs

included trichloromethane (chloroform), MTBE, tetrachloroethene (perchloroethylene), and trichloroethene (trichloroethylene). While VOCs were frequently detected in shallow groundwater, similar to pesticides, their concentrations were low and almost always below maximum contaminant levels or health advisories for drinking water.

To augment data collected by the NAWQA Program for assessment of the "occurrence" of VOCs in groundwater nationwide, the USGS has compiled a national dataset of VOC analyses of samples of groundwater collected between 1985 to 1995 by 43 federal, state, and local nonpoint source monitoring programs (Lapham et al., 1997, 1998). The dataset includes analyses representing 5,320 wells in 20 states. Eight attributes of this dataset were evaluated to determine the suitability of the data to augment NAWQA data in answering occurrence questions of varying complexity. These eight attributes are: (1) VOC analytes, (2) associated reporting levels, (3) water use, (4) well-casing materials, (5) well depth, (6) depth to water level in the well, (7) aquifer lithology, and (8) distribution of sampling points.

Twelve of the 13 most frequently analyzed VOCs are in the use category of solvents, industrial reagents, and refrigerants. Other compounds of current interest were not frequently analyzed for. MTBE was analyzed for in only about 6 percent of the samples. Three other oxygenates (diisopropyl ether, ethyl tertiary-butyl ether, and tertiary-amyl methyl ether) were not included in any of the analyses in the dataset. About 70 percent of the sampled wells have the associated water use documented in the dataset. However, the dataset generally lacks documentation of the other characteristics of interest. Three modifications to these monitoring programs that would enhance the suitability of the resulting data for determining the occurrence of VOCs are: (1) expand the VOC analyte list beyond currently regulated compounds, (2) consistently record the reporting level for each analyte for every analysis, and (3) consistently record key ancillary information about each well.

SUMMARY

The NAWQA program provides information useful in identifying emerging contaminants in the nation's streams, rivers, and groundwater used for drinking water in several ways. First, NAWQA study units cover almost half of the conterminous United States and represent some of the largest and most important hydrological systems. These hydrological systems differ widely in the natural and human factors that affect water quality and thus provide a monitoring framework that is useful for identifying existing and emerging contaminants of regional and national concern.

Second, the first major component of a study unit investigation is focused on determining the broad-scale geographic and seasonal distribution of water quality conditions in relation to major point and nonpoint contaminant sources. As part of this initial component, bed sediment, tissue, and ground and surface water samples are analyzed for a large number of potentially toxic trace elements, pesticides, and other synthetic organic contaminants of concern.

Analytical reporting limits are typically much lower than many other routine monitoring efforts. In addition, nontarget analytes are tentatively identified using computerized searches of libraries of mass spectra. This combined approach is designed to fill gaps in existing data and to help identify the most important existing and emerging contaminants of concern.

Third, the NAWQA program is perennial and places a high emphasis on repetition of measurements with time and on documentation of both the methods of data collection and analysis and the locations and characteristics of data collection sites. This type of approach is essential for identifying emerging contaminants and changes in concentrations of contaminants in relation to changes in land- and water-use activities.

Fourth, in addition to investigations of individual hydrological systems, national synthesis currently focused on pesticides, VOCs, nutrients, and trace elements helps to identify regional and national patterns in the occurrence and distribution of contaminants of concern and their relation to contaminant sources.

Finally, communication and coordination with scientists and managers in other federal, state, and local agencies are critical components of the NAWQA Program. The ongoing exchange of information about emerging water quality issues and new contaminants of concern, improved methods of measurement, and new sources of data provides some of the additional insight necessary for the program to evolve and to be relevant to future water quality information needs.

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3

CDC Perspective on Emerging Chemical Contaminants in Drinking Water

Michael A. McGeehin and Deborah M. Moll

The availability of safe drinking water is a basic cornerstone of public health. Increased access to safe water and better sanitation practices have done more to increase life span and enhance human health than any other advancements in the field of medicine (Last, 1998). Throughout the twentieth century the U.S. Public Health Service (PHS) has taken a leading role in providing safe drinking water for U.S. citizens. PHS advanced the scientific knowledge needed to implement and promote appropriate technologies by sponsoring the development of breakpoint chlorination, linking the levels of coliform bacteria in water with waterborne disease rates, and demonstrating the diarrheal and parasitic burden experienced by rural households without access to safe water or sanitary facilities (HHS, 1997). Following passage of the Safe Drinking Water Act in 1974, the U.S. Environmental Protection Agency (EPA) assumed primary responsibility in the federal effort to protect the public's drinking water supply. However, the Centers for Disease Control and Prevention (CDC), the nation's premier public health agency, remains vitally interested in the safety of the drinking water supply in the United States.

The Subcommittee on Drinking Water and Health of the U.S. Department of Health and Human Services' Environmental Health Policy Committee recently identified several areas of research and public service involving drinking water that require increased federal attention (CDC, 1997). Areas of research included (1) quantify g the association between various contaminants and adverse health effects, (2) developing methodologies and arrangements to better use existing data, (3) developing laboratory and field techniques for measuring hazards, and (4) expanding federal capacity to study waterborne outbreaks. Areas of public service that the committee identified included (1) expanding the breadth of federal responses to outbreaks and disease surveillance and (2) developing techniques for educating the public and the water industry about public health issues related to drinking water.

CDC'S EXPERTISE

The CDC is a public health research and support institution that provides technical assistance to state public health agencies on all issues concerning public

health, including those associated with contaminated drinking water. In areas where high exposure to contaminated drinking water is suspected, the CDC may undertake epidemiological studies in collaboration with the state to document the health effects of exposure. As part of linking chemical exposure to health effects, the CDC develops tests of human exposure to a wide variety of toxicants. Working in conjunction with EPA, the CDC also coordinates surveillance and documents occurrence and characteristics of waterborne disease outbreaks (WBDOs).

Epidemiology

The CDC collaborates with state health departments and other federal agencies in investigating unusual occurrences of morbidity or mortality. The scope of these investigations includes those outbreaks that may have an environmental etiology. In recent years state health agencies have asked the CDC's National Center for Environmental Health (NCEH) to help them investigate a number of water-related issues. In a study of the association between elevated sulfate levels and infant diarrhea in South Dakota, the NCEH found a low frequency of tap water use when high sulfate levels were measured in tap water provided by public water systems (CDC, 1998). During an investigation in Delaware of health effects associated with elevated copper levels in drinking water, the NCEH found that gastrointestinal symptoms consistent with copper toxicity were not higher in people living in households with high copper levels than in those in control households (CDC, 1998). The NCEH is conducting ongoing studies to assess the impact that prenatal exposure to disinfection byproducts (DBPs) has on the risk for neural tube defects among newborns and studies to determine the impact of agricultural practices on the level of environmental contamination in ground- and surface waters and the human health risks associated with such contamination. The NCEH is also investigating the possible association between high nitrate levels and adverse reproductive outcomes.

Using epidemiological methods combined with the most advanced monitoring techniques will enable the CDC to provide human health data necessary to EPA and other enforcement agencies for decision making on emerging chemical contaminants.

Biomonitoring

The NCEH's Environmental Health Sciences Laboratory (EHSL) develops tests of human exposure to toxicants (biomonitoring); when combined with epidemiological studies, these tests provide vital information about how exposures contribute to serious human disease. The EHSL has developed methods for measuring more than 200 toxicants in human biological samples and is nationally and internationally recognized for its application of these methods to assessing exposure in major environmental health studies. The laboratory has developed analytical methods for 10 metals, including lead, cadmium, mercury,

uranium, thorium, and chromium; 144 dioxins and furans; environmental tobacco smoke; 20 polychlorinated biphenyls; 42 pesticides; 32 volatile organic compounds (VOCs); and 19 polycyclic aromatic hydrocarbons.

The EHSL monitors biomarkers of disease or exposure in long-term, population-based prospective and retrospective studies such as the National Health and Nutrition Examination Survey (NHANES) and the National Human Exposure Assessment Survey. These biomonitoring results provide surveillance and susceptibility data, set background levels of various diseases and environmental exposures, and determine reference ranges for specific analytes. The EHSL also analyzes biomarkers in conjunction with epidemiological studies of drinking water contamination. For example, the EHSL will monitor blood levels of methyl *tert*-butyl ether (MTBE) for a proposed study; it analyzes trihalomethane (THM) levels in blood for populations exposed to DBPs in water through various exposure routes; and it determined blood levels of chlorinated pesticides, metals, and VOCs and urine levels of organophosphate pesticides, mercury, and cadmium for a recent study of the effects of severe flooding on levels of chemical contaminants in water in Honduras following Hurricane Mitch.

Surveillance

Since 1971, the CDC and EPA have maintained a collaborative surveillance system for collecting and periodically reporting data related to the occurrences and causes of WBDOs (CDC, 1996a). The surveillance system collects data on outbreaks associated with drinking water and those associated with recreational water, including outbreaks of infectious diseases and illness from chemical toxicity. Surveillance is a critical component in the effort to reduce the impact of waterborne illness on public health; it is necessary to document the occurrence of illness, to investigate potential etiological agents, to plan and evaluate the effects of interventions, and to ensure appropriate care for people in need of services.

Public health officials need surveillance methods that allow them to rapidly detect WBDOs and to initiate preventive measures (e.g., advisories to boil water). Surveillance data that identify the types of water systems, their deficiencies, and the etiological agents associated with outbreaks could be used to evaluate the adequacy of current technologies for providing safe drinking and recreational water. In addition, such data are being used to establish research priorities and assist in improving water quality regulations (CDC, 1996a).

State, territorial, and local public health departments are primarily responsible for detecting and investigating WBDOs and for voluntarily reporting them to the CDC. However, because of variations in how they collect data, an improved national collaborative network of state programs is necessary to coordinate the development and application of surveillance methods and uniform methods of conducting epidemiological studies of WBDOs.

PUBLIC HEALTH APPROACH

A public health approach to contaminated drinking water is an essential partner to the regulatory approach taken by EPA. Properly conducted epidemiological, occurrence, and exposure studies provide important data for the decision-making process and for investigators attempting to determine the cause, extent, and impact of WBDOs. The CDC is in a unique position to lead the public health response to emerging contaminants in drinking water. It has the crucial epidemiological and laboratory resources that are necessary to address these issues, as well as an established relationship with state health departments through its role as the federal agency tasked with supporting and interacting with state public health agencies.

Addressing the human health impacts of emerging contaminants in drinking water requires a partnership among federal agencies and state health departments. Once these partners reach a consensus on what substances should be considered emerging contaminants of concern (COC), they should develop and implement a multistate surveillance system to identify and monitor people who are exposed to water likely to contain COC. Such surveillance is a state-based function that requires federal coordination to ensure uniformity and consistency among states. As a complement to public health actions where areas of high exposure are identified, investigators could conduct epidemiological studies to document the health effects of exposure to the COC, and laboratories should develop biomarkers of human exposure to link levels of human exposure to health effects. These activities, both of which are currently being carried out by the NCEH for a wide array of chemical exposures, complement the information gained from experimental research on the effects of exposure of animals to chemical toxicants.

CURRENT NCEH ACTIVITIES WITH EMERGING CONTAMINANTS

The NCEH expects to be increasingly active in responding to health issues related to drinking water contaminated with chemicals such as MTBE and DBPs. Both MTBE and DBPs have the potential to affect large segments of the U.S. population over the next decade. Another high-profile emerging issue is the threat posed by exposure to endocrine disrupters in drinking water. Research is needed on the levels of exposure to and the health effects of chemicals with known endocrine-disrupting activity in order to identify the classes of endocrine disrupters that pose the greatest threat to human health. Extensive use of pesticides and fertilizers may adversely affect drinking water quality throughout large areas of the country; in addition, increased nutrient loading from concentrated animal feed operations (CAFOs) may increase the level of nitrates and phosphates in groundwater. These facilities may also pollute water sources that are resistant to strains of bacteria, antibiotics, hormones, and other pharmaceuticals. Along the U.S.-Mexico border, inadequate infrastructure continues to be the major impediment limiting the availability of potable drinking water. Finally, natural disasters may create both acute and long-term breaches to public water supplies, which pose severe public health problems.

MTBE

MTBE, so of its use as a gasoline additive, is becoming more ubiquitous as an environmental contaminant. Because the potential health effects of chemical exposure to this contaminant are uncertain, research should be conducted on exposure levels and associated health outcomes. The NCEH is addressing the feasibility of conducting a study to assess MTBE exposure and health effects from contaminated groundwater in two eastern states. The planned study will be a case control epidemiological survey of water use and health effects, and the EHLS will measure blood levels of MTBE to evaluate exposure, and DNA adducts and red blood cell apoptosis to evaluate health effects. The NCEH will also collect water samples at the time of the survey to determine the association between the concentration of MTBE in water and exposure levels and any health effects in the study population.

DBPS

Research on DBPs and their link to cancer has been conducted over the past two decades. However, recent findings linking DBPs with adverse reproductive outcomes, recent improvements in exposure indices, and the development of human biomarkers for these compounds should yield important results in the near future that will assist regulatory agencies in establishing health-based standards. The NCEH is currently conducting a multisite study of the association of neural tube defects in newborns with prenatal THM exposure. The NCEH is also investigating the incidence of bladder cancer in pet dogs exposed to varying levels of DBPs in their drinking water and is planning a study comparing THM exposure from drinking, showering, and bathing.

While the regulatory focus for halogenated organic DBPs is currently on THMs and haloacetic acids, approximately 50 percent of the chlorination DBPs measured as total organic halide have yet to be identified, and only about 25 percent of the total mutagenicity of chlorinated drinking water has been identified (Richardson, 1998). Further identification of DBPs is essential, along with assessments of the health effects and exposure levels of known and newly identified DBPs.

Endocrine Disrupters

In the past few years there has been increasing media interest in the possibility that chemicals in our environment can disrupt normal hormonal function in humans. Implicated chemicals include industrial chemicals such as PCBs, as well as a wide variety of pesticides, including herbicides, fungicides, nematocides, and insecticides. Potential health effects of exposure to endocrine-disrupting chemicals include adverse reproductive outcomes, birth defects, breast cancer, developmental disabilities, endometriosis, thyroid problems, and testicular cancer.

The NCEH has been at the forefront in investigating some of the health outcomes associated with exposure to endocrine disrupters. For example, it

examined the relationship between exposure to chemicals that can act like estrogen and the risk of breast cancer in a case control study of 63 Alaskan native women with breast cancer and an age-matched control group. However, there are still major areas where lack of data is limiting our ability to determine the health risks posed by endocrine disrupters. For example, there is inadequate information regarding levels of prenatal exposure to these substances and the correlation between such exposure and subsequent adverse health outcomes among children.

The NCEH has more than a dozen ongoing research projects involving endocrine disrupters. They vary from large analyses of datasets (including NHANES data) to laboratory/epidemiology studies that use biomarkers to define exposure. It is vitally important that we define the hazards that may be associated with endocrine disrupters as soon as possible and devise appropriate measures to prevent exposure and adverse health effects.

CAFO Issues

Extensive use of pesticides and fertilizers may adversely affect drinking water quality throughout large geographic areas of the country. These pesticides include organophosphates, carbamates, and pyrethroids. Some preliminary data indicate that intensive agricultural practices may increase the levels of nitrate and phosphates in groundwater. High levels of nitrate leaching into drinking water supplies increase users' risk of methemoglobinemia (excess of methemoglobin in the blood). The NCEH recently investigated a cluster of spontaneous abortions in Indiana suspected of being associated with high nitrate levels in wellwater (CDC, 1996b). The report on the results of this investigation indicated a need for further assessment of a possible relationship between ingesting nitrate-contaminated water and spontaneous abortion. The NCEH is developing a study to investigate this issue.

As mentioned above, CAFOs may pollute water sources with antibiotics, hormones, and other pharmaceuticals as well as resistant strains of bacteria. The intensive use of antibiotics is an integral feature of large-scale animal agriculture. Over 40 percent of the antibiotics sold in the United States are used in agriculture. There is growing evidence that animal use of antimicrobials is tied to the evolution of multiple drug resistance in foodborne disease agents and the loss of efficacy of drugs important in human medicine (Levy, 1998). Limited research has been conducted into the environmental fate of antibiotics given to animals, such as those in the fluoroquinolone group, which includes synthetic antibiotics that are licensed for use in poultry and are excreted in the feces largely unmetabolized. The NCEH is conducting a chemical and microbial assessment of ground- and surface waters near large-scale swine-feeding operations and is investigating the environmental effects of large poultry farming operations (CDC, 1998).

The NCEH is also collaborating with the U.S. Geological Survey to develop a cross-sectional survey to determine whether water that serves as a drinking water source contains pharmaceuticals. The NCEH is providing biomarkers of human exposure and epidemiological expertise to complement water analysis capabilities provided by the USGS, which is developing a comprehensive analytical method to determine the composition and concentrations of pharmaceuticals in U.S. waters.

Infrastructure Issues

Along the U.S.-Mexico border and in some other areas of the country, inadequate or nonexistent infrastructure continues to be the major impediment limiting the availability of potable drinking water. Some water supplies are contaminated with industrial and household wastes, pesticides, and biologic contaminants. One project currently planned will study the impact of groundwater contamination with arsenic, nitrate, and total and fecal coliforms on the health of the affected population, and another will investigate whether the prevalence of contaminated water affects the prevalence of contaminated produce that is shipped to other parts of the United States.

Natural disasters, such as floods and hurricanes, may cause both acute and long-term breaches to public water supplies that pose severe public health problems. In 1998 the NCEH responded to Hurricane Georges in Puerto Rice and Hurricane Mitch in Honduras and Nicaragua. NCEH investigators found that a clean water supply was the greatest public health need of the affected populations. Short-term lack of adequate clean water was often related to road obstruction mused by hurricane debris, which prevented supply vehicles from reaching towns and shelters. Breaches of water treatment and distribution systems may lead to long-term shortages of potable water in many communities in these localities. In Honduras pesticide contamination was of concern because of severe flood damage to pesticide factories and storage facilities. A severe hurricane or other natural disaster striking the United States may cause similar damage to local water supplies and create subsequent public health problems.

CONCLUSIONS

Ensuring the safety of our nation's drinking water supply into the next century is critically important to maintaining public health. The CDC is vitally interested in collaborating with state health departments, EPA, and other interested parties in maintaining the public's confidence in its drinking water.

An appropriate public health response to the possible emergence of new chemical threats to drinking water or the reemergence of old problems will require the cooperation of experts in a broad range of disciplines. A national public health approach, including enhanced surveillance, epidemiological studies, the development of biomarkers, and the maintenance of close working relationships with state health departments, is a central component of a comprehensive assessment of emerging chemical threats to drinking water. We at the CDC will continue to work with state and federal colleagues to address public health issues related to drinking water and to provide human health data to regulatory agencies for consideration during decision-making processes.

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4

Past and Future Strategies for Sorting and Ranking Chemicals: Applications to the 1998 Drinking Water Contaminant Candidate List Chemicals

John D. Walker, D. Anthony Gray, and Michelle K. Pepling

The 1998 Drinking Water Contaminant Candidate List (CCL) includes chemicals, chemical classes, and microorganisms. This paper discusses only chemicals and chemical classes. However, the strategies for sorting and ranking drinking water contaminant chemicals and chemical classes discussed here are probably applicable to and should be considered for sorting and ranking other types of chemicals as well as drinking water contaminant microorganisms.

EPA'S RESPONSIBILITIES

Under the August 1996 Amendments to the Safe Drinking Water Act (SDWA), the U.S. Environmental Protection Agency (EPA) must publish the CCL in February 1998 and every five years thereafter, develop the National Drinking Water Contaminant Occurrence Database (NCOD) in August 1999, publish the Unregulated Contaminant Monitoring Regulation List (UCMR) in August 1999 and every five years thereafter, and identify five drinking water contaminants for potential regulation by August 2001 and every five years thereafter.

The EPA published the Draft CCL on October 6, 1997 (EPA, 1997a). After soliciting public comment on the proposed list as mandated under Section 1412(b)(1) of the SDWA, the EPA published the 1998 CCL on March 2, 1998

Under the 1996 Amendments to the SDWA, the EPA must also consider whether drinking water contaminant chemicals should be screened for endocrine disruption potential. As a result, the 206 chemicals with Chemical Abstract Service (CAS) Registry numbers that were on the Draft CCL were included in the Endocrine Disruptor Priority Setting Database (Walker et al., 1999). During development of the Endocrine Disruptor Priority Setting Database, the strengths and weaknesses of the Draft CCL were proposed strength—prepared by screening many sources of chemicals that were likely to contaminate public drinking water systems; weaknesses-concentrations, frequencies of occurrence, and locations of contaminants were not provided, and there were uncertainties concerning the probabilities that proposed contaminants could persist in drinking water. These weaknesses are likely to be addressed as EPA develops the NCOD in August 1999 and publishes the UCMR in August 1999 and every five years

thereafter. In the interim the EPA asked the National Research Council to establish a Committee on Drinking Water Contaminants.

COMMITTEE ON DRINKING WATER CONTAMINANTS

The Committee on Drinking Water Contaminants was asked to assist the EPA with three tasks: (1) developing a scientifically sound approach for deciding whether or not to regulate contaminants on the current and future CCL(s), (2) convening a workshop that will focus on emerging drinking water contaminants and the database that should be created to support future decision making on such contaminants, and (3) creating a scientifically sound approach for developing future CCLs.

As part of its effort to assist the EPA with these tasks, the Committee on Drinking Water Contaminants issued a report entitled, *Setting Priorities for Drinking Water Contaminants* (NRC, 1999). That report described the committee's review of 10 existing prioritization schemes, review of methods for assessing microbial pathogens, approaches used to develop the 1998 CCL, and suggestions for selecting candidates on the CCL for future action. The committee concluded that processes that rank contaminants are not appropriate for selecting regulatory candidates, contaminants occurring at frequencies and concentrations that cause health effects should be regulated, and processes that rank contaminants may be useful to sort and select future contaminants.

In their discussion of processes for ranking contaminants, the committee recommended that professional judgments be used to select regulatory candidates. In addition, the Committee on Drinking Water Contaminants suggested that drinking water contaminants could be organized into four categories: Category 1, Ready for Rule-Making; Category 2, Ready for Guidance Development (e.g., health advisories); Category 3, Needing Additional Occurrence Data; and Category 4, Needing Additional Research (e.g., health effects).

The committee recognized that, as expected, the quantity and quality of information would be different for each drinking water contaminant and based its categorization criteria on that premise. The committee also recommended a staged process for assessing drinking water contaminants: Stage 1, review existing data (health effects, exposure, treatment, analytical methods); Stage 2, conduct preliminary risk assessment; Stage 3, prepare decision document (regulation, drop, additional research); and Stage 4, prepare data development plan to meet five-year SDWA Requirements.

Stages 1 through 3 of the committee's process for *assessing drinking* water contaminants could be used to assign contaminants to one of the four categories listed above. The review of existing data is more extensive than ordinarily required to categorize chemicals because options for treatment must be considered as well as analytical methods for measuring contaminants in drinking water. The preliminary risk assessment recommended by the committee is analogous to that conducted by the EPA for the premanufacture of new chemicals under the Toxic Substances Control Act (i.e., a 90-day process that uses models to estimate exposure potential and structure activity relationships (SARs) and quantitative structure activity relationships (QSARs) to predict toxicity). The

decision document is necessary to assure a consistent decision-making process. The need to prepare a data development plan is critical to publishing the CCL, publishing the UCMR List, and identifying five drinking water contaminants for potential regulation every five years to meet the statutory deadlines of the 1996 amendments to the SDWA.

PAST TECHNIQUES FOR PRIORITIZING CHEMICALS

With very few exceptions, there are two major differences between past techniques for prioritizing chemicals and those currently being developed for future use: (1) past techniques did not have distinct sorting and ranking phases and (2) past techniques were not peer-reviewed or published in peer reviewed journals or books. The exception to those that did not have distinct sorting and ranking phases and have not been published in peer reviewed journals or books were those developed by and for the Toxic Substances Control Act (TSCA) Interagency Testing Committee (ITC) (Welsh and Ross, 1982; Walker, 1993a). The exception to those that have not been peer-reviewed are those that have been proposed for public comment (e.g., those developed for the ITC, the Agency for Toxic Substances and Disease Registry, the EPA's Office of Solid Waste, and California's Office of Environmental Health Hazard Assessment). The techniques developed by and for the ITC were the first techniques used by the U.S. government to sort and rank chemicals (Davis et al., 1997). Sequential sorting and ranking are critical because they promote simultaneous allocation of resources to highest-ranking chemicals within classes that have been sorted based on chemical structure or categories that have been sorted based on uses, human exposures, environmental releases, environmental fate parameters, health or ecological effects, and so forth. Peer review is significant because it provides credibility to the chemical sorting and ranking process.

Techniques Reviewed by the Committee on Drinking Water Contaminants

The Committee on Drinking Water Contaminants reviewed 10 existing chemical prioritization schemes and considered their relevance for developing a prioritization scheme for drinking water contaminants (NRC, 1999). Three prioritization schemes were developed by private organizations for drinking water contaminants. Three schemes were developed by federal and state organizations to prioritize all contaminants. Four schemes were developed by federal organizations to prioritize contaminants for specific media.

Schemes to Prioritize Drinking Water Contaminants

The first prioritization scheme for drinking water contaminants was initiated by compiling a list of chemicals from a few of the sources proposed by the EPA (1997a). This scheme provided a risk index score based on four weighted criteria: production quantity, exposure quantity, occurrence in water, and human health effects. If one criterion was missing, the chemical was not scored. The second scheme provided a sequential prioritization process for health effects, exposure potential, controlling release and treatment technology. No chemicals were evaluated using this scheme, which apparently does not exclude a chemical if all data were not available. The third scheme for drinking water contaminants was not used to evaluate any chemicals but would exclude a chemical if all data were not available (NRC, 1999).

Schemes to Prioritize All Contaminants

The first prioritization scheme for all contaminants was used to screen a number of chemicals and provided a chemical score based on toxicity (human health or ecological effects), persistence, bioaccumulation, and mass of the contaminant in waste streams. The second prioritization scheme was used to sort chemicals by chemical substructure and associated health or ecological effects as provided by expert opinions; exposure and toxicity could be scored by using empirical data or predictions, including SARs or QSARs, and a need for data by a U.S. government organization(s) could be factored into the weighting criteria. The third scheme uses toxicity information and expert opinion to assign priorities and exposure information to determine the order in which priority toxic chemicals are assessed (NRC, 1999).

Schemes to Prioritize Contaminants for Specific Media

The first scheme to prioritize contaminants for specific media ranks hazardous waste sites and is relevant to setting priorities for drinking water contaminants, because the contaminants at the hazardous waste sites determine the potential to cause adverse effects to human health or the environment. The second scheme ranks hazardous waste sites and the contaminants at hazardous waste sites for potential to cause adverse human health effects. The third scheme to prioritize contaminants for specific media is used to indicate sediment contamination potential. The fourth scheme is used to estimate the potential for pesticides applied to apples and potatoes to contaminate groundwater (NRC, 1999).

Other Techniques

There are two other techniques for ranking chemicals that may be relevant to developing a prioritization scheme for drinking water contaminants. The Michigan Critical Materials Register ranks chemicals that may threaten water quality in

Michigan. The Ontario Ministry of the Environment Scoring System ranks chemicals that may threaten surface water quality in Ontario. Both of these techniques have been described by Davis et al. (1997).

FUTURE PROCEDURES FOR SORTING AND RANKING CHEMICALS

Future procedures for sorting and ranking chemicals must consider the continued resource and testing facility limitations for assessing the risks of chemicals, promoting pollution prevention and so forth. Strategic planning will be required to assure that these resources are effectively allocated. Formulation of strategic plan should involve development of a scheme that considers vital information and facilitates sorting and ranking of chemicals into phased programs that can be accomplished with the given resources. A scheme that considers vital information and facilitates sorting and ranking of chemicals into phased data collection and testing programs is illustrated in Figure 4-1. This scheme to sort and rank structural classes of chemicals for data collection, testing, and risk assessment includes:

1. a process to organize chemicals into structural classes;
2. a review of existing data and predictions for structural classes of chemicals;
3. consideration of legal (e.g., statutory-mandated) requirements;
4. development of a relational database, consisting of exposure, effects, fate and other compartments, chemicals sorted into categories within each compartment (e.g., within the effects compartment, there may be chemicals sorted into carcinogenicity, acute toxicity, aquatic toxicity categories, etc.), and chemicals ranked (when possible) within each category (e.g., within the aquatic toxicity category, chemicals could be ranked on fish LC_{50} values, aquatic invertebrate EC_{50} values, etc.);
5. use of the relational database to produce output scenarios (e.g., chemicals with annual production volumes exceeding a certain threshold that have been measured in surface waters (the concentration of which is given) and that are toxic to fish (the LC_{50} values are given) that can be used with professional judgments to sort chemicals into groups for which (1) no additional data are needed at that time (defer), (2) more data need to be obtained, (3) testing (including screening tests) should be conducted or, (4) risk should be assessed);
6. a phased short- and long-term program to which highest-ranking chemicals (from database categories of ranked chemicals and professional judgments) within groups needing data or testing are assigned to the first phases of data collection or testing;
7. processes that assure that results from phased data collections and testing are reviewed and decisions to defer, test, or assess risk are made; and
8. feedback loops that provide pathways for phased testing data to be (a) used for development and validation of SAPs and QSARs, (b) incorporated into risk assessments and (c) included in future data assessments of structurally related chemicals.

1998 DRINKING WATER CONTAMINANT CANDIDATE LIST

The 1998 Drinking Water Contaminant Candidate List consists of 48 chemicals with unique Chemical Abstract Service Registry numbers and chemical structures (See Table 4-1). There are 20 industrial organic chemicals, 22 pesticides, and six inorganic chemicals on the list.

TSCA Interagency Testing Committee (ITC)

The ITC is an independent advisory committee to the EPA administrator that was created in 1976 under Section 4(e) of the TSCA. Sixteen U.S. government organizations are ITC members: the Agency for Toxic Substances and Disease Registry (ATSDR), the Council on Environmental Quality (CEQ), the Consumer Product Safety Commission (CPSC), the U.S. Department of Agriculture (USDA), the U.S. Department of Commerce (DOC), the U.S. Department of Defense (DOD), Food and Drug Administration (FDA), the U.S. Department of the Interior (DOI), the U.S. Environmental Protection Agency (EPA), the National Cancer Institute (NCI), the National Institute of Environmental Health Sciences (NIEHS), the National Institute for Occupational Safety and Health (NIOSH), the National Library of Medicine (NLM), the National Science Foundation (NSF), the National Toxicology Program (NTP) and the Occupational Safety and Health Administration (OSHA). Members from these U.S. government organizations nominate industrial chemicals to the ITC when their organizations need data that can be obtained through the ITC. These data include unpublished production volume, use, exposure, monitoring, environmental fate, ecological effects, and health effects data. The ITC coordinates data needs for the nominated chemicals with those of other member organizations and determines if these chemicals should be (1) added to the Priority Testing List and recommended or designated for testing, (2) deferred for testing and not added to the list or (3) removed from the list. The ITC meets monthly to identify and coordinate federal data needs for industrial chemicals, recommends these chemicals in *Federal Register* Reports to the administrator every May and November, and establishes partnerships with manufacturers, importers, processors, and users of recommended chemicals to discuss data needed. By coordinating federal data needs and establishing partnerships, the ITC provides an infrastructure to obtain information on industrial chemicals (http://www.epa.gov/opptintr/itc/).

ITC Decisions for the 1998 CCL Chemicals

The ITC has made testing decisions on about 40,000 chemicals (Walker, 1993a). The ITC has deferred testing on 1998 CCL chemicals that are only used as pesticides because chemicals that are registered active pesticide ingredients are regulated under the Federal Insecticide Fungicide Rodenticide Act, not TSCA (See Table 4-2). However, the ITC does review data on pesticides to facilitate

toxicity and persistence predictions for structurally related industrial chemicals and to develop SARs and QSARs. Eleven of the 1998 CCL chemicals were recommended for testing by the ITC in *Federal Register* reports to the EPA administrator (Table 4-2). Eight of the recommended 1998 CCL chemicals have been removed from the Priority Testing List because the EPA implemented the ITC's testing recommendations (Table 4-2).

As result of the ITC's recommendations and EPA's implementation of the ITC's testing recommendations, many of the 1998 CCL chemicals recommended for testing by the ITC are well-characterized industrial chemicals. The most well-known 1998 CCL chemical recommended by the ITC is probably methyl-*tert* butyl ether (MTBE), because it was recommended by the ITC before it was commercially significant and at a time in the commercial life cycle of the chemical when it was easiest to request voluntary development of test data (Walker, 1993b).

TSCA Section 4 and 8(d) Studies Indexed in the TSCA Test Submissions (TSCATS) Database

As a result of ITC recommendations and related EPA actions, over 1,300 unpublished studies have been submitted to the EPA for the 1998 CCL chemicals (See Table 4-3). These studies are indexed in the TSCATS database. For each study there is a reference in TSCATS, and the reference may be a document that contains more than one study, explaining why the number of studies in Table 4-3 is equal to or greater than the number of references. Procedures for retrieving studies indexed in TSCATS were recently published (Walker and Smock, 1995). TSCATS is a pointer system—that is, it is a database that points to unpublished studies that have been submitted to EPA under TSCA. It can be accessed through the World Wide Web from the following universal resource locators: (url) http://www.rtk.net or http://igm.nlm.nih.gov/. From the Right-To-Know (RTK) page the user must search on databases. From the NLM page the user must select TOXLINE and then, under the "Apply Limits" section, choose "Toxic Substances Control Act Test Submissions."

When the EPA publishes a *Federal Register* notice under TSCA Section 4(a), manufacturers and processors of chemicals mentioned in that notice can provide TSCA Section 4(a) studies to reduce the possibility of having to conduct tests under a TSCA Section 4(a) rule or they can provide TSCA Section 4(d) studies that were conducted as a result of testing to meet the requirements of a TSCA Section 4(a) notice. The total number of TSCA Section 4 studies listed in Table 4-3 includes both TSCA Section 4(a) and 4(d) studies.

When the ITC adds a chemical to the Priority Testing List, the EPA automatically promulgates a TSCA Section 8(d) Health and Safety Data Rule. This rule requires manufacturers and processors of chemicals recommended by the ITC to submit unpublished health and safety studies (health effects, environmental fate, ecological effects, environmental and occupational monitoring, industrial hygiene, etc.) to the EPA. By comparing the chemicals recommended or designated by the ITC (Table 4-2) with the number of TSCA

Section 8(d) studies for 1998 CCL chemicals (Table 4-3), it is obvious that there are some chemicals that were deferred by the ITC for which a number of TSCA Section 8(d) studies have been submitted to the EPA. There are two explanations for this: (1) EPA published a TSCA Section 8(d) rule for chemicals other than those recommended by the ITC or (2) when manufacturers and processors submitted documents (references) in response to a TSCA Section 8(d) rule, the documents contained studies on other chemicals that were not subject to the rule. The ITC encourages manufacturers and processors of ITC-recommended chemicals to submit these and other studies electronically through the Voluntary Information Submission Innovative Online Network (VISION; http://www.epa.gov/opptintr/itc/vision/).

Uses and Substructure-Based Computerized Chemical Selection Expert System (SuCCSES) Chemical Classes for the 1998 CCL Chemicals

Uses were identified for the 1998 CCL chemicals; most are used as herbicides or insecticides (See Table 4-4). Identifying uses is important because it promotes pollution prevention through the recognition that less toxic and less persistent chemicals can be substituted for more toxic and more persistent chemicals with similar uses.

SuCCSES is the first computerized system that uses expert opinions to predict potential environmental-human health interactions of individual chemicals and chemical classes that share common substructures (Walker, 1995a; Walker and Gray, 1999). For chemical categories in SuCCSES, expert opinions were offered on the potential of chemicals containing specific substructures to cause adverse human health effects or to cause effects on the environment by adversely affecting ecologically diverse classes of organisms. SuCCSES contains over 100 chemical substructures associated with about 10,000 chemicals. Effects on human health indicated potential for chemicals containing one or more of these substructures to cause acute, chronic, mutagenic, oncogenic, developmental, reproductive, or neurotoxic effects or membrane irritation (Walker, 1991, 1995a). Effects on the environment included predictions on chemicals containing one or more of these substructures to potentially cause adverse effects to algae, aquatic invertebrates, birds, fish, mammals, microorganisms, plants, or terrestrial invertebrates (Walker and Bink, 1989; Walker, 1991).

Using SuCCSES it was possible to assign the 1998 CCL chemicals to one of 17 SuCCSES classes (Table 4-4). Organizing chemicals into SuCCSES classes is critical for estimating potential health or ecological effects of structurally related chemicals and developing or validating SARs and QSARs.

Log Octanol Water Partition Coefficient (log Kow) Values, Soil or Sediment Sorption Coefficient (Koc) Values, and Henry's Law Constant for 1998 CCL Chemicals

The log K_{ow} values, Koc values and Henry's Law constants for the 1998 CCL chemicals (arranged by SuCCSES class) are listed in Table 4-5. These three environmental fate parameters were selected to estimate the potential of chemicals to remain in drinking water. These parameters can be used when reservoirs (containing aquatic species that can bioconcentrate chemicals and sediment to which chemicals can sorb) are the source of drinking water. For other drinking water sources, different parameters may have to be used. Using previously described criteria for log K_{ow} values, Koc values, and Henry's Law constants it was possible to estimate the potential of chemicals to bioconcentrate, sorb to sediment or soil, and evaporate from water, respectively (Walker, 1995b). These criteria are listed below:

log K_{ow}	Bioconcentration Potential	Koc	Sorption Potential	Henry's Law Constant (atm m^3/ mole)	Evaporation Potential
<3	Low	<2,700	Low	$>10^{-2}$	High
3-8	Moderate to High	>2,700	High	10^{-2}- 10^{-7}	Moderate
>8	Low			$<10^{-7}$	Low

By organizing the 1998 CCL chemicals into SuCCSES classes (number of chemicals in each class in parentheses), it was possible to estimate the potential of chemicals within these classes to remain in reservoirs of drinking water:

- High potential to remain in reservoir water (low bioconcentration, sorption, and evaporation potential): acetanilides (2), phenols (2), triazines (7), and ureas (2).
- Moderate potential to remain in reservoir water (moderate bioconcentration, sorption, or evaporation potential): aliphatic halides (8) (aldrin, dieldrin, and hexachlorobutadiene may bioconcentrate or sorb to soil or sediment); aromatic halides (4) (DDE may bioconcentrate or sorb to soil or sediment); aromatic hydrocarbons (2); carbamic acid esters (1); ethers (1); halophenols (2); hydrazines (1); nitroaromatics (3); phosphonothioates (1); phosphorodithioates (2); and phosphorothioates (1).
- Low potential to remain in reservoir water (low bioconcentration and sorption potential but high evaporation potential): aliphatic halides (2) (1,1-dichloropropene and 2,2-dichloropropane); aromatic hydrocarbons (1) (*p*-isopropyltoluene).

Log K_{ow}, Koc, and Henry's Law constants may be used to estimate the potential of chemicals and chemical classes to remain in drinking water. However, some professional judgment should be used before these chemicals or chemical classes are sorted or ranked (Figure 4-1). Professional judgment would consider other environmental fate parameters that could affect the ability of some chemicals or chemical classes to remain in drinking water (e.g., hydrolysis of carbamic acid esters, hydrazines).

APPLICATION OF PAST CHEMICAL SORTING TECHNIQUES TO THE 1998 CCL CHEMICALS

As noted earlier, almost all past techniques did not have distinct sorting and ranking phases. However, a few techniques developed in the recent past do promote sorting (e.g., the Use Cluster Scoring System, SuCCSES, and the Endocrine Disruption Priority Setting Database (EDPSD).

The Use Cluster Scoring System can be used to sort chemicals into use categories (Davis et al., 1997). SuCCSES was described earlier. The EDPSD can be used to sort chemicals into structural classes and categories based on uses, production volumes, environmental fate parameters, occurrences in fish and wildlife tissues, reproductive effects, estrogen receptor binding affinity potentials, and so on (Walker et al., 1999). Past sorting techniques (uses and environmental fate parameters) were applied to the 1998 CCL chemicals; the results are summarized in Table 4-5 and discussed earlier.

APPLICATION OF PAST CHEMICAL RANKING TECHNIQUES TO THE 1998 CCL CHEMICALS

To illustrate the application of past ranking techniques, the aliphatic halides from Table 4-5 were ranked based on exposure and effects scores developed by and for the ITC (Walker, 1993b, 1995a).

Exposure Scores

Exposure scores and criteria for assigning scores to exposure factors that were relevant to ranking aliphatic halides are production volume, environmental persistence, and bioaccnmulation potential (See Table 4-6). These scores and criteria were applied to the aliphatic halides from the 1998 CCL (See Table 4-7). Ranking on production volume indicated that there were three groups of aliphatic halides: those with annual production volumes greater than 10 million pounds, greater than 1 million pounds, or less than 1 million pounds (Table 4-7). Ranking on environmental persistence indicated that there were two groups of aliphatic halides: those that could persist for years and those that could persist for months (Table 4-7). Ranking on bioaccumulation potential indicated that there were three groups of aliphatic halides based on based on log K_{ow} (Table 4-7). The three aliphatic halides that could persist for years (aldrin, dieldrin, and

hexachlorobutadiene) were the same three that could bioconcentrate or sorb to soil or sediment (Table 4-5).

Effects Scores

Four biological effects that were relevant to ranking the 1998 CCL chemicals were acute toxicity, mutagenicity, *carcinogenicity*, and ecotoxicity (See Table 4-8). The scores and criteria for these biological effects were applied to the aliphatic halides from the 1998 CCL (See Table 4-9). Positive scores (based on empirical data) and negative scores (based on predictions) for biological effects were evaluated separately. Based on acute toxicity and ecotoxicity scores, aldrin and dieldrin would rank the highest and 1,1-dichloropropene and 2,2-dichloropropane the lowest. Based on mutagenicity and carcinogenicity scores, 1,3-dichloropropane would rank the highest and 2,2-dichloropropane the lowest.

APPLICATION OF FUTURE CHEMICAL SORTING PROCEDURES TO THE 1998 CCL CHEMICALS

Procedures related to chemical properties, waste management, and resource productivity have been suggested for scoring and ranking chemicals in the future (Jensen et al., 1997). While only the procedures related to chemical properties were described in sufficient detail to warrant immediate consideration, there are merits to waste management and resource productivity approaches as evidenced by EPA's development of the Waste Minimization Prioritization Tool, which was proposed for public comment on June 23, 1997 (EPA, 1997b), substantially revised in response to public comments, and published with the Draft Resource Conservation Recovery Act Persistent Bioaccumulator Toxics list on November 9, 1998 (EPA, 1998b). Procedures related to chemical properties that might be considered in the future include flammability, ignitability, explosivity, oxidizability, reactivity, corrosivity, chemical-environmental interactions, global warming potential, ozone depletion potential, photochemical oxidant creation potential, odor threshold values, eutrophication potential, and acidification potential (Jensen et al., 1997). While criteria have been proposed to score all these chemical properties, it was not possible to use them to sort the 1998 CCL chemicals. However, two new procedures not considered by Jensen et al. (1997) could be used to sort the 1998 CCL chemicals.

The first procedure, based on a chemical's mode of toxic action, was used in conjunction with SuCCSES classes to sort the 1998 CCL chemicals (See Table 4-10). Results from testing the acute toxicity of about 600 chemicals to fathead minnows were used to develop a computer-based expert system that predicts mode of toxic action based on chemical structure (Russom et al., 1997). The models and substructure search methods were designed for the ASsessment Tools for the Evaluation of Risk (ASTER) expert system and database. ASTER is an integration of the AQUatic toxicity Information REtrieval (AQUIRE)

database and the QSAR system for use in ecological risk assessments (Russom et al., 1991). Using substructure rules based on mode of toxic action, ASTER provides high-quality data for discrete organic chemicals, when available in the associated databases, and QSAR-based estimates when there is a dearth of information. QSARs are based on the mode of toxic action of the chemical of concern. For chemicals with substructures associated with multiple modes of action, the equation that results in the highest level of hazard is selected.

Sorting the 1998 CCL chemicals based on modes of toxic action in conjunction with SuCCSES classes makes it is possible to sort groups of chemicals within and between SuCCSES classes. Within the SuCCSES class of aliphatic halides, modes of toxic action can be used to sort aliphatic halides into three groups of chemicals: those with nonpolar narcosis, reactivity; alkylation or arylation reaction and neurotoxicant; cyclodiene-type modes of action (Table 4-10). These differences are important because, while all the aliphatic halides have a common substructure that was the basis of assigning them to a particular SuCCSES class, the modes of toxic action help identify important subclasses that could be used in the future to develop more well-defined SuCCSES classes. These structural differences and subclasses are clearly illustrated in Table 4-1 (e.g., dieldrin is the epoxide of aldrin, and both are cyclodiene-type neurotoxicants, and 1,3-dichloropropene and hexachlorobutadiene are both β-chlorinated olefins, and both have alkylation reactivity). The other six aliphatic halides are all chlorinated alkanes, except 1,1-dichloropropene, an β-chlorinated olefin, but all have a nonpolar narcosis mode of toxic action. Based on modes of toxic action, the aliphatic halides could be sorted into three subclasses or three new SuCCSES classes. In contrast, consider the three SuCCSES classes—phosphonothioates, phosphorodithioates, and phosphorothioates—which all have an organophosphate-mediated acetylcholinesterase inhibition mode of toxic action and could be classified in one mode of toxic action category because of their structural similarities (Table 4-1).

The second procedure, based on a chemical's carcinogenicity concern level, was used in conjunction with SuCCSES classes to sort the 1998 CCL chemicals (Table 4-10). The carcinogenicity concern level was estimated using expert judgment and EPA's Cancer Expert System (Woo et al., 1995, 1993; Lai et al., 1996). The Cancer Expert System is a knowledge rule-based artificial intelligence system that evaluates the carcinogenic potential of chemicals based on SAR analysis and available short-term predictive data. While the system provides six semiquantitative carcinogenicity concern levels, the six levels were merged into three for this paper: high, moderate, and low. Chemicals with high concern level either have known human carcinogenicity or high probability of being potent multispecies carcinogens. For chemicals with moderate concern level, there is either evidence or reasonably high probability of being moderately active animal carcinogens or possible human carcinogens. Chemicals with low concern levels either lack evidence of carcinogenicity, are marginally active, or are considered unlikely to be of significant concern as possible human carcinogens.

Sorting the 1998 CCL chemicals based carcinogenicity concern levels in conjunction with SuCCSES classes makes it is possible to sort groups of chemicals within and between SuCCSES classes. Within the SuCCSES class of aliphatic halides, carcinogenicity concern levels can be used to sort aliphatic

halides into three groups of chemicals: those with high, moderate, and low levels of concern (See Table 4-11). While there may be some connection between modes of toxic action (Table 4-10) and carcinogenicity concern levels (Table 4-11), it would be difficult to make that connection without additional data on species tested, routes of administration, target organs and so forth. However, as with modes of action (Table 4-10), the three SuCCSES classes—phosphonothioates, phosphorodithioates, and phosphorothioates—could be sorted into a low carcinogenicity concern level category because of their structural similarities (Table 4-1).

APPLICATION OF FUTURE CHEMICAL RANKING PROCEDURES TO THE 1998 CCL CHEMICALS

As noted earlier, while Jensen et al. (1997) suggested procedures for scoring and ranking chemicals in the future, it is not possible to use any of those procedures to rank the 1998 CCL chemicals. However, two new procedures not considered by Jensen et al. (1997) could be used to do so.

The first procedure to rank the 1998 CCL chemicals uses the expert opinions generated during development of SuCCSES. The use of expert opinions to identify potential effects of chemicals is not new. However, the use of expert opinions to predict the potential of chemicals containing specific substructures to cause adverse effects to human health or the environment is new and was developed as part of SuCCSES (Walker and Gray, 1999). To illustrate how SuCCSES might be used to rank the 1998 CCL chemicals, three SuCCSES classes and their potential health effects were selected as examples:

SuCCSES Class	Potential Health Effects
Nitroaromatics	Carcinogenicity Mutagenicity Other chronic effects
Halophenols	Carcinogenicity Mutagenicity Other chronic effects
Hydrazines	Acute toxicity Membrane irritation Oncogenicity

There are three nitroaromatics, two halophenols, and one hydrazine on the 1998 CCL (Table 4-4). For carcinogenicity, mutagenicity, and acute toxicity the chemicals can be ranked based on the scores presented in Table 4-8 (note that data or predictions can be used to generate scores). In addition, they could be ranked for carcinogenicity concern levels using the estimates in Table 4-11.

The second procedure to rank the 1998 CCL chemicals uses QSARs. There are at least three QSARs that are sufficiently robust and well validated to rank the 1998 CCL chemicals: (1) fish LC_{50}, (2) rat oral LD_{50}, and (3) hologram QSAR (HQSAR) for estrogen receptor binding affinity. HQSAR describes

molecules in terms of molecular fingerprints that encode two-dimensional compositional and topological information and provides estimates of estrogen-receptor binding affinity. Estimates are generated by using a simplified 3D-QSAR model and reported as the negative log of the LC_{50} in mM (Walker et al., 1999). The HQSAR is used to illustrate how a QSAR could be used to rank the 1998 CCL chemicals. HQSAR values were available in the EDPSD for 35 of the 1998 CCL chemicals. The HQSAR values ranged from -0.61 (dieldrin) to -3.46 (DDE) and might be used to sort and rank classes of the 1998 CCL chemicals (e.g., HQSAR values for all aliphatic halides, except aldrin and dieldrin ranged from -2.32 to-2.48; HQSAR values for all triazines ranged from -2.34 to -2.97).

IDENTIFICATION OF FUTURE CCL CHEMICALS

There are many methods by which future CCL chemicals could be identified: (1) structural relationships to known drinking water contaminants, (2) uses, (3) environmental release patterns that are similar to existing drinking water contaminants, (4) environmental fate parameters and models that indicate potential to enter and persist in water, (5) frequency of occurrence in drinking water, (6) ability to persist in drinking water and so forth. Two examples illustrate how future CCL chemicals might be identified.

The first example compared environmental fate parameters used to estimate the potential of the 1998 CCL chemicals to remain in water with wildlife tissue concentrations of these chemicals or the occurrence frequency of these chemicals in wildlife tissues. The environmental fate parameters that were selected to estimate the potential of the 1998 CCL chemicals to remain in drinking water were discussed earlier and are summarized in Table 4-5. Data on occurrence or tissue concentration data for the 1998 CCL chemicals in wildlife were extracted from the Contaminant Exposure and Effects—Terrestrial Vertebrates database (Rattner et al., 1999). These data are summarized in Table 4-12. By comparing the environmental fate parameters for 1998 CCL chemicals that remain in drinking water (low bioconcentration, sorption, and evaporation potential) with the 1998 CCL chemicals in wildlife it should be possible to: (1) identify other structurally related chemicals with low bioconcentration, sorption, and evaporation potential that would contaminate drinking water and wildlife species and (2) identify wildlife species that are likely to be contaminated by structurally related chemicals with low bioconcentration, sorption, and evaporation potential that could serve as sentinel species to evaluate potential effects and contribute to the understanding of environmental-human health effects interactions.

The second example analyzed use data for structurally related chemicals. One of the aliphatic halides on the 1998 CCL (1,1,2,2-tetrachloroethane) was selected to exemplify how this procedure would work. First, consider the uses for 1,1,2,2-tetrachloroethane: a solvent in rubber manufacture, a solvent in styrene-butadiene rubber manufacture, a solvent in polystyrene production, a solvent used in machinery manufacture and repair, and a solvent for varnishes.

Second, consider similarly used aliphatic halides (See Table 4-13). There are at least three aliphatic halides (not on the 1998 CCL) with uses similar

to those of 1,1,2,2-tetrachloroethane; all have at least three uses that are similar to 1,1,2,2-tetrachloroethane, and some have more uses (Table 4-13). Third, consider the production, use, and environmental release volumes for aliphatic halides (not on the 1998 CCL) that have similar uses to 1,1,2,2-tetrachloroethane (See Table 4-14).

Fourth, consider the log K_{ow} values, Koc values, and Henry's Law constants (environmental fate parameters that can be used to estimate if chemicals will remain in drinking water) for aliphatic halides (not on the 1998 CCL) that have similar uses to 1,1,2,2-tetrachloroethane (See Table 4-15).

The information in Tables 4-13, 4-14, and 4-15 suggests that 1,1,1-trichloroethane, carbon tetrachloride, and 1,1,2-trichloroethane could be future CCL chemicals. Data that could be used to decide if they should be added to the 2003 CCL include uses that could result in environmental releases and potential to persist in drinking water. While 1,1,2-trichloroethane has the fewest uses related to 1,1,2,2-tetrachloroethane and a low-use volume, the Toxics Release Inventory (TRI) volume is higher than 1,1,2,2-tetrachloroethane and the Henry's Law constant is lower than 1,1,2,2-tetrachloroethane, suggesting that it could be a potential addition to the 2003 CCL. Carbon tetrachloride has three uses related to 1,1,2,2-tetrachloroethane, more total uses, a low-to-medium use volume, and a higher TRI volume than 1,1,2,2-tetrachloroethane, but the Henry's Law constant is high enough that it could evaporate from drinking water. 1,1,1-Trichloroethane has all uses related to 1,1,2,2-tetrachloroethane, more total uses, a medium to high use volume and a much higher TRI volume than 1,1,2,2-tetrachloroethane, but the Henry's Law Constant is high enough that it could evaporate from drinking water. However, considering the magnitude of the TRI volume, if the release rate is higher than the evaporation rate, 1,1,1-trichloroethane could be a potential addition to the 2003 CCL.

ALGORITHMS, WEIGHTING, AND SCALING FACTORS

An adequate discussion of algorithms, weighting, and scaling factors and application to the 1998 CCL chemicals is beyond the scope of this paper. However, the authors want to make readers aware of algorithms, weighting, and scaling factors that could be used to rank the 1998 CCL of chemicals. There are previously used exposure algorithms (Walker and Brink, 1989) and weighting and scaling factors (Walker, 1993a).

There is an algorithm developed for and by the ITC for producing health effects (HE) scores by summing scores for health effects endpoints (H), monitoring (M), and occupational exposures (X) and adding to that a number that is equal to three times the log of the annual production or importation volume:

$$\text{HE Score} = \sum H(1+\sum M+\sum X) + 3(\log \text{Volume})$$

Also, there is an algorithm developed for and by the ITC for producing ecological effects (EE) scores by summing scores for ecological effects endpoints

(E) and monitoring (M) and adding to that a number that is equal to three times the log of the annual production or importation volume:

$$\text{EE Score} = \sum E(1+\sum M) + 3(\log \text{Volume})$$

Finally, there is an algorithm developed for and used by the EPA's Office of Solid Waste for the Waste Minimization Prioritization Tool (W (EPA, 1997b, 1998b). This algorithm considers human toxicity (HT), mass of the substance that is produced (M), persistence (P), and bioaccumulation (B) plus ecotoxicity (ET), mass of the substance that is produced (M), persistence (P), and bioaccumulation (B):

$$\text{WMPT Score} = (HT + M + P + B) + (ET + M + P + B)$$

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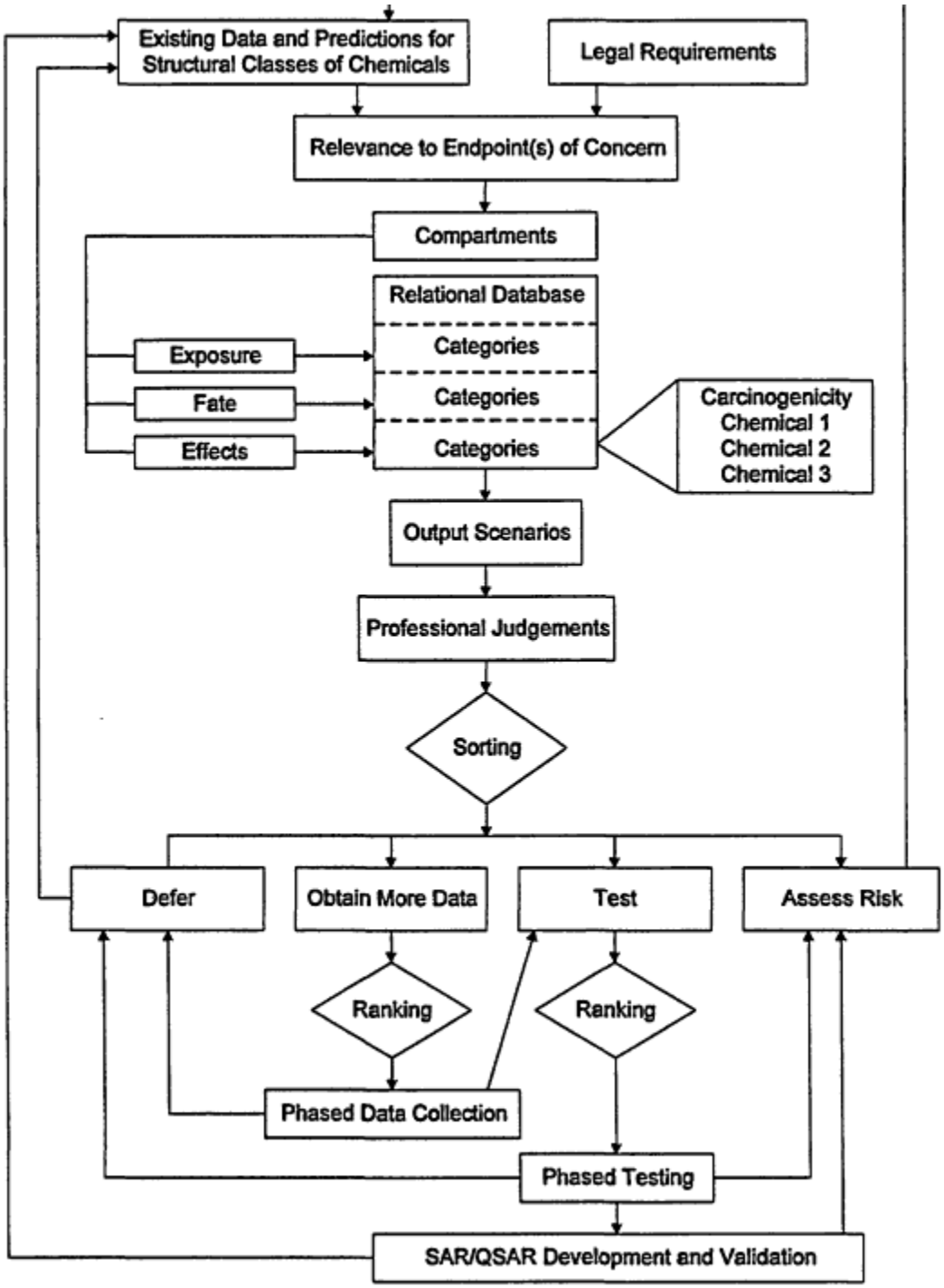
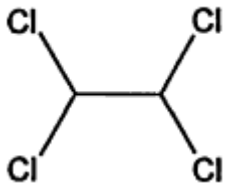
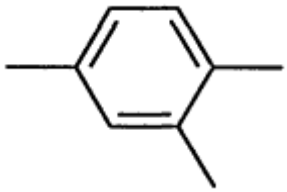
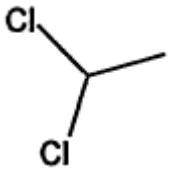
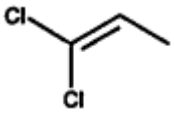
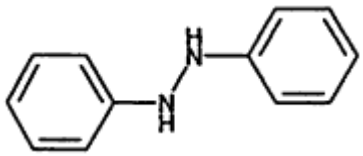
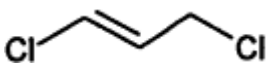
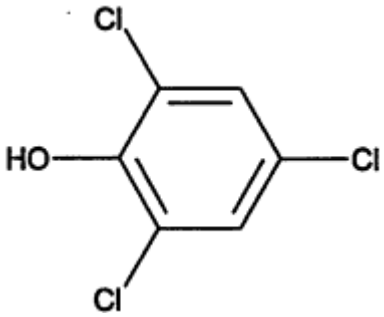
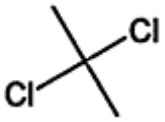
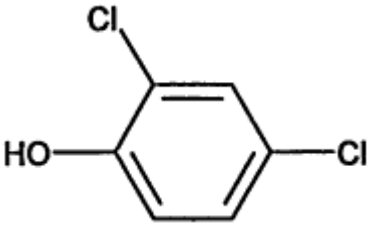
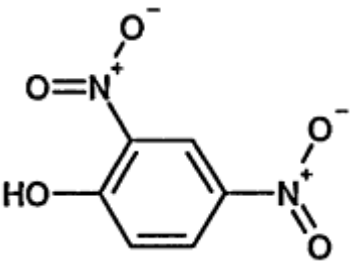
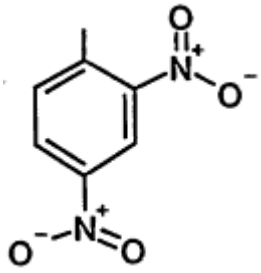
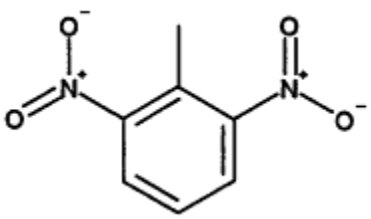
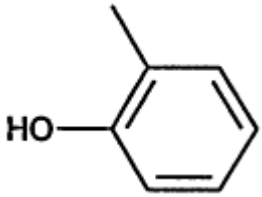
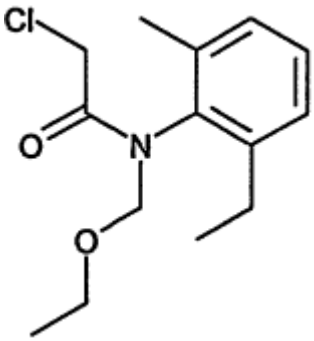
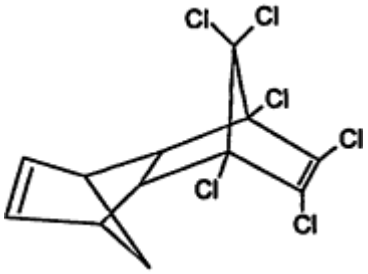


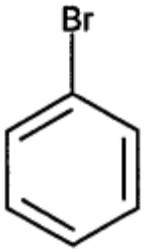
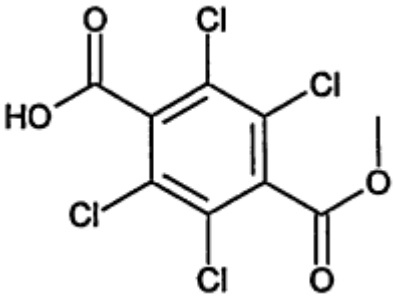
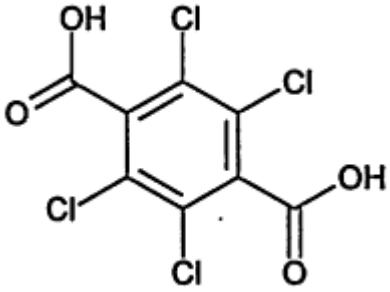
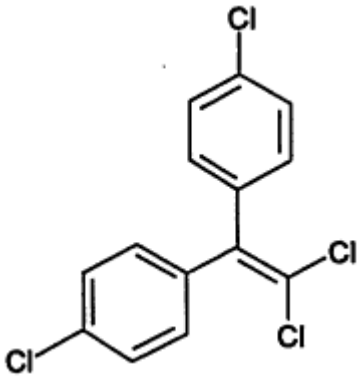
Figure 1.
Sorting and Ranking Structural Classes of Chemicals for Data Collection, Testing and Risk Assessment

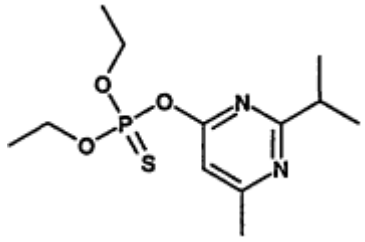
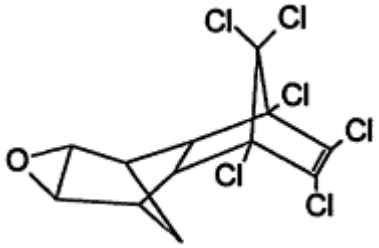
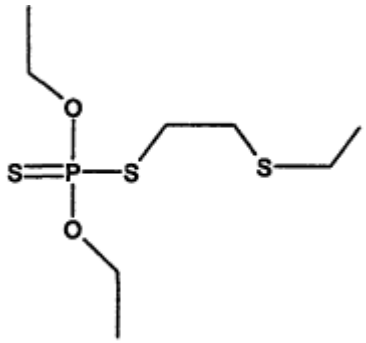
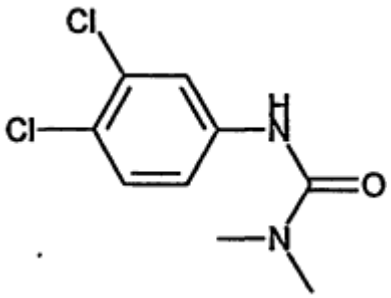
TABLE 4-1 Chemical Abstracts Service (CAS) Registry Numbers. Names and Structures for the 1998 CCL Chemicals

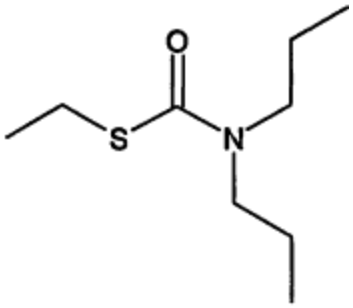
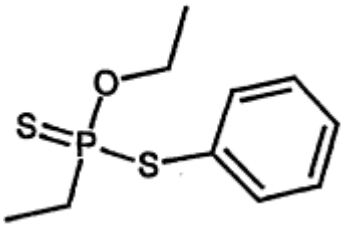
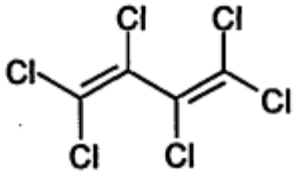
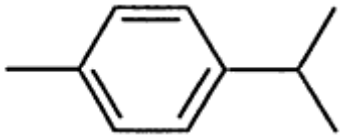
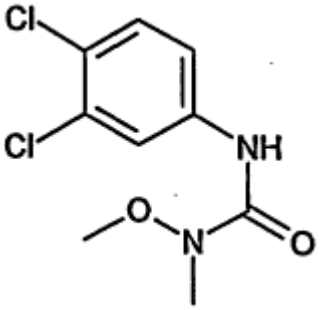
CAS No.	Chemical Name	Structure
000079-34-5	1,1,2,2-Tetrachloroethane	
000095-63-6	1,2,4-Trimethylbenzene	
000075-34-3	1,1-Dichloroethane	
000563-58-6	1.1-Dichloropropene	
000122-66-7	1.2-Diphenylhydrazine	
000142-28-9	1.3-Dichloropropane	
000542-75-6	1,3-Dichloropropene	

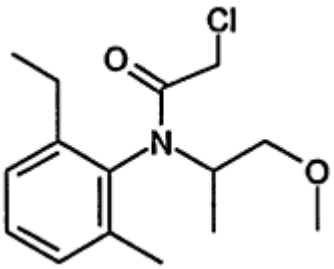
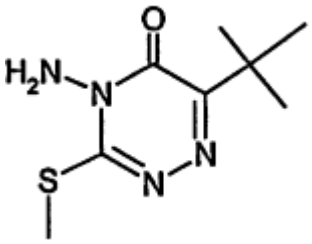
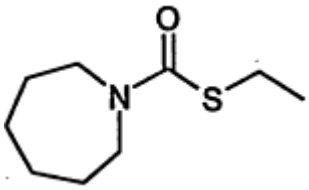
CAS No.	Chemical Name	Structure
000088-06-2	2,4,6-Trichlorophenol	
000594-20-7	2,2-Dichloropropane	
000120-83-2	2,4-Dichlorophenol	
000051-28-5	2,4-Dinitrophenol	
000121-14-2	2,4-Dinitrotoluene	

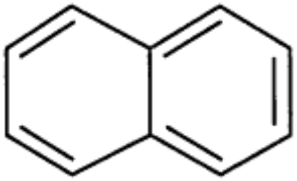
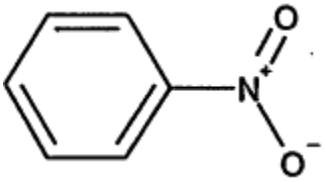
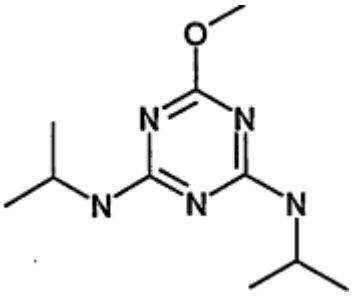
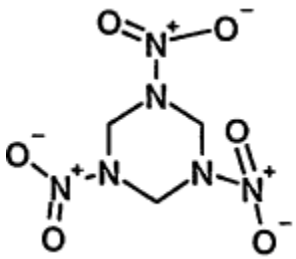
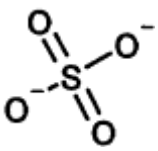
CAS No.	Chemical Name	Structure
000606-20-2	2,6-Dinitrotoluene	
000095-48-7	2-Methylphenol (*o*-cresol)	
034256-82-1	Acetochlor	
000309-00-2	Aldrin	
007429-90-5	Aluminum	$Al^{(0)}$
007440-42-8	Boron	$B^{(0)}$

CAS No.	Chemical Name	Structure
000108-86-1	Bromobenzene	
000887-54-7	DCPA mono-acid degradate	
002136-79-0	DCPA di-acid degradate	
000072-55-9	DDE	

CAS No.	Chemical Name	Structure
000333-41-5	Diazinon	
000060-57-1	Dieldrin	
000298-04-4	Disulfoton	
000330-54-1	Diuron	

CAS No.	Chemical Name	Structure
000759-94-4	EPTC (s-ethyl-dipropylthiocarbamate)	
000944-22-9	Fonofos	
000087-68-3	Hexachlorobutadiene	
000099-87-6	*p*-Isopropyltoluene (*p*-cymene)	
000330-55-2	Linuron	

CAS No.	Chemical Name	Structure
007439-96-5	Manganese	**Mn**
000074-83-9	Methyl bromide	
001634-04-4	Methyl-*t*-butyl ether (MTBE)	
051218-45-2	Metolachlor	
021087-64-9	Metribuzin	
002212-67-1	Molinate	

CAS No.	Chemical Name	Structure
000091-20-3	Naphthalene	
000098-95-3	Nitrobenzene	
001610-18-0	Prometon	
000121-82-4	RDX	
007440-23-5	Sodium	Na^+
014808-79-8	Sulfate	

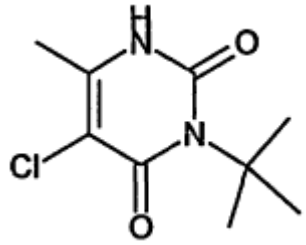
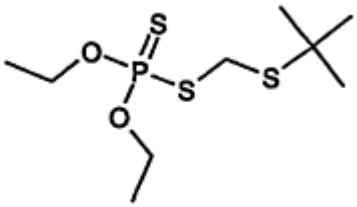
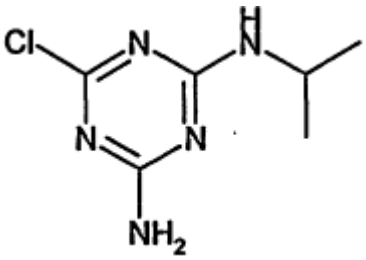
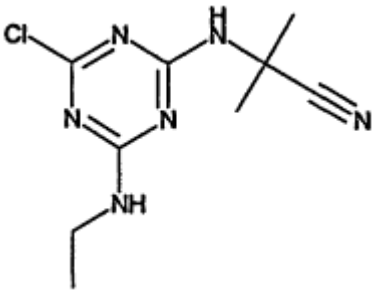
CAS No.	Chemical Name	Structure
005902-51-2	Terbacil	
013071-79-9	Terbufos	
006190-65-4	Triazines (Atrazine-desethyl)	
021725-46-2	Triazines (Cyanazine)	
007440-62-2	Vanadium	V

TABLE 4-2 ITC Decisions for the 1998 CCL Chemicals

CAS No.	Chemical Name	Decision	ITC Report No.	Federal Register Citation	Date
000079-34-5	1,1,2,2-Tetrachloroethane	Deferred			
000095-63-6	1,2,4-Trimethylbenzene	Designated	10	47FR22585	5/25/82
		Removed	13	48FR55674	12/14/83
000075-34-3	1,1-Dichloroethane	Designated	32	58FR38490	7/16/93
000563-55-6	1,1-Dichloropropene	Deferred			
000122-66-7	1,2-Diphenylhydrazine	Recommended	28	56FR41212	8/19/91
		Removed	32	58FR38490	7/16/93
000142-28-9	1,3-Dichloropropane	Deferred			
000542-75-6	1,3-Dichloropropene	Deferred			
000088-06-2	2,4,6-Trichlorophenol	Deferred			
000594-20-7	2,2-Dichloropropane	Deferred			
000120-83-2	2,4-Dichlorophenol	Recommended	28	56FR41212	8/19/91
		Removed	32	58FR38490	7/16/93
000051-28-5	2,4-Dinitrophenol	Recommended	27	56FR9534	3/06/91
		Removed	33	59FR3764	1/26/94
000121-14-2	2,4-Dinitrotoluene	Designated	32	58FR38490	7/16/93
000606-20-2	2,6-Dinitrotoluene	Deferred			
000095-45-7	2-Methylphenol	Designated	1	42FR55026	10/12/77
	(*o*-cresol)	Removed	13	48FR55674	12/14/83
034256-82-1	Acetochlor	Deferred			
000309-00-2	Aidrin	Deferred			
007429-90-5	Aluminum	Deferred			
007440-42-8	Boron	Deferred			
000108-86-1	Bromobenzene	Deferred			
000857-54-7	DCPA mono-acid	Deferred degradate			
002136-79-0	DCPA di-acid degradate	Deferred			
000072-55-9	DDE	Deferred			

CAS No.	Chemical Name	Decision	ITC Federal No.	Report Register Citation	Date
000333-41-5	Diazinon	Deferred			
000060-57-1	Dieldrin	Deferred			
000298-04-4	Disulfoton	Deferred			
000330-54-1	Diuron	Deferred			
000759-94-4	EPTC (*s*-ethyl-dipropylthiocarbamate)	Deferred			
000944-22-9	Fonofos	Deferred			
000087-68-3	Hexachlorobutadiene	Designated	1	42FR55026	10/12/77
		Removed	12	48FR24443	6/01/83
000099-87-6	*p*-Isopropyltoluene (*p*-cymene)	Deferred			
000330-55-2	Linuron	Deferred			
007439-96-5	Manganese	Deferred			
000074-83-9	Methyl bromide	Deferred			
001634-04-4	Methyl-*t*-butyl ether	Recommended	19	51FR41417	11/14/86
	(MTBE)	Designated	20	52FR19020	5/20/87
		Removed	22	53FR18196	5/20/88
051218-45-2	Metolachlor	Deferred			
021087-64-9	Metribuzin	Deferred			
002212-67-1	Molinate	Deferred			
000091-20-3	Naphthalene	Designated	35	59FR67596	12/29/94
000098-95-3	Nitrobenzene	Designated	I	42FR55026	10/12/77
		Removed	9	47FR5456	2/05/82
001610-18-0	Prometon	Deferred			
000121-82-4	RDX	Deferred			
007440-23-5	Sodium	Deferred			
014808-79-8	Sulfate	Deferred			
005902-51-2	Terbacil	Deferred			
013071-79-9	Terbufos	Deferred			

CAS No.	Chemical Name	Decision	ITC Federal No.	Report Register Citation	Date
006190-65-4	Triazines (atrazine-desethyl)	Deferred			
021725-46-2	Triazines (cyanazine)	Deferred			
007440-62-2	Vanadium	Deferred			

TABLE 4-3 TSCA Section 4 and 8(d) References and Studies Indexed in the TSCA Test Submissions (TSCATS) Database for 1998 CCL Chemicals

CAS No.	Chemical Name	No. of TSCATS Entries			
		TSCA Section 8(d)		TSCA Section 4	
		References	Studies	References	Studies
000079-34-5	1,1,2,2-Tetrachloroethane	75	100	8	9
000095-63-6	1,2,4-Trimethylbenzene	24	36	4	4
000075-34-3	1,1-Dichloroethane	110	134	8	8
000563-58-6	1,1-Dichloropropene	1	3	0	0
000122-66-7	1,2-Diphenylhydrazine	8	10	1	1
000142-28-9	1,3-Dichloropropane	12	22	2	3
000542-75-6	1,3-Dichloropropene	98	137	1	1
000088-06-2	2,4,6-Trichlorophenol	24	47	4	4
000594-20-7	2,2-Dichloropropane	0	0	0	0
000120-83-2	2,4-Dichlorophenol	31	54	5	5
000051-28-5	2,4-Dinitrophenol	12	17	4	6
000121-14-2	2,4-Dinitrotoluene	44	71	3	4
000606-20-2	2,6-Dinitrotoluene	19	23	2	2
000095-48-7	2-Methylphenol (*o*-cresol)	59	90	19	30
034256-82-1	Acetochlor	0	0	0	0
000309-00-2	Aldrin	12	12	3	3
007429-90-5	Aluminum	25	29	1	1
007440-42-8	Boron	6	6	1	1
000108-86-1	Bromobenzene	**7**	**9**	**3**	**3**
000887-54-7	DCPA mono-acid.	0	0	0	0
002136-79-0	DCPA di-acid degradate	0	0	0	0
000072-55-9	DDE	10	10	3	3
000333-41-5	Diazinon	1	1	3	3
000060-57-1	Dieldrin	13	13	3	3
000298-04-4	Disulfoton	1	1	1	1

CAS No.	Chemical Name	No. of TSCATS Entries			
		TSCA Section 8(d)		TSCA Section 4	
		References	Studies	References	Studies
000330-54-1	Diuron	0	0	0	0
000759-94-4	EPTC (*s*-ethyl-dipropyl thiocarbamate)	0	0	0	0
000944-22-9	Fonofos	0	0	0	0
000087-68-3	Hexachlorobutadiene	61	87	16	20
000099-87-6	*p*-Isopropyltoluene (*p*-cymene)	5	5	1	1
000330-55-2	Linuron	1	2	0	0
007439-96-5	Manganese	43	63	3	3
000074-83-9	Methyl bromide	88	107	4	4
001634-04-4	Methyl-*t*-butyl ether	92	216	50	78
051218-45-2	Metolachlor	0	0	0	0
021087-64-9	Metribuzin	0	0	0	0
002212-67-1	Molinate	0	0	0	0
000091-20-3	Naphthalene	161	234	12	12
000098-95-3	Nitrobenzene	33	49	6	9
001610-18-0	Prometon	0	0	0	0
000121-82-4	RDX	0	0	1	1
007440-23-5	Sodium	27	32	1	1
014808-79-8	Sulfate	17	20	1	1
005902-51-2	Terbacil	0	0	0	0
013071-79-9	Terbufos	0	0	0	0
006190-65-4	Triazines (atrazine-desethyl)	0	0	0	0
021725-46-2	Triazines (cyanazine)	1	1	1	I
007440-62-2	Vanadium	17	20	2	2

TABLE 4-4 Substructure-Based Computerized Chemical Selection Expert System (SuCCSES) Classes and Uses for 1998 CCL Chemicals

CAS No.	Chemical Name	SuCCSES Class	Use
034256-82-1	Acetochlor	Acetanilides	Herbicide
051218-45-2	Metohchlor	Acetanilides	Herbicide
000060-57-1	Dieldrin	Aliphatic halides	Insecticide
000074-83-9	Methyl bromide	Aliphatic halides	Organic synthesis, fumigant
000075-34-3	1,1-Dichloroethane	Aliphatic halides	Chemical intermediate
000079-34-5	1,1,2,2-Tetrachloroethane	Aliphatic halides	Solvent
000087-68-3	Hexachlorobutadiene	Aliphatic halides	Chemical intermediate (no longer produced in U.S.)
000142-28-9	1,3-Dichloropropane	Aliphatic halides	Unknown
000309-00-2	Aidrin	Aliphatic halides	Insecticide
000542-75-6	1,3-Dichloropropene	Aliphatic halides	Organic synthesis, soil fumigant
000563-58-6	1,1-Dichloropropene	Aliphatic halides	Unknown
000594-20-7	2,2-Dichloropropane	Aliphatic halides	Unknown
000072-55-9	DDE	Aromatic halides	Degradation product of DDT
000108-86-1	Bromobenzene	Aromatic halides	Solvent, organic synthesis
000887-54-7	DCPA mono-acid degradate	Aromatic halides	Degradation product of DCPA
002136-79-0	DCPA di-acid degradate	Aromatic halides	Degradation product of DCPA
000091-20-3	Naphthalene	Aromatic hydrocarbons	Moth repellant, fungicide
000095-63-6	1,2,4-Trimethylbenzene	Aromatic hydrocarbons	Dyes, pharmaceuticals

CAS No.	Chemical Name	SuCCSES Class	Use
000099-87-6	*p*-Isopropyitoluene (*p*-cymene)	Aromatic hydrocarbons	Heat-transferring agent
000759-94-4	EPTC (*s*-ethyl-dipropylthiocarbamate)	Carbamic acid esters	Herbicide
007429-90-5	Aluminum	Elements	Numerous consumer/industrial applications
007439-96-5	Manganese	Elements	Numerous industrial applications
007440-23-5	Sodium	Elements	Numerous applications
007440-42-8	Boron	Elements	Numerous consumer/industrial applications
007440-62-2	Vanadium	Elements	Numerous industrial applications
001634-04.4	Methyl-*t*-butyl ether (MTBE)	Ethers	Octane booster for unleaded gasoline
000088-06-2	2,4,6-Trichlorophenol	Halophenols	Mfg. of 2,4,5-T (no longer produced in U.S.)
000120-83-2	2,4-Dichlorophenol	Halophenols	Mfg. of 2,4-D, organic synthesis
000122-66-7	1,2-Diphenylhydrazine	Hydrazines	Mfg. of benzidine (no longer produced in U.S.)
014808-79-8	Surfate	Inorganics	Numerous applications
000098-95-3	Nitrobenzene	Nitroaromatics	Solvent for cellulose ethers, mfg. of aniline

CAS No.	Chemical Name	SuCCSES Class	Use
000121-14-2	2,4-Dinitrotoluene	Nitroaromatics	Explosives, dyes, organic synthesis
000606-20-2	2,6-Dinitrotoluene	Nitroaromatics	Explosives, dyes, organic synthesis
000051-28-5	2,4-Dinitrophenol	Phenols	Mfg. of explosives
000095-48-7	2-Methylphenol (*o*-cresol)	Phenols	Chemical intermediate
000944-22-9	Fonofos	Phosphonodithioates	Insecticide
000298-04-4	Disulfoton	Phosphorodithioates	Insecticide
013071-79-9	Terbufos	Phosphorodithioates	Herbicide (soil)
000333-41-5	Diazinon	Phosphorothioates	Insecticide
000121-82-4	RDX	Triazines	Explosives
001610-18-0	Prometon	Triazines	Herbicide
002212-67-1	Molinate	Triazines	Herbicide
005902-51-2	Terbacil	Triazines	Herbicide
006190-65-4	Triazines (atrazine-desethyl)	Triazines	Herbicide
021087-64-9	Metribuzin	Triazines	Herbicide
021725-46-2	Triazines (cyanazine)	Triazines	Herbicide
000330-54-1	Diuron	Ureas	Herbicide
000330-55-2	Linuron	Ureas	Herbicide

TABLE 4-5 Log Octanol-Water Partition Coefficient (Log Kow) Values, Soil or Sediment Sorption Coefficient (Koc) Values and Henry's Law Constants for the 1998 CCL Chemicals Arranged by SuCCSES Classes

CAS No.	Chemical Name	Log K_{ow}	Koc	Henry's Law Constant (atm m^3/mole)
	Acetanilides			
034256-82-1	Acetochlor	3.03	176	2.23E-08
051218-45-2	Metolachlor	3.13	292	9.00E-09
	Aliphatic halides			
000060-57-1	Dieldrin	5.40	10,600	5.80E-05
000074-83-9	Methyl bromide	1.19	14	6.24E-03
000075-34-3	1,1-Dichlowethane	1.79	35	5.62E-03
000079-34-5	1,1,2,2-Tetrachloroethane	2.39	107	3.67E-04
000087-68-3	Hexachlorobutadiene	4.78	994	1.03E-02
000142-28-9	1,3-Dichloropropane	2.00	81	9.76E-04
000309-00-2	Aidrin	6.50	105,600	4.93E-04
000542-75-6	1,3-Dichloropropene	2.29	81	3.55E-03
000563-58-6	1,1-Dichloropropene	2.53	68	5.00E-02
000594-20-7	2,2-Dichloropropane	2.92	49	1.61E-02
	Aromatic halides			
000072-55-9	DDE	6.51	152,500	3.52E-5
000108-86-1	Bromobenzene	2.99	268	2.08E-03
000887-54-7	DCPA mono-acid degradate	3.19	53	2.11E-10
002136-79-0	DCPA di-acid degradate	2.16	557	6.58E-13
	Aromatic hydrocarbons			
000091-20-3	Naphthalene	3.30	1,837	4.83E-04
000095-63-6	1,2,4-Trimethylbenzene	3.63	718	6.16E-03
000099-87-6	*p*-Isopropyltoluene (*p*-cymene)	4.10	1,324	1.10E-02

CAS No.	Chemical Name	Log K_{ow}	Koc	Henry's Law Constant (atm m^3/mole)
	Carbamic acid esters			
000759-94-4	EPTC (*s*-ethyl-dipropylthiocarbamate)	3.21	258	2.26E-05
	Elements			
007429-90-5	Aluminum	ND*	bid	ND
007439-96-5	Manganese	ND	ND	ND
007440-23-5	Sodium	ND	ND	ND
007440-42-8	Boron	ND	ND	ND
007440-62-2	Vanadium	ND	ND	ND
	Ethers			
001634-04-4	Methyl-*t*-butyl ether (MTBE)	0.94	5	5.87E-04
	Halophenols			
000088-06-2	2,4,6-Trichlorophenol	3.69	1,186	2.60E-06
000120-83-2	2,4-Dichlorophenol	3.06	718	2.19E-06
	Hydrazines			
000122-66-7	1,2-Diphenylhydrazine	2.94	3,481	4.39E-09
	Inorganics			
014808-79-8	Sulfate	ND	ND	HD
	Nitroaromatics			
000098-95-3	Nitrobenzene	1.85	191	2.40E-05
000121-14-2	2,4-Dinitrotoluene	1.98	364	130E-07
000606-20-2	2,6-Dinitrotoluene	2.10	371	7.47E-07
	Phenols			
000051-28-5	2,4-Dinitrophenol	1.67	364	7.94E-10
000095-48-7	2-Methylphenol (*o*-cresol)	1.95	443	1.20E-06
	Phosphonothioates			
000944-22-9	Fonofos	3.94	836	1.12E-04
	Phosphorodithioates			
000298-04-4	Disulfoton	4.02	819	3.99E-06
013071-79-9	Terbufos	4.48	979	2.40E-05

CAS No.	Chemical Name	Log K_{ow}	Koc	Henry's Law Constant (atm m^3/mole)
	Phosphorothioates			
000333-41-5	Diazinon	3.81	1,337	1.13E-07
	Triazines			
000121-82-4	RDX	0.87	195	6.32E-08
001610-18-0	Prometon	2.99	157	3.17E-09
002212.67-1	Molinate	3.21	286	4.10E-06
005902-51-2	Terbacil	1.89	78	1.20E-10
006190-65-4	Triazines (atrazine-desethyl)	1.51	86	1.53E-09
021087-64-9	Metribuzin	1.70	1,196	1.81E-12
021725-46-2	Triazines (cyanazine)	2.22	124	2.96E-12
	Ureas			
000330-54-1	Diuron	2.68	136	5.04E-10
000330-55-2	Linuron	3.20	350	6.60E-08

* Not determined.

TABLE 4-6 Scores and Criteria for Assigning Exposure Scores to Exposure Factors for Which Data Were Available and that are Relevant to the 1998 CCL Chemicals

Exposure Factor	Scores and Criteria for Assigning Exposure Scores			
	+3	+2	+1	0
Annual production volume (lbs.)	100,000,000	10,000,000	1,000,000	1,000,000
Environmental persistence	Years	Months	Days	Hours
Bioaccumulation potential (log K_{ow})	>5	3 to 5	1 to 3	<1

TABLE 4-7 Exposure Scores for Aliphatic Halides from the 1998 CCL Chemicals

CAS No.	Chemical Name	Annual Production Volume (lbs.)	Environmental Persistence	Bioaccumulation Potential (log K_{ow})
000060-57-1	Dieldrin	0	3	3
000074-83-9	Methyl bromide	2	2	1
000075-34-3	1,1-Dichloroethane	0	2	1
000079-34-5	1,1,2,2-Tetrachloroethane	I	2	1
000087-68-3	Hexachlorobutadiene	0	3	2
000142-28-9	1,3-Dichloropropane	I	2	1
000309-00-2	Aldrin	0	3	3
000542-75-6	1,3-Dichloropropene	1	2	1
000563-58-6	1,1-Dichloropropene	1	2	1
000594-20-7	2,2-Dichloropropane	1	2	1

TABLE 4-8 Scores nod Criteria for Assigning Effects Scores to Biological Effects for Which Data Were Available and that Are Relevant to the CCL Chemicals

	1998 Scores and Criteria for Assigning Biological Effects Scores						
Biological	+3	+2	+1	0	-1	-2	-3
Effects		Tested	Tested	Tested	Predicted	Predicted	Predicted
Acute toxicity	LD_{50} < 50 mg/kg oral LD_{50} < 5 mg/L inhal. LD_{50} < 1 mg/kg derm.	LD_{50} = 50-500 mg/kg oral LC_{50} = 5-50 mg/L inhal. LD_{50} =1-50 mg/kg derm.	LD_{50}=500-5,000 mg/kg oral LC_{50}=50-500 mg/L inhal. LD_{50}50-500 mg/kg derm.	LD_{50}>5,000 mg/kg oral LD_{50}<500 mg/L inhal. LD_{50}<500 mg/kg derm.	Suspected to be slightly to moderately toxic	Suspected to be very toxic	Suspected to be extremely toxic
Mutagenicity	Positive in two or more whole mammalian test systems	Positive in vitro and interacts with germinal-cell DNA in vivo	Positive in one test system	Negative in more than one system	Slight suspicion based on structure	Suspicion based on SARs to known mutagens or carcinogens	Strong suspicion based on SARs
Carcinogenicity	Established carcinogen in humans or two animal species	Established carcinogen in one animal species	Insufficient data but some suspicion of carcinogenicity	Negative results in two animal species	Suspect carcinogen, potent organ-specific toxin, or enzyme inducer	Structural relationship to known carcinogen	Structural relationship to a known carcinogen or strong suspicion based on SARs
Ecotoxicity	Effects at low concentrations (g/L)	Effects at moderate concentrations (mg/L)	Effects at high concentrations (g/L)	Negative results	Likely to cause effects at high concentrations	Likely to cause effects at moderate concentrations	Likely to cause effects at low concentrations based on SARs

TABLE 4-9 Biological Effects Scores for Aliphatic Halides from the 1998 CCL Chemicals

CAS No.	Chemical Name	Acute Toxicity	Mutagenicity	Carcinogenicity	Ecotoxicity
000060-57-1	Dieldrin	+3	+2	0	+3
000074-83-9	Methyl bromide	+2	+2	0	+2
000075-34.3	1,1-Dichloroethane	+1	+1	+1	+2
000079-34-5	1,1,2,2-Tetrachloroethane	+2	+2	+2	+2
000087-68-3	Hexachlorobutadiene	+2	+2	+1	+3
000142-28-9	1,3-Dichloropropane	+1	+3	-2	+2
000309-00-2	Aldrin	+3	+2	+2	+3
000542-75-6	1,3-Dichloropropene	+2	+2	+3	+2
000563-58-6	1,1-Dichloropropene	-1	+1	-1	-2
000594-20-7	2,2-Dichloropropane	-1	-1	-1	-2

TABLE 4-10 Modes of Toxic Action for the 1998 CCL Chemicals Arranged by SuCCSES Classes

CAS No.	Chemical Name	Mode of Action
	Acetanilides	
034256-82-1	Acetochlor	Nonpolar narcosis
051218-45-2	Metolachlor	Nonpolar narcosis
	Aliphatic halides	
000060-57-1	Dieldrin	Neurotoxicant: Cyclodiene-type
000074-83-9	Methyl bromide	Nonpolar narcosis
000075-34-3	1,1-Dichloroethane	Nonpolar narcosis
000079-34-5	1,1,2,2-Tetrachloroethane	Nonpolar narcosis
000087-68-3	Hexachlorobutadiene	Reactivity: Alkylation or arylation reaction
000142-28-9	1,3-Dichloropropane	Nonpolar narcosis
000309-00-2	Aldrin	Neurotoxicant: Cyclodiene-type
000542-75-6	1,3-Dichloropropene	Reactivity: Alkylation or arylation reaction
000563-58-6	1,1-Dichloropropene	Nonpolar narcosis
000594-20-7	2,2-Dichloropropane	Nonpolar narcosis
	Aromatic halides	
000072-55-9	DDE	Nonpolar narcosis
000108-86-1	Bromobenzene	Nonpolar narcosis
000887-54-7	DCPA mono-acid degradate	Nonpolar narcosis
002136-79-0	DCPA di-acid degradate	Nonpolar narcosis
	Aromatic hydrocarbons	
000091-20-3	Naphthalene	Nonpolar narcosis
000095-63-6	1,2,4-Trimethylbenzene	Nonpolar narcosis
000099-87-6	*p*-Isopropyltoluene	Nonpolar narcosis
	(*p*-cymene)	
	Carbamic acid esters	
000759-94-4	EPTC (s-ethyl-dipropylthio-carbamate)	Nonpolar narcosis

CAS No.	Chemical Name	Mode of Action
	Elements	
007429-90-5	Aluminum	N.A.*
007439-96-5	Manganese	N.A.
007440-23-5	Sodium	N.A.
007440-42-8	Boron	N.A.
007440-62-2	Vanadium	N.A.
	Ethers	
001634-04-4	Methyl-*t*-butyl ether (MTBE)	Nonpolar narcosis
	Halophenols	
000088-06-2	2,4,6-Trichlorophenol	Polar narcosis
000120-83-2	2,4-Dichlorophenol	Polar narcosis
	Hydrazines	
000122-66-7	1,2-Diphenylhydrazine	Reactivity: hydrazines
	Inorganics	
014808-79-8	Sulfate	N.A.
	Nitroaromaties	
000098-95-3	Nitrobenzene	Nonpolar narcosis
000121-14-2	2,4-Dinitrotoluene	Reactivity: dinitroaromatic group
000606-20-2	2,6-Dinitrotoluene	Reactivity: dinitroaromatic group
	Phenols	
000051-28-5	2,4-Dinitrophenol	Uncoupler of oxidative phosphorylation
000095-48-7	2-Methylphenol (*o*-cresol)	Polar narcosis
	Phosphonothioates	
000944-22-9	Fonofos	Organophosphate mediated acetylcholinesterase inhibition
	Phosphorodithioates	
000298-04-4	Disulfoton	Organophosphate mediated acetylcholinesterase inhibition
013071-79-9	Terbufos	Organophosphate mediated acetylcholinesterase inhibition

CAS No.	Chemical Name	Mode of Action
	Phosphorothioates	
000333-41-5	Diazinon	Organophosphate mediated acetylcholinesterase inhibition
	Triazines	
000121-82-4	RDX	Nonpolar narcosis
001610-18-0	Prometon	Nonpolar narcosis
002212-67-1	Molinate	Nonpolar narcosis
005902-51-2	Terbacil	Nonpolar narcosis
006190-65-4	Triazines (atrazine-desethyl)	Nonpolar narcosis
021087-64-9	Metribuzin	Nonpolar narcosis
021725-46-2	Triazines (cyanazine)	Nonpolar narcosis
	Ureas	
000330-54-1	Diuron	Nonpolar narcosis
000330-55-2	Linuron	Nonpolar narcosis

* N.A. = not available.

TABLE 4-11 Carcinogenicity Concern Levels for the 1998 CCL Chemicals Arranged by SuCCSES Classes

CAS No.	Chemical Name	Carcinogenicity Concern Levels	Comments
	Acetanilides		
034256-82-1	Acetochlor	Moderate	+Data
05121845-2	Metolachlor	Moderate	
	Aliphatic halides		
000060-57-1	Dieldrin	Moderate	+Data
000074-83-9	Methyl bromide	Moderate	
000075-34-3	1,1-Dichloroethane	Low	- Data
000079-34-5	1,1,2,2-Tetrachloroethane	Moderate	+ Data
000087-68-3	Hexachlorobutadiene	Moderate	+ Data
000142-28-9	1,3-Dichloropropane	Moderate	
000309-002	Aldrin	Moderate	+ Data
000542-75-6	1,3-Dichloropropene	High	+ Data
000563-58-6	1,1-Dichloropropene	Moderate	
000594-20-7	2,2-Dichloropropane	Low	
	Aromatic halides		
000072-55-9	DDE	Moderate	+ Data
000108-86-1	Bromobenzene	Moderate	
000887-54-7	DCPA mono-acid degradate	Low	
002136-79-0	DCPA di-acid degradate	Low	
	Aromatic hydrocarbons		
000091-20-3	Naphthalene	Moderate	+ Data
000095-63-6	1,2,4-Trimethylbenzene	Low	
000099-87-6	*p*-Isopropyltoluene (*p*-cymene)	Low	
	Carbamic acid esters		
000759-94-4	EPTC (*s*-ethyl-dipropylthiocarbamate)	Moderate	
	Elements		
007429-90-5	Aluminum	Low	
007439-96-5	Manganese	Low	
007440-23-5	Sodium	Low	
007440-42-8	Boron	Low	
007440-62-2	Vanadium	Low to moderate	

CAS No.	Chemical Name	Carcinogenicity Concern Levels	Comments
	Ethers		
001634-04-4	Methyl-*t*-butyl ether	Moderate	+ Data
	Halophenols		
000088-06-2	2,4,6-Trichlorophenol	Moderate	+ Data
000120-83-2	2,4-Dichlorophenol	Low	- Data
	Hydrazines		
000122-66-7	1,2-Diphenylhydrazine	Moderate	
	Inorganics		
014808-79-8	Sulfate	Low	
	Nitroaromatics		
000098-95-3	Nitrobenzene	Moderate	
000121-14-2	2,4-Dinitrotoluene	High	+ Data
000606-20-2	2,6-Dinitrotoluene	Moderate	+ Data
	Phenols		
000051-28-5	2,4-Dinitrophenol	Moderate	
000095-48-7	2-Methylphenol (*o*-cresol)	Low	
	Phosphonothioates		
000944-22-9	Fonofos	Low	
	Phosphorodithioates		
000298-04-4	Disulfoton	Low	- Data
013071-79-9	Terbufos	Low	- Data
	Phosphorothioates		
000333-41-5	Diazinon	Low	
	Triazines		
000121-82-4	RDX	Moderate	
001610-18-0	Prometon	Low	Equivocal data
002212-67-1	Molinate	Moderate	+ Data
005902-51-2	Terbacil	Low	- Data
006190-65-4	Triazines (atrazine-desethyl)	Moderate	+ Data for parent compound

CAS No.	Chemical Name	Carcinogenicity Concern Levels	Comments
021087-64-9	Metribuzin	Low	Equivocal data
02172546-2	Triazines (cyanazine)	Moderate	+ Data for parent
	Ureas		
000330-54-1	Diuron	Low	- Data
000330-55-2	Linuron	Moderate	+ Data

TABLE 4-12 Wildlife Species Contaminated with the 1998 CCL Chemicals

Chemical	Species	Records	Individuals	Matrix	Range (µg/g)
Aldrin	Blue jay	1	1	Brain	0.04
	Fulvous whistling duck	2	30	Liver	0.0021, 0.0094
	Sharp-shinned hawk	1	1	Brain	0.04
Aluminum	American alligator	3	13	Egg	1.3-2.0
	American	2	12	Eggshell	52.36
	crocodile			Egg	10.86
	Black-crowned night-heron	1	7	Egg	9.55
	Muskrat	3	76	Kidney	3.45-13.19
	Peregrine falcon	10	10	Egg	6.74-17.4
	Short-tailed shrew	5	5	Carcass	130.0-561.0
	Snapping turtle	2	19	Liver	15.97, 78.83
	White-footed mouse	4	4	Carcass	45.0-180.0
Boron	Common tern	10	10	Egg	22.4-36.8
	Peregrine falcon	3	3	Egg	0.75-1.29
	Snapping turtle	1	12	Liver	3
	Tree swallow	3	9	Egg	1.52-3.55
Diazinon	American brant	2	21	Liver	0.003
				Small intestine	0.002-3.2
				Gizzard	0.12-0.77
	American robin	2	3	Gizzard	1.5
	Blackbird	1	60		blot given
	Blue jay	2	3	Alimentary canal	0.09-3.48
	Boat-tailed grackle	1	3	Gizzard	12
	Bobwhite quail	1	160	Wing	2.93
	Canada goose	12	112	Gizzard	0.34-9.13
				Liver	0.014-0.05
	Common grackle	4	72	Gizzard	16
	Mallard	9	74	Brain	161
				Gizzard	0.32-3000

Chemical	Species	Records	Individuals	Matrix	Range (µg/g)
Disulfoton	American robin	1	9		Not given; birds poisoned
Naphthalene	Common tern	6	6	Egg	0.01 for all
Vanadium	Common tern	7	7	Egg	0.005-0.007
	Muskrat	3	76	Kidney	0.045-1.10
	Short-tailed shrew	3	3	Carcass	0.5-0.7
	Snapping turtle	1	12	Liver	0.85
	White-footed mouse	1	1	Carcass	0.3
Manganese	Birds: 20 species	94	1,006	Nine	0.005-20.2
	Muskrat	3	76	Kidney	5.23-6.60
	White-footed mouse	4	4	Carcass	8.6-16.00
	American alligator	3	16	Egg	0.14-0.15
	Pine snake	8	248	Carcass	11.72-16.27
				Skin	1.35-7.26
DDE	102 bird species; 8 mammal species; 6 reptile species; 1 amphibian species	1,608	21,585		0.002-228.00
Dieldrin	77 bird species; 9 mammal species; I reptile species; I amphibian species	1,067	14,889		0.0007-21.60

NOTE: These data were extracted from the Contaminant Exposure and Effects—Terrestrial Vertebrates database (Rattner et al., 1999). The column labeled "records" refers to the number of records in the database for each species that contain the given contaminant. (A record can represent one or many individuals and usually gives a mean concentration of the chemical.) "Individuals" represents the total number of individuals for all records. "Matrix" is where the chemical concentration was measured, and "range" is the concentration range in the given matrix for each species (generally dry weight for metals and wet weight for organics).

TABLE 4-13 Aliphatic Halides (not on the 1998 CCL) with Uses Similar to Those of 1,1,2,2-Tetrachloroethane (on the 1998 CCL)

		Uses					
CAS No.	Chemical	Machinery	Polystyrene	SBR Rubber	Rubber	Varnish	Total Uses
79-34-5	1,1,2,2-Tetrachloroethane	X	X	X	X	X	5
71-55-6	1,1,1- Trichloroethane	X	X	X	X	X	15
56-23-5	Carbon tetrachloride	X			X	X	9
79-00-5	1,1,2-Trichloroethane		X	X		X	3

TABLE 4-14 Production, Use, and Environmental Release Volumes for Aliphatic Halides (not on the 1998 CCL) that Have Similar Uses to 1,1,2,2-Tetrachloroethane (on the 1998 CCL)

Chemical Name	Production Volume	Use Volume	Toxics Release Inventory Volume (lbs.)
1,1,2,2-Tetrachloroethane	High	Low	16,000
1,1,1-Trichloroethane	Extremely high	Medium to high	8,800,000
Carbon tetrachloride	Extremely high	Low to medium	400,000
1,1,2-Trichloroethane	Very high	Low	340,000

TABLE 4-15 Log Octanol-Water Partition Coefficient (log Kow) Values, Soil, or Sediment Sorption Coefficient (Koc) Values, and Henry's Law Constants for Aliphatic Halides (not on the 1998 CCL) that Have Similar Uses to 1,1,2,2-Tetrachloroethane (on the 1998 CCL)

Chemical Name	Log K_{ow}	Koc	Henry's Law Constant (atm m^3/mol)
1,1,2,2-Tetrachloroethane	2.39	107	3.67E-04
1,1,1-Trichloroethane	2.49	85	1.72E-02
Carbon tetrachloride	2.83	71	2.76E-02
1,1,2-Trichloroethane	1.89	97	8.24E-04

5

Sorting And Screening of Potential Drinking Water Contaminants: New and Existing Chemicals Under the Toxic Substances Control Act

Charles M. Auer, Christopher Blunck, Flora Chow, and David R. Williams

This paper reviews the chemical assessment and testing programs under the U.S. Toxic Substances Control Act (TSCA) of 1976 and considers elements relevant to screening and assessment of new and existing industrial chemicals as drinking water contaminants. TSCA established a number of new requirements and authorities for identifying and controlling existing and potential toxic chemical risks to human health and the environment. The TSCA programs are implemented by the U. S. Environmental Protection Agency's (EPA) Office of Pollution Prevention and Toxics. Generally, TSCA gives EPA the authority to gather certain kinds of basic data relevant to determining chemical risks from those who manufacture and process chemicals. The law also enables EPA to require companies to test chemicals for toxic effects and requires the agency to review most new chemicals before they are manufactured commercially. To prevent unreasonable risks, EPA may select from a broad range of control actions under TSCA, from requiring hazard-warning labels to outright bans on manufacture and/or use. EPA may regulate a chemical's risks at any stage of its life cycle: at manufacture, processing, distribution in commerce, use, or disposal. TSCA coverage does not extend to certain product categories, including tobacco, munitions, food additives, drugs, cosmetics, and pesticides.

NEW CHEMICALS

Section 5 of TSCA provides EPA with the authority to regulate new chemical substances (i.e., those not on the TSCA inventory) of existing chemicals) prior to their commercial manufacture. Anyone who plans to manufacture or import a new chemical substance for a commercial purpose is required to provide the EPA with a premanufacture notice (PMN) at least 90 days prior to the activity.

Section 5 of TSCA thus gives EPA the role of gatekeeper between the laboratory and the commercial marketplace. EPA reviews the new chemical to determine whether its manufacture, processing, distribution in commerce, use, or disposal "may present an unreasonable risk" to human health or the environment or cause exposures of concern. The program's assessment includes exposures

and risks to workers, consumers, and the general population (including from drinking water or fish consumption) as well as risks to wildlife. From its inception in 1979 the program has reviewed over 30,000 new chemical notices (currently about 2,000 a year) and taken action to control or require testing on approximately 10 percent of the new chemicals notified.

Notification Requirements

PMN submissions require all available data on chemical identify, production volume, byproducts, use, environmental release, disposal practices, and human exposure. TSCA does not require the submission of "base set" testing with the notice, although the submitter is required to provide all health and environmental data in the possession of the submitter.

EPA Evaluation

EPA assesses the potential risks to humans or the environment of each new substance based on data submitted with the notice, other information available to the agency, and exposure and release modeling. As noted, TSCA does not require prior testing of new chemicals and, as a consequence, approximately 50 percent of submissions contain no test data of any type. When submitted, health test data rarely extend beyond acute studies (~40 percent) or genotoxicity tests (~15 percent; Auer and Gould, 1987). In the absence of test data, EPA bases its health and environmental toxicity review of new substances primarily on structure activity relationships (SARs)(Auer and Gould 1987; Auer et al., 1990, 1994, 1995; Leeman et al. 1995).

Almost 90 percent of the PMNs submitted to the program complete the review process without being restricted or regulated in any way. Ten percent of the PMNs, however, are regulated by EPA, either under a TSCA Section 5(e) consent order or by a Significant New Use Rule (SNUR).

Section 5(e) Consent Orders

EPA may determine that activities involving the new substance "may present an unreasonable risk of injury to health or the environment" (referred to as a risk-based finding) and that the information available is insufficient to permit a "reasoned evaluation" of the new chemical. When EPA makes these two findings it acts under Section 5(e) of TSCA to regulate the new substance and can control uses and/or releases until test data or other information sufficient to adequately assess the potential risks become available. Section 5(e) consent orders have specified a variety of control measures, including protective equipment, use limitations, process restrictions, labeling requirements, and limits on environmental release. In other instances EPA may determine that a new substance will be produced in substantial quantities (currently set at 100,000 kg/year) and there is or may be significant or substantial human or environmental exposure to the substance (referred to as an exposure-based finding) and that the

available information is insufficient. Consent orders issued to address exposure-based concerns include testing requirements similar to the Minimum Premarket Dataset (MPD) used in the European Union (see Auer and Gould, 1987, for a description).

SNURS

Section 5(e) orders apply only to the submitter of the PMN. When a PMN notifier submits a Notice of Commencement of Manufacture to EPA, EPA adds the former new substance to the TSCA inventory. When a substance is listed on the inventory, other persons are able to manufacture, import, or process it without EPA review and without any restrictions imposed by a Section 5(e) order. Under TSCA Section 5(a)(2), EPA may determine by rule that a use of a chemical substance is a "significant new use." Once EPA determines that a use of a chemical substance is a significant new use, TSCA requires persons to submit a Significant New Use Notice (SNUN) to EPA at least 90 days before they manufacture, import, or process the chemical substance for that use. Thus, EPA can use its SNUR authority to extend limitations in Section 5(e) orders to companies beyond the original submitter. After receiving and reviewing a SNUN, EPA has the option of either permitting the new use or acting to regulate the new submitter's activities.

Accomplishments

Since 1979, EPA has reviewed over 32,000 new chemical substances and taken action to prevent potential risks to people and the environment on nearly 3,000. PMN actions based on health concerns for exposures from contaminated drinking water are uncommon (typically fewer than five such cases per year (Becky Jones and Flora Chow, OPPT, personal communication, 1998).

EU/U.S. Structure Activity Relationship/Minimum Premarketing Dataset Study

As noted above, EPA does not receive any test data with most PMNs. When data are submitted, they often do not go beyond acute toxicity endpoints. Quantitative structure activity relationships (QSARs) are the technique EPA uses to carry out preliminary hazard assessments of new chemicals in the absence of test data. These QSARs are predictive methods that estimate the properties of a chemical (e.g., melting point, vapor pressure, toxicity, ecotoxicity), on the basis of its structure and test data on analogous chemicals. A joint U.S./ EU study was initiated to evaluate the predictive power of the QSAR by applying QSAR methods to chemicals for which MPDs were already available in the EU and then

comparing the properties predicted by QSAR with the properties observed from MPD testing (OECD, 1994). Analysis of the results of this study showed that the SAR approach was relatively successful in identifying chemicals of concern. Nevertheless, the study concluded, the approach could be improved by selectively incorporating specific testing schemes into the process. Such a focused effort would provide valuable data while not presenting large overall cost implications.

Persistent/Bioaccumulative/Toxic (PBT) New Chemicals

EPA recently proposed a new chemical category for PBT new chemicals (EPA, 1998a) that possess characteristics of persistence, bioaccumulation, and toxicity that cause such chemicals to present potentially significant hazards and risks. The proposed category is intended to alert manufacturers to EPA's concerns and facilitate assessment and risk management of such new chemicals. The policy statement includes boundary conditions, such as environmental half lives (>2 months and >6 months) and bioaccumulation factors (>1,000 and >5,000) that would determine inclusion in the category, recommended testing to address PBT concerns, and EPA's regulatory strategy for chemicals meeting the category requirements.

EXISTING CHEMICALS

EPA's TSCA inventory currently contains over 70,000 chemicals, many of which are produced or imported at low or negligible volumes, while others are polymers that, because of their size (e.g., high molecular weight) and other characteristics, are unlikely to present significant risk concerns. Excluding low-volume chemicals (~25,000 chemicals produced in amounts less that 10,000 pounds per year) and polymers (which tend to be poorly absorbed by organisms and typically exhibit low toxicity), there are ~15,000 nonpolymeric chemicals that are produced at levels above 10,000 pounds per year. This 15,000 chemicals subset has been identified as being the broad focus of EPA's existing chemical testing and assessment program with the primary focus being on the ~3,000 U.S. high production volume (HPV) chemicals that are produced/imported at levels above 1 million pounds per year.

Existing Chemical Testing

Section 2 of TSCA states that "it is the policy of the United States that adequate data be developed with respect to the effect of chemical substances and mixtures on health and the environment and that development of such data be the responsibility of those who manufacture [and import] and those who process such chemicals and mixtures." Section 4 of TSCA gives EPA the authority to issue rules to require chemical producers, importers, and processors to conduct specified testing for health and environmental effects as well as chemical fate and exposure.

Testing Actions

EPA must make certain Statutory "findings" to require chemical testing under a TSCA Section 4 Test Rule, as follows. The chemical may present an unreasonable risk; and/or is produced in substantial quantities and enters the environment in substantial quantities, or there is or may be substantial or signifier human exposure; and existing data are inadequate; and testing is necessary. As a result of litigation in the 1980s, EPA and other stakeholders developed an alternative to the TSCA Section 4 rule-making process that involves the negotiation of formal TSCA Section 4 enforceable consent agreements. EPA also looks to voluntary industry testing initiatives to supplement its formal chemical testing program. A primary example of such a voluntary initiative is the Screening Information DataSet (SIDS) program, an important program focused on cooperative voluntary testing of international HPV chemicals. The program is operated under the auspices of the Organization for Economic Cooperation and Development (OECD). Thus, EPA relies on a mix of TSCA Section 4 test rules, ECAs, orders, and voluntary testing agreements. Since 1979, approximately 550 chemicals have been the subject of final testing actions. Virtually all of the actions taken to date have involved U.S. HPV chemicals and more than 50 percent of the testing actions have been developed since 1990. Other recent developments related to existing chemical testing are discussed below.

TSCA Section 4 Final Test Rule for EPA's Office of Drinking Water

On November 10, 1993, OPPT published a final TSCA Section 4 Test Rule (58 FR 59667) covering four chemicals of interest to the Office of Drinking Water (ODW) in EPA's Office of Water. The chemicals subject to this rule (chloroethane, 1,3,5-trimethylbenzene, 1,1-dichloroethane, and 1,1,2,2-tetrachloroethane) were unregulated drinking water contaminants for which ODW needed data in order to develop 1-day, 10-day, and long term/lifetime health advisories. The required testing included 14- and 90-day oral toxicity studies in rats on each of the subject chemicals.

In consultation with ODW and following receipt of adequate data from studies conducted by the National Toxicology Program or conducted by industry as a result of settlement of lawsuits challenging the test rule, OPPT[1] revised the

[1] Testing included in the OECD Screening Information DataSet (SIDS). The SIDS test battery includes the following basic screening endpoints: physical-chemical properties, environmental fate, ecotoxicity, acute toxicity, genetic toxicity, repeat-dose toxicity, and developmental and reproductive toxicity, which are listed in Section 2.2 of the Screening Information DataSet Manual of the OECD Programme on the Co-operative Investigation of High Production Volume Chemicals, published in July 1997. This manual (also called the SIDS Manual) is available at www.epa.gov/opptintr/sids/sidsman.htm or can be obtained as hard copy from the OECD Environment Directorate, Environmental Health and Safety Division; 2, rue Andre-Pascal F-75775; Paris Cedex 16, France; Tel: 3314-4524 9844. Specific information on the SIDS test protocols can be found at:

final test rule to remove (1) the 14- and 90-day testing requirements for chloroethane and 1,1-dichloroethane and (2) the 90-day subchronic testing requirement for 1,1,2,2-tetrachloroethane. The remaining studies have been completed and the results forwarded to ODW for review and disposition.

Existing Chemical Assessment

Historically, the existing chemical assessment effort focused on screening efforts to identify potential problem chemicals that were then subjected to increasingly detailed reviews to determine their hazards, exposures, and risks. Recent developments have occurred that have fundamentally changed the focus of this EPA program.

Chemical Hazard Data Availability Study

In an Earth Day 1998 announcement, Vice President Gore and EPA Administrator Carol Browner committed EPA to testing initiatives aimed at strengthening the public's right and ability to know about the potential health and environmental risks from HPV existing chemicals. The announcement on the testing of HPV chemicals is a direct result of a recent EPA (1998a) analysis of the public availability of basic testing and screening information on chemicals produced or imported at a rate of more than 1 million pounds per year. EPA researched public information sources for data contained in the internationally agreed-upon Screening and Information DataSet (SIDS), considered the minimum set of tests that can allow an informed screening-level evaluation of a chemical's hazards. The study found that of the 3,000 U.S. HPV chemicals a full set of SIDS testing was publicly available for only 7 percent of the chemicals and that no SIDS data were available for 43 percent of the chemicals. The report also considered specific subsets of chemicals, including EPA's Toxics Release Inventory-listed chemicals, those with occupational exposure standards, and consumer chemicals. A similar analysis could be conducted for chemicals found in drinking water.

This recent EPA study is similar in several respects to a 1984 National Research Council (NRC) report. The NRC report considered the availability of

www.oecd.org/ehs/hpv.htm. The tests needed for each of the six screening endpoints are (a) physical/chemical property tests: melting point, boiling point, vapor pressure, *n*-octanol/water partition coefficient (shake flask method), water solubility; (b) environmental fate tests: photodegradation, hydrolysis stability in water, transport/distribution, inherent biodegradation; (c) ecotoxicity tests: acute toxicity to fish, acute toxicity to *Daphnia*, toxicity to aquatic plants (algae), chronic toxicity to *Daphnia*, when appropriate, terrestrial organism toxicity, when appropriate; (d) mammalian acute toxicity test: acute inhalation or acute oral or acute dermal test (if testing is needed, oral is default route except for gases); (e) mammalian genotoxicity tests: gene mutation (e.g., ames salmonella), chromosomal aberrations (in vive mouse micronucleus preferred if testing is needed); and (f) mammalian repeated dose/reproductive/developmental effects: combined repeated-dose with reproductive/developmental toxicity screen (45-day exposure) or repeated dose oral toxicity (28-day) and first generation reproductive toxicity test.

test data for various groups of chemicals, including industrial chemicals. It concluded that "minimal" toxicity information (defined as availability of any one or more of the following test types included in the NRC study: acute toxicity, subchronic toxicity, reproductive/developmental toxicity, mutagenicity) was available for only 22 percent of HPV chemicals. The EPA study found, in comparison, that while there is much work to be done, some progress has been made in improving our understanding of chemical hazards.

HPV Challenge Program

On October 9, 1998, the Vice President, EPA Administrator Browner, the Chemical Manufacturers Association, the American Petroleum Institute, and the Environmental Defense Fund made a joint announcement of a cooperative program to test 2,800 U.S. HPV chemicals and invited the chemicals industry to participate in a voluntary HPV Challenge Program to provide the public with basic screening data on the high-volume chemicals they produce. Under the HPV Challenge Program, companies can commit to voluntarily develop complete SIDS test datasets for their chemicals by the end of 2004. In addition, EPA will, as necessary, propose and finalize TSCA Section 4 test rules to require SIDS testing of HPV chemicals not handled under the Challenge Program. EPA is taking actions to secure these data so that individuals and communities can better evaluate the chemical hazards and risks they face.

Because of Vice President Gore's initiative, the United States expects to have complete SIDS test results on all U.S. HPV chemicals by 2005. It is also hoped that the U.S. action will spur other countries to step up their rate of testing under the closely related OECD SIDS effort.

TOXICS RELEASE INVENTORY

EPA requires annual reports of toxic chemical releases and transfers under Section 313 of the Emergency Planning and Community Right-to-Know Act. These reports provide the public with information on the releases of 600 listed toxic chemicals and chemical categories in their communities. Additionally, the information is used by EPA to support the development of EPA regulations and programs. Generally, facilities must report the quantities of both routine and accidental releases of listed toxic chemicals, including releases to the atmosphere, surface water, and land (Title HI of the Superfund Amendments and Reauthorization Act, 1986).

APPROACHES TO SORTING AND SCREENING INDUSTRIAL CHEMICALS AS DRINKING WATER CONTAMINANTS

New Chemicals

EPA currently attempts to identify potential drinking water contaminants (both ground- and surface water) as part of its new chemicals review program. The potential hazards are generally identified using SARs, while exposure is estimated using a combination of measured and estimated physical-chemical properties, estimates of the amount released, estimates of removal in treatment processes, fate and transport in the environment, and the extent of dilution by the receiving environmental medium. Releases to surface water can occur from manufacture, processing, use (including industrial, commercial, and consumer), and disposal. The primary fate and transport processes that are considered in estimating removal during treatment include biodegradation, sorption, volatilization, and hydrolysis. For rivers and streams, complete mixing can be assumed and a simple dilution model can be used to estimate surface water concentrations. If the specific site of release and the point of entry into a drinking water treatment facility are known, the analysis can account for the additional dilution that can occur before entry into the drinking water treatment facility. Estimates of potential dose rates from ingestion of surface water are developed using surface water concentrations based on mean stream flow values multiplied by the daily drinking water ingestion rate and the annual frequency of ingestion (EPA, 1998b).

Potential carcinogenicity is the most frequently identified risk involving drinking water. The potential carcinogenicity of a PMN chemical is generally identified based on structural or functional analogy to known carcinogens and consideration of absorption and metabolic potential; consideration of mechanisms is also important when information is available (for more information on the approach, see Auer and Gould, 1987, and Auer et al., 1990). Using carcinogenicity test results on the analog, the data are modeled to produce a unit risk factor that can then be coupled with estimates of exposure to estimate drinking water risks. Carcinogenicity risk estimates of greater than 10^{-6} are generally considered significant for general population exposure.

As noted earlier, identification of new chemicals presenting significant concerns about risk based on drinking water exposures occurs at most several times per year (i.e., typically less than five such cases are identified each year out of over 2,000 new chemical notifications).

Existing Chemicals

As for new chemicals, existing chemical hazards can also be screened using available data and SARs to identify chemicals of potential concern. Several large compilations of SAP, estimates for the health effects of industrial chemicals have been developed by EPA, although most are several years old (Becky Jones, OPPT, personal communication, 1998). However, in light of the HPV Challenge Program and the likelihood that basic screening test data will be available for almost 3,000 HPV industrial chemicals by 2005, the best strategy

may be to wait for the development and reporting of this information to support identification of industrial chemical drinking water contaminants warranting more detailed assessment.

In addition, emissions and release data contained in the toxic release inventory can be analyzed to identify chemicals presenting potential concerns owing to releases into drinking water sources.

CONCLUSION

This paper describes major components of EPA's program to assess, test, and manage the risk of new and existing industrial chemicals under TSCA. The paper also explores possible approaches to sorting and screening these chemicals to identify possible candidates that present drinking water concerns.

More information about TSCA and other EPA activities and programs can be found on EPA's Internet home page on the World Wide Web at http://www.epa.gov.

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6

Emerging Chemical Drinking Water Contaminants

Walter Giger

The fate of contaminants in the aquatic environment is strongly influenced by their biodegradability and physico-chemical properties. The latter can be illustrated by a matrix showing polarity and volatility as coordinates (see Figure 6-1). Most of the aquatic pollutants, which have been studied up to now, are situated in the lower part of the polarity-volatility diagram. With regard to the potential of entering drinking water resources, the highly polar and hydrophilic contaminants in the upper right quadrangle of the polarity-volatility diagram are of elevated importance because of their high mobility in water. These contaminants, must be determined by liquid chromatography if not derivatized to make them amenable to gas chromatography. Currently, a breakthrough is occurring for analytical methods based on directly coupled liquid chromatography and mass spectrometry (LC/MS). It can be inferred that LC/MS will greatly enlarge the number of hydrophilic contaminants that can be determined at trace concentrations in wastewaters, ambient waters, and drinking waters.

This paper reviews current knowledge on the environmental occurrence of hydrophilic organic contaminants, including herbicide degradates, pharmaceuticals, and various high production volume chemicals.

HERBICIDE DEGRADATES

Numerous studies have been and are being conducted to determine the occurrence and environmental fate of herbicides, which are extensively applied to control weeds. Only few studies have considered degradates of these herbicides (e.g., Lerch et al, 1997; Muller et al., 1997). Herbicide degradates were prevalent in about 75 percent of 88 municipal wells studied in aquifers across Iowa (Kalkhoff et al., 1998; Kolpin et al., 1998). The sulfonic and oxanilic metabolites of acetoclor, alachlor, and metolachlor were determined along with their parent compounds. Altogether, 13 herbicides and 17 herbicide degradates were determined (Kolpin et al., 1998). With the exception of atrazine, the frequencies of detection in groundwater for a given herbicide increased multifold when its degradates were also considered.

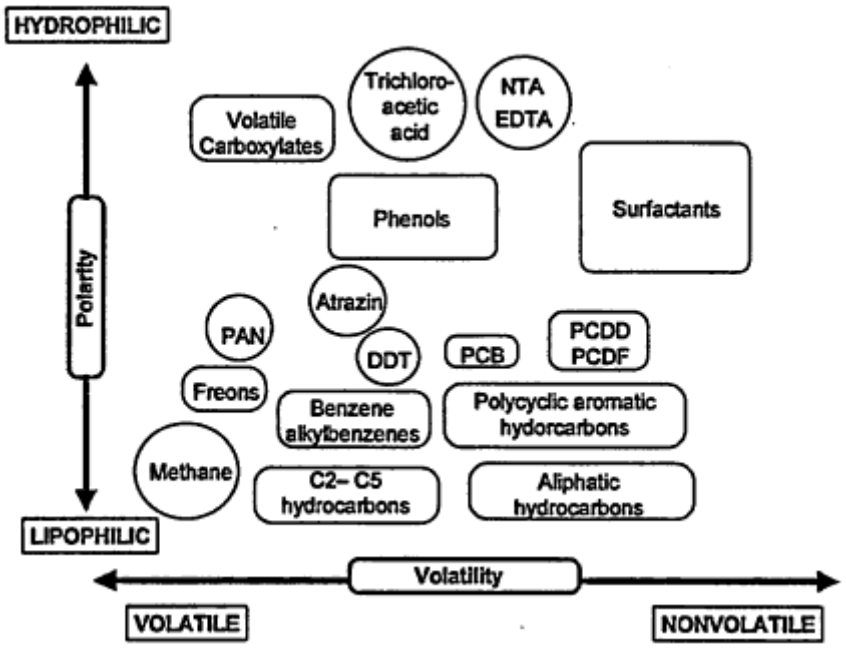

Figure 6-1
Polarity-volatility diagram for chemical contaminants.

Furthermore, a majority of the measured concentration for a given herbicide was in the form of its degradates, even for a relatively persistent compound such as atrazine. The degradates comprised 60 to over 99 percent of a herbicide's measured concentration. It was shown that potentially stable and persistent degradates are being formed in the environment before complete herbicide mineralization occurs. Kolpin and coworkers (1998) concluded that any investigation of herbicides such as their occurrence and effects on the environment and human health would be missing a significant piece of the puzzle if data on herbicide degradates are not also obtained. It can be extrapolated that for other pesticides similar observations will be made regarding the environmental occurrence of more polar metabolites.

PHARMACEUTICALS

In several European countries research activities have been accelerated that are aimed at enlarging our knowledge of environmental occurrences of pharmaceutical chemicals. Good overviews are given by Stun and Heberer (1997) and Ternes (1998a,b) as well as for a public audience by Raloff (1998).

One important route to follow is the collection of information on the types and amounts of pharmaceuticals used for human care and veterinary applications. Such a survey has been published by Halling-Sørensen et al. (1998) for the situation in Denmark. From a principal perspective, most drugs have a relatively high risk of causing residual levels in the environment because these chemicals are, to a large extent, excreted in urine or feces and are consequently contained in municipal wastewaters. For some chemicals their use as veterinary drugs is an important contamination source (Montforts, 1998).

In 1992, clofibric acid the active metabolite of the drugs clofibrate, etofibrate, and etofyllin—was found for the first time as a contaminant in groundwater at considerable concentrations. This discovery occurred during screening analyses for phenoxyalkanoic herbicides in the Berlin area (Stan and Linkerhäger, 1992). In more recent studies it has been reported that a series of drugs and drag metabolites were found at concentrations up to the microgram per liter level in groundwater samples taken from a drinking water treatment plant (see Table 6-1; Heberer and Stan, 1997; Stan and Heberer, 1997; Heberer et al., 1997, 1998). These contaminants leach from the neighboring sewage-contaminated surface waters by bank filtration through the subsoil into the groundwater of the waterworks. In the same investigation *N*-(phenylsulfonyl)-sarcosine was measured, which is considered to be a metabolite of a corrosion inhibitor.

Similarily, Buser and coworkers (1998a,b) came across the detection of clofibric acid as a trace contaminant in waters of the North Sea and in Swiss lakes (Table 6-2). The relatively higher residual concentrations of clofibric acid in the North Sea indicate that this contaminant is more persistent than mecoprop. The antirheumatic drug diclofenac was detected in rivers and lakes in Switzerland

TABLE 6-1 Concentrations of Pharmaceutical Contaminants and of N(Phenylsulfonyl)-Sarcosine in 17 Groundwater Wells of a Drinking Water Treatment Plant and in Bank Filtrates of the Rhine River

Contaminant	Pharmaceutical Compound Class	Concentration Range (ng/L)
		Groundwater
Clofibric acid	Metabolite of lipid regulator	70-7,300
Diclofenac	Antirheumatic	N.D. - 3 80
Fenofibrate	Lipid regulator	N.D. - 45
Ibuprofen	Antireumatic	N.D. - 200
Phenazone	Analgesic	<10 - 1,250
Propyphenazone	Analgesic	N.D. - 1,465
Clofibric acid derivative	Metabolite of clofibric acid, tofibrate, and etofyllin	50- 2,900
N-methylphenmacetin	Metabolite of phenacetin	<5 - 470
N-(phenylsulfonyl)-sarcosine	Metabolite of a corrosion inhibitor	165 - 1,440
		Bank Filtrate
Carbamazepin	Antiepileptic	130 (50^{th} percentile)
		360 (90^{th} percentile)

SOURCES: Adapted from Heberer et al. (1997) and Sacher et al. (1998).

(Table 6-2, Buser et al., 1998b). Based on the lake data and on the results of laboratory experiments it can be deduced that photodegradation is the predominant process affecting the environmental fate of diclofenac.

TABLE 6-2 Clofibric Acid, Mecoprop, and Diclofenac in Swiss Ambient Waters and in the North Sea

	Compound Concentration (ng/L)	
Location	Clofibric acid	Mecoprop
North Sea	0.5 - 7	0.6 - 11
Lakes	<1 - 9	<1 - 45
	Diclofenac	
Rivers	<1 - 370	
Lakes	<1- 12	

SOURCE: Adapted from Buser et al., 1998a, 1998b.

The occurrence of 32 drug residues belonging to different medicinal classes such as antiphlogistics, lipid regulators, psychiatric drugs, antiepileptic drugs, betablockers, and beta(2)-sympathomimetics as well as five metabolites has been investigated in German municipal sewage treatment plant (STP) discharges and river and stream waters (Ternes, 1995a). Owing to incomplete removal of drug residues during passage through an STP, more than 80 percent of the selected drugs were detectable in at least one municipal STP effluent with concentration levels up to 6.3 µg/L (carbamazepine), thus resulting in contamination of the receiving waters. Twenty different drugs and four corresponding metabolites were measured in river and stream waters. Mainly acidic drugs such as the lipid regulators bezafibrate, and gemfibrozil; the antiphlogistics diclofenac, ibuprofen, indometacine, naproxen, and phenazone; and the metabolites clofibric acid, fenofibric acid, and salicylic acid as well as neutral or weak basic drugs such as the betablockers metoprolol, propranolol, and the antiepileptic drug carbamazepine were found to be ubiquitously present in rivers and streams, mostly in the nanogram per liter range. However, maximum concentrations were determined up to 3.1 µg/L and median values as high as 0.35 µg/L (both for bezafibrate). The drugs detected in the environment were predominantly applied in human medicine. It can therefore be assumed that the load of municipal STP effluents in surface water highly influences the contamination.

Table 6-3 gives an overview on the concentrations found in surface waters (Ternes, 1998b). The relatively high environmental persistence of many pharmaceutical chemicals is documented by their widespread occurrence in ambient waters. Commonly applied wastewater treatment is obviously not

sufficient for the complete removal of these residues. There is a certain probability that metabolites formed by conjugation (e.g., glucoronates and sulfates) can be cleaved during wastewater treatment, and thus the parent chemicals are being discharged to the receiving surface waters.

TABLE 6-3 Ranges of Concentrations Found in German Surface Waters

Median (>0.050 µg/L)	Median (0.050-0.01 µg/L)	Median < LOD[a]; 90th Percentile > LOD;	90th percentile < LOD Maximum < LOD
Lipid regulators			Zytostatica
Bezafibrate			Cyclophosphamid Ifosfamid
Metabolites			
Clofibric acid	Fenofibric acid	Salicylic acid	
		Gentisic acid	
Antiphlogistics			
Diclofenac Ibuprofen Naproxen	Indometacin Phenazon	Ketoprofen	Dimethylaminophenazon
Antiepileptic	Betablockers		
Carbamazepin (Rhine River. C_{max} =<1 µg/L, 50th-percentile = 290 µg/L)	Metoprolol Propranolol	Bisoprolol Carazolol	Betaxolol
			Bronchospasmolytics Salbutamol Fenoterol

[a] Limit of detection.
SOURCE: Adapted from Ternes (1998b) based on data from Ternes (1998a) and Sacher et al. (1998).

The antiepileptic drug carbamazepin was detected in several German rivers and at elevated concentrations in the Rhine River (Sacher et al., 1998). It was inferred from these data that industrial wastewaters from companies manufacturing this pharmaceutical might add to its lead in the Rhine River. These authors also report on preliminary results of investigations assessing the behavior of carbamazepin during bank filtration and water treatment processes. Analogous studies in Brazil showed the sporadic presence of pharmaceuticals in rivers at concentrations below 10 ng/L, indicating a lower environmental contamination in this country (Stumpf et al., 1998).

ANTIBIOTICS

Hirsch et al. (1998a,b) have determined 18 antibiocidal chemicals, among them betalactams, makrolides, and tertracyclines as well as chloramphenicol, sulfamethaxol, and trimethroprim. Erythromycin was shown to occur only as a metabolite after water cleavage. Among the five antibiotics detectable in treated sewage effluents and in surface waters, erythromycin-water was most abundant with a median value of 2.5 µg/L and a maximum concentration of 6.0 µg/L. Roxitromycin, clarithromycin, sulfamethaxol, and trimethoprim occurred at concentrations below 1 µg/L.

No tetracyclines or penicillins could be detected in five sewage treatment effluents and in 14 samples from surface waters. A large number of groundwaters were screened for possible *occurrence* of antibiocidal substances. Some of these samples were strongly contaminated by liquid manure as was evident from the high nitrate levels. In four samples trace levels of residual sulfonamides were detectable.

Fluoroquinolone (FQ) antibiotics, inhibitors of the bacterial DNA unwinding enzyme gyrase, are important broad-spectrum antibiotics licensed for use in both humans and animals. Concentration of the prevalent FQ in human medicinal use, ciprofloxacin, was determined by reversed-phase high pressure liquid chromatography (HPLC) with fluorescence detection in hospital wastewaters and qualitatively confirmed by electrospray mass spectrometry (Alder et al., 1998; Hartmann et al., 1998). Concentrations ranged from 5 to 100 µg/L. Ciprofloxacin was found to be bioeliminated to 56 ±11 percent in 24 days using a modified OECD 302B in hospital wastewater. Bioavailability was unexpectedly high, as indicated by a bacterial genotoxicity assay (umuC test), which is highly sensitive for FQ antibiotics. Therefore, substantial amounts of bioavailable FQ antibiotics could be expected in wastewaters. The concentrations of ciprofloxacin in 24-hour composite samples in municipal wastewaters ranged from 0.2 to 0.4 µg/L in primary effluents and 0.1 µg/L in secondary effluents. Elimination of ciprofloxacin from the wastewater stream during aerobic treatment varied from 55 to 75 percent.

HIGH PRODUCTION VOLUME CHEMICALS

Among the high production volume chemicals (HPV), those with a high biopersistency and high polarity are potential drinking water contaminants. Table 6-4 gives a small collection of such chemical compound classes.

CONCLUSION

Based on the literature cited in this paper and related publications the following conclusions can be drawn:

- Introduction of directly coupled LC/MS techniques allows reliable and quantifiable determination of many polar hydrophilic water pollutants.
- Polar degradates of herbicides are increasingly important.
- Many pharmaceutical chemicals are detectable in the aquatic environment, antibiotics with an elevated level of concern.
- A large number of HPV chemicals should be investigated in more detail.

TABLE 6-4 HPV Chemicals Either Documented as Drinking Water Contaminants or Having a Certain Potential

Class of Chemical/Compound
Organic complexing agents
EDTA
Surfactant metabolites
Alkylphenols, alkylphenolpolyethoxylates, alkylphenolethoxcarboxylates
Musk fragrances
Benzenesulfonates naphthalenesulfonates
Sulfonated naphthalene formaldehyde condensates
Fuel additives
Methyl *tert*-butyl ether (MTBE)
Corrosion inhibitors (e.g. tolylbenzotriazoles)
Haloacetic acids

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7

New and Emerging Analytical Techniques for the Detection of Organic Contaminants in Water

Martin Reinhard and Jean-François Debroux

Detailed chemical analysis of water is a prerequisite for assuring the safety of water supplies. Limitations in our ability to identify contaminants in water also limit our ability to assure water quality and to assess environmental impacts. Recent improvements in analytical techniques have expanded the "analytical window," that is, the compound range that is amenable to specific identification. Using these improved tools, much has been learned about the occurrence, fate, and transport of organic chemicals in the environment. The boundaries of the analytical window represent the "analytical frontiers" and are continuously expanded. These boundaries are defined loosely by the contaminant concentration and chemical properties, such as molecular weight, polarity, chemical lability, and structural complexity.

In typical natural water samples, the mass of compounds that is within the analytical window (i.e., that can be specified in terms of both a specific structure and concentration) is small compared to the total organic carbon. Using coupled gas chromatography/mass spectroscopy (GC/MS) in conjunction with derivatization, the specifically identified compounds accounted for less than 12 percent (or < 1 mg/L) of the organic carbon in different groundwater samples (Reinhard et al., 1994). For 80 percent (or 2 to 10 mg/L) of the total organic carbon, this fraction typically remains uncharacterized or only in aggregate form (e.g., in terms of average chemical properties, functional group content, or size distribution) (Fujita et al., 1996).

Even though good mass spectra are obtained from a majority of the contaminants that are detected, most remain unidentified and/or unquantified because of a lack of reference spectra and/or reference compounds. The information that can be deduced from the mass spectra may be sufficient to propose structures using spectral determinations. However, verification and quantification of the proposed structures are often impossible because of a lack of reference spectra.

Since the majority of the organic carbon in environmental samples is not amenable to specific identification, aggregate properties (or group parameters) are often used as indicators of general water quality. Included in this category are such parameters as elemental composition, functionality, acidity, metal binding properties, total halogen content, ultraviolet (UV) absorption,

fluorescence properties, and molecular size distribution. Although very important, analysis of these parameters is not discussed in detail here.

Concern about the presence of potentially harmful contaminants is particularly relevant in cases where drinking water sources are impacted by point sources, such as wastewater effluents, landfills, and industrial dump sites. Other threats to water quality stem from the use of agricultural pesticides, leaking fuel and solvent storage tanks, and byproduct formation during disinfection with oxidants. To deal with these concerns, regulatory agencies have responded by establishing maximum contaminant limits (MCLs) for hazardous organic compounds (priority pollutants) known to have significant potential to contaminate drinking water, including pesticides, aromatic hydrocarbon compounds, disinfection byproducts, chlorinated solvents, and a number of other synthetic chemicals. MCLs are as low as 50 ng/L for ethylene dibromide and 200 ng/L for 1,2-dibromo-3-bromopropane. The European Union Commission has set a maximum limit for pesticide residues of 100 ng/L in drinking water.

Specifying MCLs for selected compounds addresses the potential threat of chemicals known to be hazardous. However, water quality can be threatened by numerous unidentified compounds that may be of anthropogenic origin or that may originate from natural sources. Compounds of anthropogenic origin include byproducts in consumer products, additives to fuels, waste products of manufacturing processes; natural sources for organics include detritus and exudates of plant and animal matter. The lowest MCLs are in the low nanogram per liter range, and it is evident that target concentrations for detailed characterizations of individual compounds should be in the low nanogram per liter range as well. This paper reviews new and emerging analytical approaches for the analysis of aqueous environmental samples.

Examples of compounds that have emerged recently as particularly relevant are indicated in Table 7-1. The new and emerging analytical techniques are discussed in the context of these compound classes.

ANALYTICAL PROCEDURES

Basic Analytical Approaches

Analytical procedures consist of several interdependent operations carefully tuned to provide maximum efficiency. Some of the analytical operations that may apply are shown in Figure 7-1. The sensitivity of the method defines the lower limit of the sample size that must be processed. The sample is processed to preserve, recover, isolate, and/or concentrate the analytes to produce extracts that are compatible with subsequent instrumental analyses. The processes that lead to a concentrate that can be analyzed using instrumental methods are called sample preparation. Derivatization is a microanalytical technique that serves one or several of the following purposes: increase recovery from the aquatic matrix, facilitate separation from other organic constituents,

and/or improve identification or detection. Because reference compounds for most contaminants are not available, synthesis is often necessary for structure verification and the development of rapid detection and quantification procedures.

TABLE 7-1 Emerging Compound Classes

Compound Category	Examples
Pharmaceuticals	Antibiotics, hormones and contraceptives
Pesticides, herbicides, and their transformation products	Triazines, phenoxy acids
Surfactants and surfactant residues	Aliphatic alcohol polyethoxylates, octyl-and nonylphenol polyethoxylates, octyl-and nonylphenol ethoxycarboxylates, linear alkyl benzene sulfonates
Industrial additives and agents	Aromatic sulfonates, chelating agents, amino carboxylic acids
Taste and odor compounds	Xylenes, aldehydes, disulfides, chlorophenol
Gasoline additives	Dialkyl ether, alcohol, methyl tertiary butyl ether
Disinfection byproducts	Trihalomethanes, haloacetic acids

Methods used to characterize aggregate dissolved organic carbon (DOC) reflect the physical-chemical properties of the heterogeneous mixture of organic molecules present. The molecular size distribution (selective membranes or gel permeation chromatography), the absorbance and fluorescence of UV and visible light, the bonding configurations (^{13}Carbon, ^{1}Hydrogen nuclear magnetic resonance (NMR), infrared spectroscopy), and acidity (potentiometric titrations) are all commonly investigated properties. A thorough review of these techniques has been prepared by members of the International Humic Substances Society and can be found in Aiken et al. (1985) and Hayes et al. (1989).

SAMPLING AND SAMPLE PREPARATION METHODS

Sampling Considerations

Sample size is one of the most important considerations in designing analytical protocols. If the needed sample size exceeds one liter many studies are not feasible. For instance, the sampling and shipping costs in large-scale field investigations may become prohibitive if the sample size is large and samples are

shipped by air. Preservation depends on the biodegradability of the analyte. For biolabile compounds, acidification to pH < 2, refrigeration at 4°C, physical separation of microbes by filtration, and the exclusion of light are often sufficient to preserve the sample for a few days. Chemically and biologically stable analytes such as the triazine pesticides are stable under refrigeration in dark conditions for a few years (Bucheli et al., 1997).

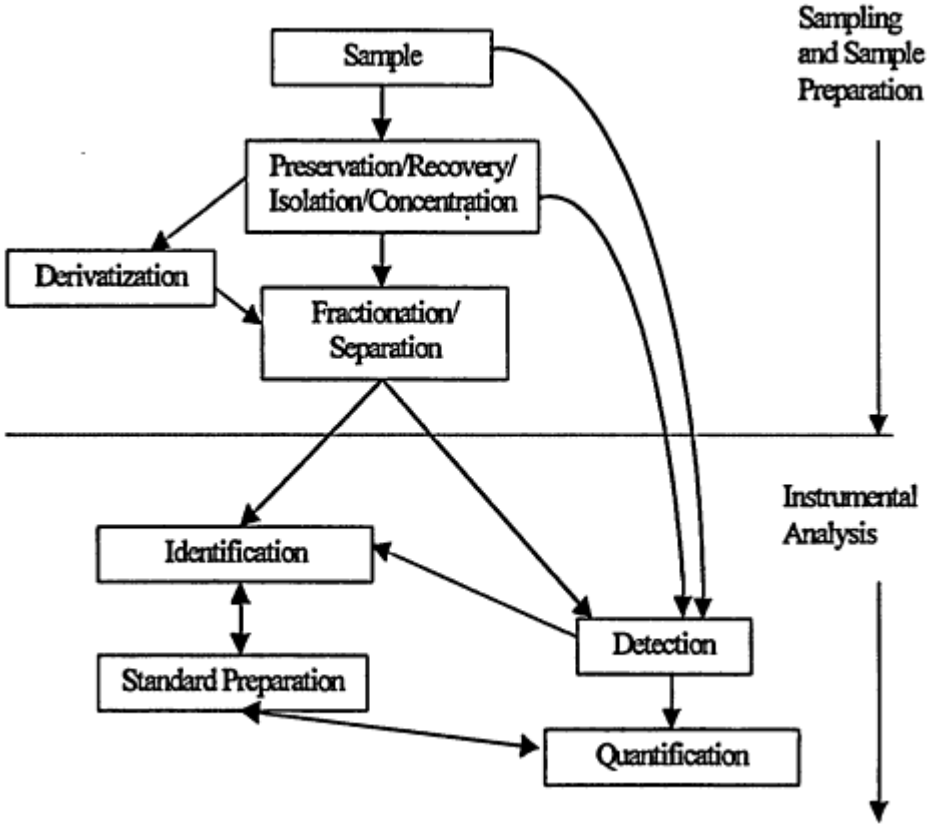

Figure 7-1
General analytical protocol for the analysis of organic trace compounds in water.

Some contaminants, such as chelating agents or some steroid alcohols, are strongly bound to the matrix or to co-contaminants. For the analysis of total testosterone, for example, the sample may have to be subjected to enzymatic hydrolysis prior to extraction to make the testosterone extractable. For ethyl-enediaminetetraacetic acid (EDTA) analysis the speciation (i.e., type of central ion) is an important analytical factor since it influences the stability of the complex and its spectroscopic properties.

Liquid-Liquid and Solid-Phase Extraction

Liquid-liquid extraction (LLE) is a commonly used method of removing organic analytes from an aqueous matrix. LLE methods are used in most official pesticide analysis methods. As LLE methods can be laborious, may cause emulsification problems, involve the evaporation of large solvent volumes, and the disposal of large volumes of hazardous wastes, ways are sought to replace LLE. One increasingly popular alternative is solid-phase extraction (SPE; Altenbach and Giger, 1995; Crescenzi et al., 1997; Pan et al., 1997; Suter et al., 1997). SPE uses hydrophobic sorbents, such as cartridges or discs. Solid-phase microextraction (SPME) utilizes small volumes of sorbents that are extracted using thermal desorption or a small volume of solvent after contacting the sample with the solvent containing the analyte(s) of interest. An elegant form of SPME involves the sorption by a sorbent phase that is coated onto a silica rod mounted into a syringe (Zhang et al., 1994). The compounds can be introduced into the GC by simply injecting the needle and pushing the silica rod into the hot injector.

Another alternative to conventional LLE is supercritical fluid extraction (SFE), which typically uses carbon dioxide as the extractant. SFE can be used indirectly by first concentrating solutes onto solid sorbents, such as SPE cartridges or SPME discs.

As LLE methods are successful at isolating relatively nonpolar organics from water, resin chromatography and membranes are currently used to increase the recovery of organic matter when isolation and concentration are necessary for analysis. A series of ionic and nonionic resins are utilized to exploit the low solubility, and hence absorption, of organic molecules onto resin surfaces. These isolation procedures can be carried out at neutral as well as depressed pH values, relying on the natural or modified (by pH) polarity of organic compounds. Desorption is performed by aqueous eluents possessing different pH values, altering the polarity, or by less polar organic solvents. The resulting fractions of the organic matter pool possess operational definitions that pertain to similar chemical properties.

Concentration by Semipermeable Membranes

Membrane filtration (i.e., reverse osmosis, nanofiltration, and ultrafiltration) is used to separate larger organic molecules from smaller water molecules, increasing the concentration of organic matter in the retentate. As this method has been shown to be successful in retaining a substantial fraction of the larger organic molecules present, retention of smaller organic molecules as well as inorganic components is dependent on membrane pore size and charge. A tradeoff emerges, with smaller pore sizes increasing the fraction of organic matter isolated corresponds to increasing inorganics retention. A comprehensive review of resin chromatography and membrane isolation is presented by Aiken et al. (1985).

Derivatization

Derivatization techniques are used to modify the properties of polar analytes such that they can be processed with a given analytical technique. Typical analytes that must be derivatized prior to analysis include relatively large compounds with thermolabile functional groups (hydroxyl, carboxyl, aminogroups) or small molecules with multiple functional groups. The derivatization chemistry utilizes an agent that reacts selectively with the functional group to form a stable product that can be separated from the water matrix by extraction or sorption, from other analytes by chromatography, detected by chromatographic detectors, or identified by mass spectrometry. Selected examples relevant to water analysis are indicated in Table 7-2.

Most derivatization agents are water reactive and can only be used in water-free extracts. Recent research has been directed toward the development of procedures that allow derivatization directly in water (Minero et al., 1994; Vincenti et al., 1995; Angelino et al., 1997). One approach is to react amino alcohols, amino phenols, polyhydroxy polycarboxylic acids, glycols, and polyhydroxybenzenes with *n*-hexyl chloroformate. The products hydrolyze slowly owing to their increased hydrophobicity. When fluorinated with an *n*-hexyl chloroformate, the detection limit could be lowered from the low µg/L to the low ng/L range.

Owing to public health concerns, there is a strong interest in the analysis of some low molecular weight carbonyl compounds, such as glyoxal and methyl glyoxal. One approach to analyzing such compounds involves a reaction with 2,4-dinitrophenylhydrazine and subsequent HPLC analysis. A method for GC analysis has been presented by Glaze and Weinberg (1997), who modified the method by Yamada and Somiya for the analysis of C_1 to C_3 carbonyls in water. A

TABLE 7-2 Examples of Derivatization Reactions

Derivatization Reaction	Common Derivatizing Agent
Methylation of carboxylic acids	Diazomethane, methanol/sulfuric acid
Oxime formation of carbonyl functionality	PFBHA
N-hexyl carbonate, carbamate, and ester formation from hydroxylic, aminic, and carboxylic functionality	*N*-hexyl chloroformate
Heptafluorobutyramide formation from aromatic amines	Heptafluorobutyramide

review of aqueous carbonyl derivatization by the use of *O*-(2,3,4,5,6-pentafluorophenyl) methylhydroxylamine hydrochloride (PFBHA) is presented by Cancilla and Que Hee (1992). PFBHA makes an excellent derivatizing agent Since this reaction can be performed in water, resulting oximes are readily extracted into an organic solvent and separate well during GC, and ECD detectors am particularly sensitive to multifluorinated aromatics.

Although diazomethane is a commonly used carboxylic acid methylating reagent, it is very toxic and unstable. Alternative methylating reagents, such as the combination of methanol and sulfuric acid, can be advantageous as they can be time saving and safer to use in the laboratory (Xie et al., 1998). Methylation is also performed in combination with other derivatizing reactions. Multiple derivatizations can enhance the separation of desired compounds from aqueous matrix.

There are numerous derivatizing reagents in use to produce numerous products that can then be separated and quantified. The above text discusses only a select few. Articles or books that solely discuss derivatization chemistry present a more thorough review of the topic (Knapp, 1979; Drozd, 1981; Lingeman and Underberg, 1990). A current review of the various derivatizations utilized to quantify herbicide residues by gas chromatography is presented by Tadeo et al. (1996).

INSTRUMENTAL ANALYSIS

Fractionation and Separation

Conventional fractionation and separation involve preparative column chromatography, followed by GC or high-performance liquid chromatography. Combinations of derivatization and extraction techniques with either liquid chromatography (LC) or GC allows for the separation of numerous families of compounds. The objective of recent research is to circumvent these laborious techniques by using highly selective MS techniques.

Mass Spectrometry

Mass spectrometry is the method of choice for the identification of trace contaminants in water. State-of-the-art MS has been reviewed elsewhere (Burlingame et al., 1996). The spectrometry of biomacromolecules represents one of the major breakthroughs of the past decade. This breakthrough became possible because of the discovery that polar labile substances could be ionized by sputtering from viscous liquid surfaces using energetic atom and ion beams. Over the past five years, soft ionization techniques with high ion yields have become available, such as electrospray ionization (ESI) and matrix-assisted laser desorption (MALD) ionization. ESI involves the formation of low-energy, even-electron ions by polyprotonation or deprotonation solutions (Burlingame et al., 1996). To achieve a unimolecular compound-specific fragmentation of these low-energy (cold) species, energy is added in tandem mass spectrometers. ESI is applicable for compounds up to 200 kDa.

MALD ionization involves laser-induced ablation as it is protonated or deprotonated from a cocrystalline solid in the matrix chosen. The laser energy is deposited selectively into the solids. Burlingame et al. (1996) have predicted that these technologies will "become as commonplace as HPLC did in the early 1980s." If one looks at the recent environmental literature, this prediction is clearly becoming a reality, as research papers that are using ESI are becoming more and more frequent.

The high selectivity of MS/MS offers the possibility for direct injection of water samples without chromatographic separation and derivatization. An increasingly important tool is molecular modeling techniques for the interpretation of mass spectral fragmentations.

Identification of Chiral Compounds

Many environmental contaminants occur as enantiomeric mixtures. The widely used pesticide mecoprop (2-(4-)chloro-2-methyl-phenoxy propionic acid) is an example. Because different enantiomers often respond selectively in biochemical systems, there is a need for enantioselective determination.

EXAMPLES

Pharmaceuticals

Pharmaceuticals are used in large quantities in human and veterinary medicine or as a food additive in animal production. In a series of studies, Stan and Heberer (1997) detected 29 different pharmaceutical compounds. Methods for the analysis of drugs are typically adapted from methods used in pharmacology. Pharmaceuticals have long been known to occur in sewage effluents (Reinhard and McCarty, 1980), but the widespread occurrence of these compounds has been documented only recently, mainly by researchers in Germany (Heberer and Stan, 1997).

Antibiotics

In a bioassay-directed study using umuC genotoxicity, Hartman et al. (1998) analyzed the occurrence of fluoroquinone antibiotics in the sewage of a Swiss hospital.

Hormones and Contraceptives

Ramsey et al. (1997) analyzed for estrone, hexestrol, and zeranol by interfacing an aqueous SFE vessel to an LC/MS instrument equipped with an amino column and a UV/vis diode-array detector. The analyses progressed in

two steps: first, the sample was extracted with super critical carbon dioxide and then the analytes were concentrated on the octadecasylane (ODS) column. Second, by means of a 10 port valve the ODS column inlet was connected to an HPLC pump, and the outlet was connected in series to the chromatographic amine column and the LC/MS. Hexane is used as the extractant for the ODC column and the moile phase for the amine column. The method is suitable for the detection of analytes at the 200 ng/L level.

Stumpf et al. (1996) developed a method for trace analysis of steroids in water with a detection limit of 1 ng/L. The method is suitable for the detection of natural and synthetic estrogen as well as the phytoestrogen β-sitosterol in matrices containing high organic contents (such as secondary effluents). One-liter samples are filtered using 0.45-mm glass fiber filters and then acidified to pH 3. Analytes are concentrated using SPE with a mixture of Lichrolut-EN and Lichrolut C18 (Merck). The extracted materials are eluted with acetone and cleaned up using slica gel chromatography with hexane/acetone as the eluent. The analytes are silylated and then analyzed using GC/MS. Recovery rates at 10 ng/L were 76 to 97 percent. The detection limit ranges from 1 ng/L for estrone, estradiol, estriol, mestranol, 17-ethinylestradiol to 5 ng/L for estradiol-17-valerate and 10 ng/L for β-sitosterol. In river water the observed concentrations for synthetic steroids exceeded the detection limit only occasionally; for β-sitosterol, 50 ng/L was observed in most cases.

Schlett and Pfeifer (1996) report a method for the detection of steroidal hormones that is similar to that of Stumpf et al. (1996). The sample is not acidified prior to SPE, and cleanup of the e tract is not necessary. For derivatization a 1,000:2:2 mixture of MSTFA/TMIS/DTE is used.

Nichols et al. (1997) evaluated the hypothesis that poultry litter applied to pasture contributes to the estrogen 17-β-estradiol in runoff using an enzyme-linked immunoassay. Environmental concentrations in poultry litter (water-extractable fraction) were found to be 133 μg/kg. The observed concentrations in municipal waterwater were 0.03 μg/kg, and in runoff 0.3 to 1.3 μg/kg. The detection limit was found to be 0.02 μg/L. The reported limitation of the study was that only one of many hormones found in poultry waste was measured. Other hormones, including testosterone and estrone, were not measured.

Drug and Drug Metabolites

Heberer and Stan (1997) reported on a procedure for analyzing clofibric acid and *N*-(phenylsufonyl)-sarcosine. Clofibiric acid (2-(4-)-chlorophenoxy-2-methyl propionic acid) is the metabolite of several blood lipid-regulating drugs (clofibrate, etofyllincolfibrate, etofibrate). Clofibiric acid was detected in wastewater effluents in the 1970s by several investigators in raw and treated sewage. Cartridges containing 1 g of C_{18} reversed-phase adsorbent were used to extract 1L samples after acidification at pH < 2. Two and one-half milliliters of ethanol were used to elute the analytes from the SPE cartridge. For derivatization, pentafluorobenzoyl bromide is used with triethylamine as the catalyst. The extracts were analyzed using a GC/MS system in the multiple ion detection mode. Concentrations of clofibric acid artificially recharged

groundwater ranged from below the detection limit to 170 ng/L. *N*-(phenyl)-sarcosine was found at concentrations up to 105 ng/L. In drinking water the concentrations of clofibric acid and *N*-(phenyl)-sarcosine were as high as 270 and 105 ng/L, respectively; near wastewater infiltration ponds, concentrations were 4 and 150 µg/L, respectively. Occurrence of these compounds in European rivers is consistent with the widespread use of these compounds.

In another series of studies, Stem and Heberer (1997) screened sewage, surface, groundwater, and drinking water for drug and drug metabolites. The observed concentrations in sewage and surface concentrations were as high as 4.5 and 0.5 µg/L, respectively. In a groundwater well used by a drinking water treatment plant, for example, maximum concentrations of clofibiric acid where found to be 7.3 µg/L, diclofenac, 0.4 µg/L; ibuprofen, 0.2 mg/L; and phenazone, 1.2 µg/L.

Buser et al. (1998) report the occurrence of diclofenac, a nonsteroidal antiinflammatory drug, in Swiss rivers and streams, and its photodegradative removal. The analytical procedure involved adsorption at pH < 2 using a macroporous polystyrene adsorbent, extraction, methylation with diazomethane, and GC/MS analysis using selected-ion monitoring.

Pesticides

Environmental contamination with pesticides remains an important topic in environmental chemistry (Barbash and Resek, 1996). The classes of chemicals used as pesticides are expanding, and the chemical structures of the chemicals are increasing in complexity, especially when compared to the chlorinated hydrocarbon pesticides used during the 1950s and 1960s.

Banoub et al. (1997) describe an ESI MS/MS method for the detection of tebufenozide (*N'-t*-butyl-*N*'-(3,5-dimethylbenzoyl)-*N*-(4-ethylbenzoyl)hydrazine) in lakewater samples without either derivatization or further purification. These authors used an ESI with collision-activated decomposition MS/MS for detection of the analyte. The detection limit is approximately 5 ng/L.

Bucheli and coworkers (1997) investigated the occurrence and behavior of three groups groups of herbicides (triazines, acetamides, and phenoxy acids) in roof runoff. Their analytical approach involved concentration on GCB, followed by sequential elution of the neutral and acidic fractions and derivatization of the acidic fraction with diazomethane. ^{13}C-labeled internal standards were used for quantification. Recoveries were 84 percent or better. Mecoprop, which occurs in two enantiomeric forms, was separated with a fused silica capillary column. The detection limits in rainwater are approximately 1 ng/L.

Crescenzi et al. (1997) reported that 45 pesticides, representing 15 compound classes and possessing a wide range of polarity, were quantified using SPE followed by LC/ESP/MS. All compounds but One were greater than 80 percent recovered during SPE, with the majority of the compounds > 95 percent. Detection limits ranged between 1 and 9 ng/L. This method was also used to

quantify polyethylene glycols (ethoxy chain lengths >3) in environmental samples (Crescenzi et al., 1997). Mangiapan and coworkers (1997) report quantification of arachlor and its degradation products by using SPE followed by GC/MS. Select samples were also analyzed by LC/MS.

Surfactants

Although most high-volume surfactants are classified as biodegradable, residual concentrations of the parent product and/or metabolites are frequently found in effluents and surface waters impacted by effluents. Of greatest interest have been the linear alcohol polyethoxylates (AE), alkyl phenol polyethoxylates, and the linear alkyl sulfonates.

Aliphatic Alcohol Polyethoxylates

Marcomini and Pojana (1997) describe an approach to simultaneously characterize both neutral and carboxylated AE biointermediates using liquid chromatography. Biointermediates include linear alcohols, polyethylene glycols (PEGs) of varying lengths, AE carboxylated at the hydrophilic end or on the hydrophobic end, polyethylene glycol monocarboxylates (PEGC), polyethylene glycol dicarboxylates (PEGDC), and short-chain dicarboxylated PEGs. Depending on the type of sample, 10- to 1,000-ml aliquots are used. The approach is based on SPE using 0.3 to 1.0 g GCB as the sorbent. The reported advantage of GCB is that it exhibits properties of reversed-phase sorbents and cation exchange resins. Using elutions of increasing strength, analyte fractions of increasing acidity are obtained. Because of the lack of chromophores, the analytes were converted into derivatives that could be analyzed using HPLC. To take advantage of the great sensitivity and specificity of the fluorescence detector, Marcomini and Pojana (1997) utilize a fluorescent derivatizing agents. For the two neutral compound classes AE and PEG, 1-naphthoyl chloride (NC) and 1-naphtyl isocyanate (NIC) are used, respectively. The authors note that the two derivatizing agents are highly complementary in terms of the attainable separations by reversed-phase HPLC.

The AE and PEG derivatives of NIC can be separated by homologues and total ethoxymer elution, whereas the NC derivatives allow the separation of each AE ethoxymer and the oligomer-by-oligomer separation of PEGs. Hence, the choice of NC or NIC depends on the information red. The reported detection limit for the neutrals is 100 ng/L.

The carboxylated metabolites (carboxylated PEG and carboxylated AE) are derivatized using 9-chloromethyl anthracene and separated using normal-phase and reversed-phase HPLC. Normal-phase chromatography using an amine column separates PEGC and PEGDC, proving a full separation of all intermediates. Reversed-phase chromatography separates the PEGC and the DPEGDC from the AEC but not from each other. The reported recoveries from environmental matrices were better than 90 percent for AEC and CAEC and 67 to 84 percent for PEGC and PEGDC (Macromini and Pojana, 1997) possibly because of matrix effects.

Linear Alkylbenzene Sulfonates (LAS) and Alkylphenol Polyethoxylates (APEO)

LAS and their associated degradation products sulfophenyl carboxylates (SPC), were measured by Gonzales-Mazo et al. (1997) using SPE followed by HPLC. Multiple detection (fluorescence and diode array) was used prior to definitive identification with ISP/MS (operated in the negative ion mode). Detectable levels of C_7 to C_{13} SPCs in environmental samples were reported.

Di Corcia et al. (1994) present a method wherein LAS and SPC can be isolated and quantified in conjuction with APEO, specifically nonylphenol polyethoxylate and its degradation products. These compounds were initially captured by utilizing cartridge SPE and then separated and quantified using liquid chromatography.

Industrial Additives and Chelating Agents

This compound class includes chemically diverse compounds that are used as additives in plastic or concrete, foundry mold, as tanning agents. Of recent interest here are the aromatic sulfonates (Suter et al., 1997). Altenbach and Giger (1995) used SPE and ion-pair chromatography combined with UV absorption and fluorescence detection to detect aromatic sulfonates in a landfill leachate. Compound identification is based on UV/vis and fluorescence spectral libraries. Surer et al. (1997) used SPE in conjunction with LC/MS for the quantitative analysis of aromatic sulfonates (*p*-toluenesulfonic acid and naphthalene mono and disulfonic acids) from the same site. The LC/MS system utilized was equipped with a single quadrupole mass filter and employed ESI in the negative ion mode.

Taste and Odor Compounds

Taste and odor compounds include relatively simple compounds such as toluene, the xylenes, geosmin, disulfides, and low molecular weight aldehydes (Bruchet and Hochereau, 1997). Odor-thresholds are typically at the nanogram per liter level or below. Most odorous compounds are volatile and although there are exceptions, including chlorophenol and triiodomethane. Bruchet and Hochereau summarize the analytical approaches used for taste and odor compounds: closed-loop and open-loop stripping analysis; purge-and-trap, liquid-liquid, and liquid-solid extraction coupled to high-resolution GC/MS. Solvent-less procedures are important for the detection of highly volatile compounds that would elute within the window of the solvent. Bruchet and Hochereau note that SPE methods have found limited applications owing to background problems,

although they see a potential for SPME. The human nose is very sensitive, and for many taste and odor compounds the sensitivity of available analytical techniques is insufficient to identify the odor-causing compound. Efforts are under way to increase the sensitivity of analytical techniques. New approaches aim to directly inject water volumes up to 100 µl using an ion-column injector.

Disinfection Byproducts

Disinfection byproducts (DBPs) are primarily a drinking water issue. However, because effluents are often chlorinated before discharge, halogenated disinfection byproducts can reach surface waters and groundwater on discharge. Over 100 different reaction products were identified by GC/MS when natural organic matter was chlorinated (Christensen et al., 1983), but Krasner et al. (1989) state that the most abundant DBPs found in chlorinated drinking waters are trihalomethanes, haloacetic acids, haloacetonitriles, haloketones, chlorophenols, chloral hydrate, chloropicrin, and cyanogen chloride.

Gasoline Additives

Church et al. (1997) describe a method that quantifies various gasoline oxygenates: methyl *tert*-butyl ether (MTBE), ethyl *tert*-butyl ether (ETBE), and *tert*-amyl methyl ether (TAME) and also characterizes their most characteristic degradation products. Direct aqueous injection (DAI) was utilized in a GC/MS system. Although purge-and-trap methods have been successful at measuring MTBE, ETBE, and TAME, the DAI/GC/MS method was used to simultaneously measure these compounds and their common metabolites. Detection limits were reported as 0.1 µg/L for all compounds except one metabolite (5 µg/L).

SUMMARY AND CONCLUSIONS

The size of the analytical window is expanding but still limits our ability to characterize organics in water. The second major limitation is the lack of reference spectra and reference compounds. Even if detected, contaminants often cannot be identified.

The target concentrations for trace organics are being pushed from the microgram to the nanograms per liter range. The trend to lower detection limits is driven by the low MCLs and the potency of some endocrin disruptors. As a consequence, sample preparation techniques require new levels of refinement.

The contaminants that are analyzed include more and more reactive contaminants, contaminants that interact with matrix or sediment components by complexation or other chemical-bonding mechanisms. Chemical speciation is an increasingly important consideration in water quality analysis.

HPLC/MS in conjunction with ESI is becoming more and more a standard method for organic trace analysis. HPLC/MS offers the possibility to circumvent costly and time-consuming derivatization procedures.

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9

Methods to Identify and Detect Microbial Contaminants in Drinking Water

Mark D. Sobsey

The transmission of infectious diseases via contaminated water continues to be a risk to public health in the United States and throughout the rest of the. world. Source and finished drinking waters are vulnerable to microbial pathogen contamination from a variety of sources of human and animal fecal wastes and from the introduction and proliferation of nonfecal pathogenic microbes. Throughout most of the modem history of drinking water supply, concerns about pathogenic microbes have focused on enteric bacteria of human fecal origin. These concerns led to the development of criteria and standards for bacteriological quality intended to protect against excessive risks from enteric bacterial pathogens such as *Salmonella typhi* and other nontyphoid *Salmonella* spp., *Shigella* spp., and *Fibrio cholerae. The* infectious disease risks in drinking water supplies from enteric viruses (such as hepatitis A virus), enteric parasites (such as *Entamoeba histolytica and Giardia lamblia*), and nonfecal bacterial pathogens (such as *Legionella* spp.) were not recognized until more recent times. These risks were recognized initially by the occurrence of waterborne outbreaks of disease mused by these pathogens.

Until recently there were no formal, legally required processes to identify or consider new or emerging water. me pathogens in the United States. It was only with reauthorization of the Safe Drinking Water Act in 1996 that the U.S. Environmental Protection Agency (EPA) was required to identify through a structured process candidate microbial pathogens for possible regulation in drinking water supplies. Prior to this the agency used an informal and largely reactive process to recognize, identify, and prioritize microbial pathogens for possible regulation. The new requirement for a proactive rational process to identify and consider microbial pathogens for possible regulation in drinking water is the essential motivation for this paper. As part of this process it is necessary to detect and quantify microbial pathogens in drinking water and its sources; to establish dose-response relationships as an essential step in health effects characterization for waterborne pathogens; and to identify, characterize, and quantify the virulence properties of these pathogens that influence their human health effects.

PURPOSE

The purpose of this report is to consider and address the following questions: How should microbial contaminants for possible regulation in drinking water be identified, characterized, and quantified with respect to their risks to public health? What should be the essential elements of the process for waterborne microbial pathogen identification and characterization? What should be the basis for prioritizing, ranking, or choosing among the many potential drinking water pathogens for possible regulation? How should the microbial pathogen identification and selection process be integrated into the overall process of improving drinking water quality and reducing health risks through drinking water regulations? How should analytical methods for detection, characterization, and quantification of microbial contaminants be applied to the process of identifying, characterizing, and quantifying the risks from waterborne pathogens being considered for regulation? What. analytical methods are available for use in identifying, quantifying, and characterizing microbial pathogens in drinking water for possible regulation?

ANALYSIS

Need for a Risk-Based Approach

The recognition, identification, prioritization, and characterization of microbial pathogens in drinking water should be risk based and should consider the relationships and interactions of the microbes, their *hosts, and the* environment. The microbial world consists of a wide variety of different types or classes of microbial agents potentially present in water. Viruses, bacteria, protozoans, fungi, and algae are widespread in soil, sediments, water, air, and food and on objects and surfaces with which humans have contact ("fomites"). Most of these microbes are not pathogenic (harmless) and are incapable of infecting or colonizing immunocompetent persons unless they somehow gain access to sterile internal sites in the body (such as the bloodstream and various organs) through trauma, surgery, or other such means. However, persons with immunodeficiencies are at risk of infection, colonization, and illness from microbes considered nonpathogenic for immunocompetent persons. Therefore, recognition and identification of a possible waterborne pathogen depends in part on the susceptibilities of the population to infection, colonization, and illness from a microorganism. Some pathogens are always potentially pathogenic and are often referred to as "frank" pathogens. Other pathogens are never or rarely pathogenic for immunocompetent and otherwise "healthy" people. However, these microbes can sometimes cause infection, colonization, and illness in persons who have an immune deficiency, have other conditions that make them susceptible, or because they encounter the microbe in an unusual or atypical way. Such microbes are sometimes referred to as "conditional" or "opportunistic" pathogens. As previously noted, there are nonpathogenic microbes in the environment that are capable of infecting, colonizing, and causing illness in humans only if they are able to dramatically breach the body's natural barriers

and proliferate in normally sterile sites within the body. These nonpathogenic or "saprophytic" microbes are common in aquatic and other environments.

A waterborne pathogen may emerge or acquire increased public health importance because of changes in host susceptibility to infection. Factors influencing host susceptibility in the population include increases in the number of immunocompromised persons, increased use of immunosuppressive agents (among persons receiving cancer chemotherapy or undergoing organ transplants), increases in the elderly segment of the population, and poor nutrition. In identifying and prioritizing emerging waterborne pathogens the susceptibilities of these higher-risk population subgroups to specific infectious diseases is an important consideration (Morris and Potter, 1997).

The relationships between waterborne microbes and their human hosts are complex and are influenced by a variety of factors involving the characteristics and conditions of the microbe, the human and in some cases animal hosts, and the environment. Therefore, it seems necessary to identify, characterize, and quantify these relationships in order to determine if a potentially waterborne microbe should be considered or classified as a drinking water contaminant for possible regulation. Furthermore, the need to prioritize or otherwise determine the importance of a microbe for possible regulation in water suggests that a structured and quantitative approach must be used for such an evaluation or assessment.

Adapting Quantitative Risk Assessment to Recognize, Identify, Prioritize, and Characterize Drinking Water Pathogens

Over the past two decades considerable progress has been made in quantitative risk assessment (QRA) for making management decisions about waterborne pathogens. Initially, the National Academy of Sciences/ National Research Council risk assessment strategy was adapted to assess microbial risks (Regli et al., 1991; Rose and Gerba, 1991; Rose et al., 1991; Sobsey et al., 1993). This process consists of hazard identification, exposure assessment, effects assessment, and risk characterization. Using this approach, quantitative risk assessments were done initially for several recognized waterborne pathogens, such as *Giardia lamblia* and rotaviruses. More recently, the process of quantitative risk assessment for pathogens in water was reconsidered and revised through a consensus-building International Life Sciences Institute (ILSI) workshop process (ILSI Risk Science Institute Pathogen Risk Assessment Working Group, 1996). This effort resulted in a modified quantitative risk assessment system that specifies the criteria, information needs, and analytical approaches for quantitative risk assessment for waterborne microbes (See Figure 9-1).

Presently, the EPA/ILSI system for quantitative risk assessment of microbes in water is being applied by several research groups to determine its utility, and other researchers will peer review the QRA products for utility,

clarity, and transparency. The EPA/ILSI QRA approach was not intended for the purpose of selecting microbial contaminants for possible regulation in drinking water. Furthermore, it certainly is not the only way to identify, prioritize, and assess the risks from microbes in drinking water. However, this microbial QRA system does specify information needs and analytical methods that can be readily adapted to the recognition, identification, prioritization, and initial characterization of risks from a possible waterborne microbe. Considering that the EPA and many of the nation's scientists in the areas of water microbiology, infectious diseases, water treatment, epidemiology, and risk assessment invested much effort and time in the development of this system, it seems appropriate to interface it with the process for microbial contaminant selection. Furthermore, it can be said that the elements of the EPA/ILSI QRA system for microbes rely on the same types and sources of data and at least some of the same analytical methods that would be used in any structured process to identify, select, characterize, and prioritize candidate microbial contaminants for possible regulation in drinking water (See Figure 9-2).

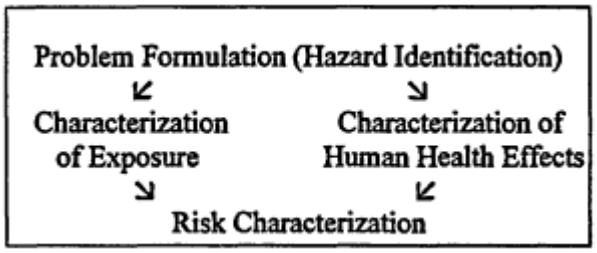

Figure 9-1
Risk assessment for waterborne microbial pathogens: EPA/ILSI paradigm.

Human Pathogens in Water: Classification, Sources, and Properties

Known and potential human pathogens in water include the spectrum of agents ranging, in order of increasing complexity, from prions, to viruses, to bacteria, and other prokaryotes, and the microbial eukaryotes (the protists), including protozoans, fungi, and algae (Moe, 1997). Prions have not been implicated in waterborne disease, but recent evidence for human spongiform encephalopathies from ingestion of beef contaminated with bovine spongiform agents suggests that vehicles such as food and possibly water contaminated with prions pose a risk of exposure (Ironside, 1998; Knight and Stewart, 1998). Furthermore, these agents are very small compared to other microbes, which makes them difficult to remove by physical-chemical processes, and they are extremely resistant to virtually all physical and chemical agents, which makes them persistent in the environment and resistant to virtually all drinking water disinfectants.

A. ELEMENTS CONSIDERED IN PATHOGEN OCCURRENCE
Spatial distribution (clumping, particle-association, clustering)
Concentrations in environmental vehicles and foods
Seasonality and climatic effects
Temporal distribution, duration, and frequency
Niche (potential to multiply or survive in specific media)
Amplification, die-off, persistence
Indicators/surrogates predictive of pathogen
B. ELEMENTS CONSIDERED IN EXPOSURE ANALYSIS
Identification of water and other media
Unit of exposure
Temporal nature of exposure (single or multiple; intervals)
Route of exposure and transmission potential
Demographics of exposed population
Size of exposed population
Behavior of exposed population
C. ELEMENTS CONSIDERED IN PATHOGEN CHARACTERIZATION
Virulence and pathogenicity of the microorganism
Pathological characteristics and diseases caused
Survival and multiplication of the microorganism
Resistance to environmental control measures
Host specificity
Infection mechanism and route; portal of entry
Potential for secondary spread
Taxonomy and strain variation
D. ELEMENTS CONSIDERED IN HOST CHARACTERIZATION
Demographics of the exposed population (age, density, etc.)
Immune status
Pregnancy
Concurrent illness or infirmity
Nutritional status
Genetic background
Behavioral and social factors
E. ELEMENTS CONSIDERED IN HEALTH EFFECTS
Morbidity, mortality, sequelae of illness
Severity of illness
Duration of illness
Chronicity or recurrence
Potential for secondary spread
Quality of life

FIGURE 9-2 Microbial contaminant identification, selection and characterization using elements of the EPA/ILSI risk-based approach: Description of the information needs.

Viruses

A variety of enteric and respiratory viruses of humans and in some cases other animals as well are potential agents of waterborne disease. For many of these viruses the role of water has been clearly established because of documented waterborne outbreaks, or it is strongly suspected because the viruses have been detected in drinking water or its sources. Some of these viruses are shown in Table 9-1, but other viruses and virus groups may also pose risks from exposure via drinking water. A notable feature of all of these viruses except the coronaviruses and picobirnaviruses is that they are nonenveloped (consisting only of a nucleic acid surrounded by an outer protein coat or capsid).

Nonenveloped viruses tend to be more resistant to various physical and chemical agents and more stable in the environment than the enveloped viruses, which probably contributes to their potential to cause waterborne disease. Another important feature of some of these viruses, as well as many of the bacterial and parasitic pathogens of concern in drinking water, is that they have known or suspected animal hosts and therefore are transmissible directly or indirectly from other animals to humans. The potential for animal-to-human transmission creates concerns about contamination of drinking water supplies with animal wastes containing these pathogens. As previously noted, similar concerns also apply to many bacterial and parasitic pathogens.

Bacteria

Many enteric and respiratory bacteria infect and cause morbidity and mortality in humans via the water route. Some of these bacteria also infect other

TABLE 9-1 Important Viral Contaminants of Drinking Water

Virus or Virus Group	Outbreak or Detected in Water	Animal Sources
Enteroviruses: (polios, echos[2], coxsackies[2], etc.)	Yes	No
Hepatitis A virus[2]	Yes	No
Hepatitis E virus	Yes	Pigs?
Reoviruses	Yes	Yes
Rotaviruses	Yes	Yes[b]
Adenoviruses[2]	Yes	Yes[b]
Caliciviruses[2]: Norwalk, Snow Mountain, etc.	Yes	No for some; maybe for others
Astroviruses	Yes	No
Parvoviruses; picornaviruses	Maybe	Uncertain
Coronaviruses	No	Uncertain
Picobirnaviruses and picotrirnaviruses	Unknown	Maybe

[2] On EPA's microbial contaminants priority list.
[b] Humans and animals are usually infected by different ones but not always.

animals, often asymptomatically, and some, such as the *Legionella* spp., the *Mycobacteria* spp., and the heterotrophic plate count bacteria, have abiotic environmental reservoirs. For many of these bacteria the role of waterborne transmission has been documented by waterborne outbreaks, or it is strongly suspected because the bacteria have been detected in drinking water and its sources (see Table 9-2). In the case of some of these waterborne bacteria their risks to human health from ingestion or inhalation of water or contact with water are uncertain because they have not been conclusively documented by outbreaks or other epidemiological evidence of waterborne disease. However, their presence in drinking water and the uncertainty of their risks to human health from drinking water exposure suggest the need for further investigation and analyses.

The risks posed by various bacteria potentially present in drinking water differ among the various genera and species as well as within the same genus and species of a bacterium. These differences in risks to human health pose considerable challenges to the detection and identification of these bacteria in water. Similar concerns apply to the protozoan parasites, algae, and fungi. Strains or variants of the same genus and species of bacterium can differ dramatically in their ability to cause disease because this ability is largely dependent on the presence of virulence factors or properties.

In some cases the virulence factors or properties of the bacterium responsible for disease are essential constituents of the cell. This appears to be the case for *Salmonella typhi, the* causative agent of typhoid fever, whose essential virulence properties are the O antigen (the lipopolysaccharide outer membrane of the cell wall; an endotoxin) and the Vi antigen (a capsule polysaccharide) (Salyers and Whitt, 1994; Levine, 1998). For many other bacteria, such as strains of *Escherichia coli, Aeromonas hydrophila, and Yersinia enterocolitica, the* ability to be a pathogen and cause disease is clearly associated with the presence of specific virulence properties that may or may not be present in specific strains or types. These virulence factors are often transmissible from one cell to another via transmissible plasmids or bacterial viruses (bacteriophages). Plasmids are extrachromosomal, small, circular DNA molecules that replicate separately from the bacterial chromosome and can move from one cell to another by a process called conjugation. Bacteriophages also can transmit virulence factors from one host cell to another, especially if the infecting bacteriophages do not kill the cell and instead integrate their DNA into the bacterial chromosome. Strains of a species bacterium possessing no virulence factors generally are not pathogenic and do not produce disease. Strains of the same species of bacterium possessing one or more specific virulence factors are pathogenic and capable of producing disease. Furthermore, the pathology and clinical features of the disease depend on the properties and activities of these virulence factors. For example, strains of *E. coli* lacking virulence properties generally are not pathogenic, and most humans and other mammals harbor about a billion *E. coli* cells per gram in their lower intestinal

tracts with no adverse effects. However, *E. cell* strains possessing one or more virulence properties are capable of causing different diseases. For example, enterohemorrhagic strains of *E. cell* strains possess the Shiga-like toxin (SLT). They are infectious at relatively low doses (< one thousand cells) and cause a bloody diarrhea without fever that can advance to life-threatening hemolytic-uremic syndrome, a form of hemolytic anemia and kidney failure, especially in young children. Other strains of *E. coli* possess a heat-stable toxin (ST) and/or heat labile toxin (LT; similar to the cholera toxin of *Fibrio cholerae). These* enterotoxigenic strains of *E. coli are* infectious at higher doses (> one million cells) and cause disease by increasing adenylate cyclase (LT) and guanylate cyclase (ST) activities in the small intestine that lead to watery diarrhea, electrolyte imbalance, and dehydration.

TABLE 9-2 Some Important Bacterial Contaminants of Drinking Water

Bacterium/Group	Outbreak or Detected in Water	Animal Feces	Non-Fecal Sources
Salmonella spp. (except S. *typhi*)	Yes	Yes	No
Salmonella typhi	Yes	No	No
Campylobacter spp.	Yes	Yes	No
Escherichia cell	Yes	Yes	Maybe
Helicobacter pylori[a]	Yes	Unknown	Unknown
Heromonas hydrophila[a]	Yes	Yes	Yes
Yersinia enterocolitica	Yes	Yes	Yes
Fibrio cholerae and some other *Fibrio* sp.	Yes	Yes	Yes
Shigella spp.	Yes	No	No
Legionella spp[b].	Yes	No	Yes
Mycobacterium avium-intracellulare[a] and other *Mycobacterium* spp.	Yes	Yes	Yes
Leptospira spp.	Yes	Yes	Yes
Heterotrophic plate	Yes	Yes	Yes
Count bacteria	Yes	Yes	Yes

[a] On EPA's microbial contaminants priority list.
[b] On EPA's microbial contaminants priority list in groundwater.

The roles of human and animal hosts as well as the environment in the selection for and emergence of new strains of virulent bacteria are becoming increasingly appreciated. For example, there is growing evidence that cattle and other agricultural (livestock) animals are major reservoirs of such waterborne and foodborne bacterial pathogens as enterohemorrhagic *E. coli, Salmonella spp., and Yersinia enterocolitica* (Tauxe, 1997).

The role of the aquatic environment as a reservoir for and source of emergence of new virulent strains of bacteria is becoming increasingly recognized in the case of some bacteria. For example, the genes coding for the cholera toxin of *Fibrio cholerae* are borne on and can be infectiously transmitted

by a filamentous bacteriophage (Faruque et al., 1995). The natural history of V. *cholerae*, including the mechanisms and evolution of virulence and pathogenicity, as well as its taxonomy, appear to be intimately linked to the aquatic environment and the interactions of humans with this environment. Molecular epidemiological studies reveal clonal diversity among toxigenic *V. cholerae* strains. The continual emergence of new epidemic clones may be taking place in aquatic ecosystems through interaction of the phages bearing the cholera toxin with different strains or antigenic types of V. *cholerae*. These new strains may then be selected for during epidemics in human populations. This appears to be an example of the evolution of new toxigenic strains of a human pathogen in natural aquatic ecosystems systems and its selection during outbreaks in human hosts. Within the aquatic ecosystem, interactions of the genetic elements of the microbes and their host reservoirs mediate the transfer of virulence genes, thereby resulting in the creation and the subsequent selection in humans of these new pathogenic strains. The extent to which such evolution and selection occurs for other human pathogens in aquatic ecosystems is unknown and deserves further investigation.

Protozoan Parasites

In the past three decades, protozoan parasites have emerged as important waterborne pathogens (Marshall, 1998). Some of the important protozoan parasites infecting humans and found in water are listed in Table 9-3. The ameba *Entamoeba histolytica, the cause* of amebic dysentery, has long been recognized as a waterborne pathogen. However, outbreaks of waterborne amebic dysentery have not been reported for decades in the United States and there are no major nonhuman reservoirs of this parasite. It was only with the recognition in the 1960s and 1970s of *Giardia lamblia* as a waterborne pathogen having important animal reservoirs and considerable resistance to *chlorination* and other drinking water disinfection practices that serious attention began to focus on this agent and other human pathogenic protozoans in drinking water. Since then, *Cryptosporidium parvum* has become a high-priority pathogen for regulation in drinking water because of documented waterborne disease, many animal reservoirs, ubiquitous presence in drinking water sources, relatively small size, and resistance to chlorine and other drinking water disinfectants. Other protozoan parasites, including the free-living amebas (e.g., *Acanthamoeba* spp), the coccidians *Cyclospora cayatenensis and Toxoplasma gondii, the* microsporidia, and the ciliate *Balantidium coli are* now recognized as human pathogens that deserve consideration in drinking water. Some of these agents, such as the free-living amebas, have a natural aquatic habitat. Many of the others, including *Giardia lamblia, Cryptosporidium parvum, Toxoplasma gondii, Balantidium coli, as* well as the microsporidia have nonhuman animal reservoirs that contribute to their presence in drinking water supplies and sources. The microsporidia are among the most ubiquitous protozoan parasites of animals and

infect hosts ranging from insects and other invertebrates to fish, birds, and mammals. Only a few species of human microsporidia have been recognized, and the Significance to human health of the many microsporidia of other animals is unknown at this time.

TABLE 9-3 Important Protozoan Parasite Contaminants of Drinking Water

Parasite	Outbreak or Detected in Water	Animal Feces	Non-fecal Sources
Acanthcanoeba spp.[a]	Yes	No	Yes
Cryptosporidiurn parvum	Yes	Yes	No
Cyclospora cayatenensis[a]	Yes	Unknown	Unknown
Giardia lamblia	Yes	Yes	No
Entarnoeba histolytica	Yes	Rare	No
Balantidium cell	Yes	Yes (pigs)	No
Microsporidia[a] (*Enterocytozoon and Septata*)	Yes?	Yes	Maybe
Toxoplasma gondii[a]	Yes	Yes	No

[a] On EPA's microbial contaminants priority list.

A particular challenge to the detection of protozoans of public health concern in drinking water is that many of the currently available and widely used analytical methods, especially the various microscopic techniques (such as brightfield, immunofluorescent, phase contrast, and differential interference contrast microscopy) cannot always distinguish the human pathogenic genera, species, and strains from the many others that are noninfectious and therefore harmless to humans (EPA, 1996, 1998). Furthermore, these microscopic methods cannot distinguish the infectious parasites posing a human health risk from the noninfectious inactivated ones no longer posing risks to human health. Even the latest of sensitive and specific molecular genetic methods, such as polymerase chain reaction (PCR) amplification and restriction fragment length polymorphism (RFLP) analyses, may not distinguish human pathogenic from nonhuman nonpathogenic strains of a parasite such as *Cryptosporidium* (Champliaud et al., 1998). The limitations of currently available detection methods in identifying species and strains of protozoans capable of causing human infection and disease also apply to the methods of detecting other classes of microbes in drinking water that pose risks to human health.

Methods for Detecting Pathogenic Microbes in Water

Introduction

The detection of pathogenic microbes in water typically involves three main steps: (1) recovery and concentration, (2) purification and separation, and (3) assay and characterization. In most cases the concentrations of pathogenic microbes in drinking water are so low that practical detection requires an initial

step of concentration or enrichment from the water. Because many concentration and recovery procedures for pathogens also recover and concentrate other microbes and other constituents in the water sample, subsequent purification procedures are needed to separate the target pathogens from these other materials. Furthermore, the volumes of concentrated samples often are still too large for sensitive detection and analysis of the target pathogens, and therefore additional steps of concentration as well as purification are needed.

The physical and chemical properties of the microbes have an important influence on their ability to be recovered by the various physical and chemical separation methods available. The size, shape, and density of the microbes influence various physical methods of recovery, such as filtration, sedimentation, and flotation. The surface properties of the microbes, such as their hydrophilicity, surface charge, isoelectric point, hydrophobicity, permeability, and chemical reactivity, will influence chemical and physical-chemical methods of recovery and separation. Most microbes are hydrophilic and negatively charged near neutral pH, but most are also somewhat hydrophobic and their surface has both hydrophobic and hydrophilic domains. The environmentally stable stages or forms of some microbes, including bacterial spores and protozoan cysts, oocysts, and spores, have thick outer "walls." Some bacteria have other surface features influencing physical-chemical behavior, such as outer polysaccharide layers (capsules), and appendages such as flagella and pili (fimbrae). These many and varied physical and chemical properties must be considered in the development and application of methods to recover and concentrate microbes from water.

A variety of assay and characterization procedures can be applied to the detection and quantitation of target pathogens in drinking water. These include enumeration or quantal assays of total, viable, active, or infectious target microbes and their distinction from nontarget microbes based on identification or characterization of genus, species, type, strain, and virulence or other relevant properties. Recently, nucleic acid amplification methods such as PCR and nucleic acid identification and characterization methods, such as hybridization (gene probes), RFLP analysis, and nucleotide sequencing, have been applied to the detection of microbes in water. Despite the potential sensitivity and specificity of these methods, they are not always capable of reliably detecting and quantifying infectious or viable organisms because they often detect the nucleic acid of noninfectious inactivated microbes (Sobsey et al., 1998). There are similar concerns about the various immunochemical methods to detect and quantify microbes in water; these methods detect and quantify antigens that may still be present and reactive in noninfectious or inactivated microbes.

Initial Recovery and Concentration of Pathogens from Water

Sedimentation by Centrifugation

For bacteria, parasites, and other cellular microbes, initial concentration and recovery are sometimes done by sedimenting the cells using centrifugation. Typically, bacteria and parasites can be sedimented from water and other aqueous samples at relative centrifugal forces (RCFs) of several thousand times gravity for several minutes to several tens of minutes. The supernatant water is removed, and the sedimented cells are resuspended in a small volume of water or other aqueous solution for subsequent analysis and characterization, with or without further purification or concentration. A modified centrifugation method recently applied to *Cryptosporidium* is the use of a blood cell separator (Borchardt and Spencer, 1998). Water is continuously centrifuged through the device at about 1,000x gravity, and *Cryptosporidium* oocysts and other particles are deposited in a separation channel. The deposited *Cryptosporidium* oocysts and other particles are then recovered from the separation channel and collected for microscopic examination.

Viruses also can be recovered and concentrated by centrifugation, but because of their small size this requires ultracentrifugation (Sobsoy, 1976). Typical ultracentrifugation conditions for viruses are RCFs of 50,000 to 100,000x gravity for periods of several hours. Ultracentrifugation is not widely used to concentrate and purify viruses from water because of the high cost and lack of portability of ultracentrifuges and the tendency for low levels of viruses to be recovered with poor and variable efficiency. Using simple centrifugation methods, other particles in the same size and density range of the target microbes also are recovered and concentrated. This lead of other nontarget particles often greatly exceeds the concentration of target microbes, and these excess nontarget particles can 'interfere with further separation, concentration, assay, and characterization of the target microbes.

Filtration

Microbes can be recovered and concentrated from water by a variety of filtration methods (Brock, 1983). The most widely used filtration method for recovering bacteria is membrane filtration using microporous membranes typically composed of cellulose esters. This method is the basis of the widely used membrane filtration methods for detecting indicator bacteria, including total and fetal coliforms, enterococci, and *Clostridium perfringens* (Eaton et al., 1995). These methods and modifications of them are also widely used for initial concentration and recovery of bacterial pathogens in water, including *Salmonella, Shigella, and Campylobacter. The* cells recovered on a membrane filter can be directly cultured on differential and selective broth (liquid) or agar (solid) media in order to detect and assay the recovered bacteria by enrichment (or presence-absence) or by the development of bacterial colonies. The enriched bacteria or bacterial colonies are further characterized to confirm their identity.

Alternative filtration methods have been used to recover and detect bacteria and parasites, including microporous filters composed of nylon,

polycarbonate, fiberglass, porous ceramics, and other media. Track-etched polycarbonate and other membrane filters have been used to concentrate and recover bacteria and parasites for direct microscopic detection. These microscopic methods often employ immunofluorescence assays to facilitate identification, assays for determination of cellular activity as a measure of viability (e.g., inclusion or exclusion of vital dyes or other compounds), and infectivity assays, such as cultivation of bacteria on solid media for the development of microcolonies detectable by microscopy or fluorometry.

Another filtration method used for recovery and concentration of bacteria as well as viruses, parasites, and other microbes is ultrafiltration. As the name implies, ultrafilters have much smaller pore sizes that are expressed as the molecular weight of the smallest retained particles or molecules (molecular weight cutoff or MWCO). Typically, this is in the range of several thousand to 100,000 MWCO. Ultrafiltration is often done using tangential flow systems in which the water is made to flow parallel to the membrane surface. This is done in order to keep the microbes and other particles suspended in the retained water (retentate) and prevent them from accumulating at the filter surface where they would cause clogging and reduce hydraulic flux. Tangential flow ultrafiltration systems include stirred cells, hollow fibers, spinning cartridges, and stacked sheets.

Because of the small size of viruses, they are recoverable from water by pore size exclusion filtration only with ultrafilters or even smaller pore size filters (nanofilters and reverse osmosis filters). Ultrafiltration has been used for virus concentration from water for decades, although the high costs of ultrafiltration hardware and the ultrafilters themselves have limited the use of these methods (Sobsey, 1976). Recently economical, disposable hollow fibers have been used to concentrate viruses as well as bacteria and the parasite *Cryptosporidium parvum* from raw source water and finished drinking water (Juliano and Sobsey, 1997).

Size exclusion filtration is widely used to concentrate parasites from water, with most of the historical and current focus on *Giardia and Cryptosporidium. The* filters initially and still widely used are yarn-wound, 10-inch-long, cartridge filters composed of polypropylene or other media, and having nominal pore sizes of one to several micrometers in diameter (EPA, 1996). A disadvantage of these filters is the need to remove them from the filter housing and manually cut them apart in order to recover the parasites and other retained particles by physically washing them from the filter medium using an aqueous detergent solution. Parasite cysts and oocysts in the recovered solution of several liters volume are further concentrated and recovered by centrifugation to sediment them. Because these depth filters have only nominal pore size ratings and the cartridges are typically pressure held in their plastic housings by flexible O-ring or gasket seals, *Cryptosporidium* oocysts have penetrated or bypassed the filters, resulting in appreciable losses. Furthermore, recoveries from the filters are highly variable, resulting in large coefficients of variation. Additionally, because the target sample volumes are 100 L or more, there are

high loads of other particles in the resulting pellets. These other particles can interfere with subsequent purification and microscopic examination of the parasite cysts and oocysts.

Other filters having absolute pore size ratings smaller than the size of the target cysts, oocysts, and spores are alternatives for concentrating parasites from water. These filters are preferred because they are expected to achieve absolute retention of the protozoan cysts, oocysts and spores and because their physical characteristics facilitate easier and more efficient recovery of the retained microorganisms by simpler elution methods than cutting apart and macerating the filter material. Formats for these filters include flat track-etched polycarbonate disks, cellulose acetate membranes (that are dissolved in acetone to recover *Cryptosporidium* oocysts), pleated capsule filters (1 um pore size polyether-sulphone filters in a polycarbonate housing), and ultrafilters (spinning cartridge and hollow fiber units). Such filters, as well as the smaller water sample volumes, are now recommended by the EPA, and some of them are specified in the recently developed Method 1622 (EPA, 1998). Another type of filter being used to concentrate C*ryptosporidium* from water is a compressible "sponge" filter. This filter is compressed into a water pipe to achieve a small pore size, and water is allowed to flow through the compressed filter for a period of time. The filter is recovered from the pipe, and the parasite cysts and oocysts are readily washed off of the now decompressed sponge-like filter medium for further processing and analysis.

The most widely used methods for initial concentration and recovery of viruses from water employ microporous filters that retain viruses primarily by adsorption to the filter medium (Sobsey, 1976; Sobsey, 1982; .De Leon and Sobsey, 1991). These filters retain viruses by both electrostatic and hydrophobic interactions between the surfaces of viruses and the filter media. Formats used for virus adsorbent filters include membranes, disks, and pleated cartridges. The media used initially as virus adsorbent filters were negatively charged cellulose esters, fiberglass, and other materials. These filters adsorb viruses efficiently only at lower (acidic) pH levels (pH of 3 to 6) and/or in the presence of multivalent cation salts, such as divalent calcium or magnesium or trivalent aluminum salts. Relatively large volumes of conditioned water are passed through the filter, and viruses adsorb to the filter medium surfaces. Subsequently, filters that are electropositive near neutral pH and adsorb viruses directly without acidifying or adding cations salts to the water were developed for virus concentration (De Leon and Sobsey, 1991).

Electropositive filter media are composed of charge-modified fiberglass sold commercially as disks or pleated cartridges, fiberglass filter disks that are coated with precipitated aluminum or iron salts, or positively charged, natural quartz fiberglass that one packs into a column to make an adsorbent filter. The current EPA-approved ICR method to detect culturable enteric viruses in drinking water supplies specifies use of commercially available, electropositive filter (EPA, 1996). Viruses adsorbed to both electronegative or electropositive filters are subsequently eluted and recovered by passing a relatively small volume of aqueous elution medium through the filter. Viruses in the resulting filter eluates are assayed directly or after further steps of concentration, purification, and extraction.

Initial Recovery and Concentration of Pathogens from Water by Chemical Precipitation Methods

Pathogens can be recovered and concentrated from water by chemical precipitation methods, and such methods have been used primarily for vital and protozoan pathogens. Chemical precipitation of viruses is done typically with either polyethylene glycol or cation salts (aluminum, iron, magnesium, etc.; Sobsey, 1976; Dobberkau et al., 1981), and for protozoans such as *Cryptosporidium* it is done primarily with calcium carbonate (Vesey et al., 1993). Virus concentration from water by aluminum hydroxide flocculation and *Cryptosporidiurn* concentration from water by calcium carbonate precipitation has been used for recoveries from sample volumes up to about 10 to 20 L. For virus recovery, aluminum sulfate is added to the water, the water is acidified, and after several hours of settling the supernatant is aspirated and the remaining floc or sediment is centrifuged to remove additional water. The resulting floc is dissolved in an acidic or other buffer, such as citric acid. Viruses in the dissolved floc are assayed directly or after further concentration and purification. For *Cryptosporidium parvum* oocyst recovery, water is supplemented with calcium chloride and sodium bicarbonate and brought to pH 10 with NaOH to precipitate calcium carbonate. After settling for several hours, the supernatant is removed and the remaining precipitate is dissolved in dilute sulfamic acid. The *Cryptosporidiurn* oocysts are recovered by centrifugation, resuspended, and microscopically enumerated after fluorescent antibody staining.

Other Primary Recovery and Concentration Methods

Other solid-phase or granular media, including minerals (such as iron oxide, talc and quartz sand), glass beads, and synthetic resins (ion exchange and adsorbent) have been used to concentrate microbes from water by adsorption, filtration, and related processes. These methods are not as widely used as the others described above because they are less effective, often cumbersome, and often not readily portable for field use. Furthermore, elution, desorption, or flushing of the target microbes from these media is often inefficient and cumbersome. Other filtration and adsorption media that are better defined, more portable, and more amenable to efficient microbial recovery are now preferred.

Purification Methods for Waterborne Pathogens

Purification, separation, and concentration of target microbes in primary samples or sample concentrates is intended to separate target microbes from other particles and solutes and reduce the sample size by further concentration. A variety of physical, chemical, and immunochemical methods are used for this purpose. Sedimentation and flotation using density solutions or gradients are

techniques used primarily for parasites, but they have also been applied to viruses, bacteria, and other eukaryotes besides protozoans. Chemical precipitation methods are used for viruses and parasites, and some of these are similar if not identical to those used for primary concentration of these same microbes from large volumes of water. Filtration methods are applied for purification and further concentration of all classes of microbes, and often they are similar to those filtration methods used for primary concentration of these same microbes from large volumes of water.

Immunomagnetic separation (IMS), sometimes referred to as immunocapture or antibody capture, is a method now being applied to all classes of microbes. The method uses paramagnetic synthetic beads, other magnetic or paramagnetic particles, or other solid surfaces (e.g., microcentrifuge tubes and the wells of microtiter plates) that have been coated with antibodies directed against the target microbes to recover the microbes from the sample by an antigen-antibody reactions. The retained microbes can be analyzed directly or after they or their components (e.g., their nucleic acids) have been subsequently released or extracted from the antibody and solid phase by various physical or chemical methods. IMS methods have the advantage of selecting, separating, and purifying specific target microbes from other microbes and particles of similar size and shape and as well as from solutes, based on the specificity of the antigen-antibody reaction. This is a powerful approach for recovering, enriching, purifying, and concentrating the target organisms from the sample matrix.

Other purification and concentration methods include ion exchange, adsorption, chelation, chromatography, and related chemical and physical-chemical techniques to remove or separate impurities from the sample containing the target microbes. For example, particle size exclusion chromatography using Sephadex gel has been used to separate enteric viruses from solutes in the sample matrix and achieve a high degree of purification for subsequent detection by cell culture or nucleic acid amplification-nucleic acid hybridization methods (Sobsey et al., 1996). Extraction methods using organic solvents, detergents, lytic enzymes, and other chemicals have been used to partition target microbes from impurities in the sample (phase partitioning) or to solubilize sample impurities and facilitate their physical separation from the microbes in the sample. However, care must be used in applying these chemical treatments in order to avoid injury or damage of the target microbes that would interfere with their detection by cultivation or other methods.

Another physical separation and purification method, as well as a detection method, becoming more widely applied to the purification, separation, and concentration of pathogens in water is flow cytometry. Flow cytometry is a laser-based technology to measure cells or other particles made to flow single file through a sensing area. The cells are measured by both forward and 90° angle laser light scatter as well as by fluorescence (when labeled with a fluorochrome such as fluorescent antibody). These systems can also sort the detected cells by electronically charging them when detected and then deflecting them into a separate liquid stream. Recently, flow cytometry has been applied to the detection, separation, and purification of *Cryptosporidium parvum* oocysts concentrated from water (Vesey et al., 1997). Despite the advances in applying flow cytometry to the concentration, purification, and detection of *C. parvum* and potentially other pathogens in water, there remain technical and other barriers to

the application of this technology. The instruments are expensive and require a skilled, dedicated analyst; infectious and non-infectious organisms can not be reliably distinguished and sample cross-contamination is a high risk because field samples and positive control (calibration) samples pass through the same chambers and channels.

Assay Methods for Waterborne Pathogens

Introduction

Assay methods include all of the approaches involving either propagation or other analyses of microbes. These assay methods include (1) culture or infectivity, (2) viability or activity measurements, (3) immunoassays, (4) nucleic acid assays, and (5) microscopic and other optical or imaging methods. Often, several of these assays are combined or used concurrently in order to provide more definitive information on the quantity, identity, characteristics and state of the target organisms. Detection of microbial pathogens by culture or infectivity assays is preferred because it demonstrates that the target microbe is alive and capable of multiplication or replication. From a public health and risk assessment standpoint, microbial pathogen assays based infectivity are the most relevant and interpretable ones.

Culture or Infectivity Assays for Bacteria

Culture of bacterial pathogens is widely used in clinical diagnostic microbiology, and, for many waterborne bacterial pathogens, culture methods are adapted from those initially developed for medical diagnosis. Typical approaches are culturing the target microbes from specified volumes of water by preenrichment and enrichment methods using broth media or filtering the organisms from specified volumes of water and placing the filters in broth or agar culture media. Using membrane filters, the bacteria are often cultured directly by placing the filter on differential and selective media and incubating at appropriate temperatures to allow the development of discrete colonies of the target pathogens. Usually, the identity of the cultured bacteria must be confirmed by one or more of several methods. These methods include (1) subculturing on other differential and selective media; (2) biochemical, metabolic and other phenotypic analyses (for substrate utilization or conversion, enzyme activity, oxidation and reduction reactions, antibiotic resistance, motility, etc.); (3) immunological analyses (e.g., serological, immunofluorescent, enzyme-immune, or radio-immune assays); and (4) nucleic acid or genetic analysis. The nucleic acid methods include hybridization (gene probe), nucleic acid amplification (by PCR and other methods), restriction enzyme fragment length analyses (restriction fragment length polymorphism; RFLP), and nucleotide sequencing.

Detection of bacterial pathogens in water continues to be of interest because of newly recognized, newly appreciated, and evolving agents. Despite the ability to culture many bacterial pathogens for more than a century, culturing them from water continues to be technologically underdeveloped and has not advanced greatly beyond the application of methods used routinely in clinical diagnostic microbiology (Eaton et al., 1995). While conventional culture and antibiotic sensitivity methods are often suitable for medical diagnostic microbiology applications, these methods are not always suitable for application to the detection of bacteria in water. This is because of the need for sensitive, specific, and efficient detection and quantitation of low levels of bacterial pathogens in water and the ability to distinguish them from nonpathogenic strains of the same or similar genera and species. For some of the recognized enteric bacterial pathogens such as various species of the *Salmonella, Shigella, Campylobacter, and Vibrio* genera, culture methods for their detection in clinical, food, and water samples have changed little beyond attempts to improve recoveries and provide more distinctive recognition using modified preenrichment and enrichment broths and differential and selective agars.

For some other enteric bacterial pathogens, such as the recently appreciated enterohemorrhagic strains of *Escherichia coli* (O157:H7), for example, culturing from water and other samples continues to be a challenge because of the relative abundance of other nonpathogenic strains of *E. coli*. Culturine the target pathogenic strains from water then becomes an exercise in attempting to select for their growth based on distinctive biochemical or other properties that would facilitate their separation from the other nontarget strains. In the case of *E. coli* O157:H7, for example, it can be separated from other E. *coli* strains by its inability to ferment sorbitol. Therefore, its detection is facilitated by using a modification of the standard MacConkey agar as the differential and selective medium by including sorbitol in it. On sorbitol MacConkey agar, *E. coli* O157:H7 colonies appear atypical because sorbitol is not fermented. However, such colonies must be further confirmed by serological or other methods to confirm their identity *as E. coli* O157:H7.

Other waterborne pathogenic bacteria for which culture methods remain underdeveloped and inadequate are those for *Yersinia enterocolitica, Aeromonas hydrophila* and other *Aeromonas* species, *Helicobacter pylori, Legionella* species, and *Mycobacterium avium-intracellulare*. These bacteria are still difficult to reliably culture using currently available media and methods because their growth is inefficient (low plating efficiency), growth rates are slow, and they are often overgrown by other nontarget bacteria. Efforts to culture some of these bacteria include the use of antibiotics as well as physical (heat) and chemical (acid) treatments to reduce or eliminate nontarget bacteria. Even when these bacteria are cultured, they often must be separated or distinguished from other, nontarget bacteria that were also cultured from the sample. In some cases, it is impossible to distinguish nonpathogenic strains from pathogenic strains of the same bacterial genus and species unless advanced immunochemical, nucleic acid, or bioassay methods are used to detect specific antigens, genes, or activities found only in the pathogenic strains of the bacterium. For example, in recent efforts to detect potentially pathogenic *Aeromonas* species in water and food, isolates were tested for cytotoxins by cell culture and PCR assays, enterotoxins by PCR assays, and invasiveness in cell cultures (Granum et al., 1998). All

Aeromonas hydrophila strains, as well as two *A. trota* strains and the single *A. veronii* isolate, produced and secreted cytotoxins at 37°C; one *A. schubertii strain* and one *A. caviae* strain were invasive. The ability to detect specific virulence factors in water isolates of *Aeromonas* species helps elucidate their possible role in waterborne disease.

Detection of Stressed, Injured, and Viable-But-Nonculturable (VBNC) Bacteria

Studies over the past several decades demonstrate that many waterborne bacterial pathogens and indicators are physiologically altered such that they are not efficiently cultured using standard selective and differential media (Ray, 1989; Colwell and Grimes, 1998). This results in considerable underestimation of the hue concentrations of these bacteria in water and therefore underestimation of their risks to human health. It is contended that stressed, injured, and VBNC bacteria are still fully infectious for humans and other animal hosts, although there is disagreement on this matter. Some studies report human and animal experimental infection by VBNC or injured bacteria, and other studies report no animal infectivity by such cells. Despite disagreement about the public health significance of VBNC, injured, and stressed bacteria, a number of experimental procedures clearly demonstrate that the number of culturable cells in a population of VBNC, injured, or stressed bacteria can be increased using modified assay methods. These methods include the use of nonselective media (yeast extract, nonselective broth, or agar media), less selective media (containing fewer or reduced concentrations of inhibitory agents), and other, less stressful culture conditions (such as, lower incubation temperatures, optimum pH levels, optimum concentrations of salts and nutrients, etc.). Despite evidence that such injury repair and resuscitation methods improve the detection of viable and potentially cultural bacteria, these methods are rarely used to detect pathogens in drinking water. Estimates of the occurrence and risks from pathogenic bacteria in water would be improved if injury repair and resuscitation methods were more widely used for detection in water.

Detection of Viral Pathogens by Culture

As obligate intracellular parasites, many enteric viruses can be propagated or cultured in susceptible hosts of either whole animals or mammalian cells grown in culture (Payment and Trudel, 1994; Payment, 1997). Some enteric viruses can be grown in experimental animals, such as mice (certain enteroviruses, adenoviruses, reoviruses), pigs (rotaviruses and hepatitis E virus), or subhuman primates (hepatitis A and E viruses and rotaviruses). However, experimental animals are almost never used for enteric virus detection in water because of high costs, technical demands, and ethical considerations of animal rights. Some enteric viruses are readily cultured in susceptible

mammalian host cells, and cell culture techniques for their cultivation have been available for nearly 50 years. Some viruses, such as certain enteroviruses, reoviruses, adenoviruses, and astroviruses, will propagate in susceptible host cell cultures and produce morphologically distinct cytopathogenic effects (CPEs). Other viruses, including some enteroviruses, reoviruses, adenoviruses, rotaviruses, astroviruses, and hepatitis A virus, grow poorly or slowly in cell cultures and produce little or no CPE. Detection of these viruses requires the use of additional analytical techniques directed at detecting viral antigens (immunofluorescence, immunoenzyme, and radioimmune assays) or nucleic acids (nucleic acid hybridization and amplification assays). Other viruses, such as certain enteroviruses, caliciviruses, parvoviruses, coronaviruses, picobirnaviruses, and hepatitis E virus, cannot be propagated in any known cell cultures. Such viruses will not be detected in water unless sensitive and specific analytical methods, such as nucleic acid amplification by PCR or reverse transcription (RT)-PCR, are applied directly to concentrated samples.

Assays of viruses in cell cultures can be quantified using quantal or enumerative methods. In quantal methods different volumes (or dilutions) of sample are inoculated into replicate hosts (cell cultures or animals) and the numbers of infected (positive) and negative (uninfected) hosts for each volume are scored to calculate a most probable number (MPN), 50 percent tissue culture infectious dose ($TCID_{50}$), or other expression of concentration. Enumerative methods are typically done by plaque assays in cell cultures where virus infection of inoculated cells is confined by the presence of solidified (agar-containing) medium so that the viruses can infect only adjacent cells. This results in the formation of localized areas or lesions of infection and host cell lysis called plaques, and each plaque is assumed to have originated from a single infectious virus. Virus concentrations are expressed as plaque-forming units, analogous to colony-forming units for bacteria on solid media.

Detection of Protozoan Parasites by Culture

The environmental forms of some protozoan parasites, such as spores, cysts and oocysts, can be cultured on susceptible host cells. Cysts of the free-living ameba, such as *Naegleria* spp. and *Acanthamoeba* spp., can be excysted and cultured on lawns of host bacteria, such *as E. coli*, on nonnutrient agar, on which they form local lesions that can be directly counted. Spores of some of the important human microsporidia, such as *Encephalitozoon intestinalis and Enterocytozoon bieneusi*, and oocysts of *Cryptosporidium parvum* can be cultured on mammalian host cells where spores germinate or oocysts excyst and active stages of the organisms can proliferate in the cells (Arrowood et al., 1994; Upton et al., 1994; Visvesvara et al., 1995a,b). The living stages can be detected (after immunofluorescent or other staining) and quantified by scoring positive and negative microscope fields or cell areas (slide wells) or by counting the numbers of discrete living stages of groups (loci) of them. Concentrations can be expressed as an MPN or in some other unit, such as numbers of live stages. Detection is also possible by PCR, immunoblotting, and electron microscopy. For other waterborne parasites, such as *Giardia lamblia and Cyclospora*

cayatenensis, culture from the environmental stage (the cyst or oocyst, respectively) recovered in a water sample is still not possible.

Combined Cell Culture and Nucleic Acid Detection and Amplification of Waterborne Pathogens

For some enteric viruses and protozoan parasites, detection and quantitation of the infectious pathogens are improved by using the combined techniques of cell culture and then nucleic acid hybridization and/or amplification. The sample is inoculated into susceptible host cell cultures, and the cultures are incubated to allow the viruses or parasites to infect the cells and proliferate. After an incubation period sufficient to produce enough nucleic acid for direct detection or further amplification, the nucleic acid is denatured and fixed either in situ or after extraction. Then the target nucleic acid is detected by hybridization with a gene probe either directly or after further amplification by PCR or RT-PCR. These methods facilitate the detection of infectious but noncytopathogenic viral and protozoan pathogens that are capable of proliferating in cell cultures. Combining cell culture and PCR or RT-PCR also reduces the incubation time to detect pathogen nucleic acid, because even small amounts of the target nucleic acid produced in culture can be rapidly and specifically amplified in vitro using these techniques. Combined cell culture and nucleic acid detection has been used to detect HAV and other fastidious enteric viruses in water (Shieh et al., 1991; Reynolds et al., 1996; Sobsey et al., 1996). Recently, a combination of cell culture and PCR was used successfully to detect *Cryptosporidium parvum* recovered from water using centrifugation and immunomagnetic separation methods (Di Giovanni et al., 1998).

Detection of Waterborne Pathogens by Viability or Activity Assays

Bacterial pathogens concentrated and purified from water can be assayed for viability or activity by combining microscopic examination with chemical treatments to detect activity or "viability." These chemical treatments include measurements of enzymatic activities, such as dehydrogenase, esterase, protease, lipase, and amylase. An example is tetrazolium dye reduction by bacteria, such as reduction of 2-(*p*-iodophenyl)-3-(*p*-nitrophenyl)-5-phenyltetrazolium chloride, which measures dehydrogenase activity. Reduction of tetrazolium dye leads to precipitation of reduced products in the bacterial cells that are seen microscopically as dark crystals. Another assay of viable gram-negative bacteria is the cell elongation assay using nalidixic acid ("Kogure" method). Nalidixic acid inhibits RNA synthesis in live gram-negative cells, thereby causing them to elongate and be distinguished from dead cells.

Application of these methods to pathogens in water often involves combinations of methods, such as combining an activity measurement with an

immunochemical assay (for specific bacteria). An example of this approach combines fluorescent antibody (FA) with tetrazolium dye reduction and involves looking for reduced crystals in cells specifically stained with fluorescent antibodies. For example, Pyle et al. (1995) combined incubation using cyanoditolyl tetrazolium chloride (CTC) to detect respiratory activity with a modified FA technique, for the enumeration of viable *E. coli* O157:H7 in water in three to four hours. Bacteria were captured by filtration on nonfluorescent polycarbonate membranes, incubated on absorbent pads saturated with CTC medium, and reacted with a specific antibody conjugated with fluorescein isothiocyanate. The membrane filters were examined by epifluorescence microscopy with optical filters permitting concurrent visualization of fluorescent red-orange CTC-formazan crystals in respiring cells that were also stained fluorescent apple-green with specific FA.

"Viability" or activity assays for protozoan cysts and oocysts include reaction with DAPI (the fluorogenic stain 4',6-diamidino-2-phenylindole), which is taken up by live oocysts and propidium iodide (PI), which is taken up by dead oocysts. Viable *Cryptosporidium oocysts are* DAPI positive and PI negative, and nonviable oocysts are DAPI negative and PI positive. Other fluorogenic compounds that react specifically with targets in "viable" cells also have been used to detect bacteria cells and protozoan cysts and oocysts. Another activity or viability approach is based on detecting a nucleic acid target consistent with viability in the ribosomal RNA, messenger RNA, or genomic RNA of the pathogen. Detection of pathogen nucleic acid by fluorescent in situ hybridization has been applied to detecting bacteria, protozoan cysts, and oocysts, as well as viruses in infected cell cultures. Nucleic acid methods for pathogen detection, quantitation and characterization in water are described in the next section.

Detection of Waterborne Pathogens by Nucleic Acid Methods

Methods for nucleic acid cloning, synthesis, hybridization, sequencing, and other analyses now make it possible to detect pathogens in environmental samples. However, the application of direct nucleic acid hybridization using cDNA or RNA ("gene") probes to detect and quantify environmental pathogens is inadequate owing to (1) high detection limits (about 100 to 1000 generate targets), (2) large sample volumes that are impractical for most hybridization protocols without further pathogen concentration, (3) hybridization reaction failures (false negatives) and ambiguities (false positives) due to sample-related interferences and nonspecific reactions, and (4) uncertainties about whether positive reactions are truly indicative of infectious pathogens.

Some of the limitations of direct nucleic acid hybridization for pathogen detection in environmental samples are overcome by first culturing bacteria and by inoculating viruses and protozoans into cell cultures for replication prior to gene probing. This approach, which was introduced in a previous section of this paper, has several advantages. Allowing pathogens to multiply amplifies target viral nucleic acids prior to extraction and gene probing and thereby facilitates detection. Culturing also helps to accommodate environmental sample or sample concentrate volumes, which are much larger than the volumes accommodated by direct gene probing. In addition, inoculating samples for culture dilutes and

facilitates the removal of sample-related interfering components. Furthermore, because the pathogens have the opportunity to multiply, it becomes possible to relate gene probe detection to pathogen infectivity. Despite these advantages, this approach still relies on culturing and so it cannot be applied to noncultivable pathogens.

Nucleic Acid Amplification

With the recent development of PCR and other in vitro enzymatic amplification techniques for target gene sequences, the direct detection of low levels of human pathogens in environmental samples becomes more plausible, practical, and economically feasible than ever before (Persing et al., 1993; Dieffenbach and Dveksler, 1995; Persing, 1996; Sobsey et al., 1996). For example, methods to detect enteric viruses in water by nucleic acid amplification using PCR and RT-PCR have advanced in recent years to the point where they have been successfully applied to investigating waterborne outbreaks caused by nonculturable human caliciviruses viruses (Bellar et al., 1997) and surveying for enteric viruses in drinking water sources (Abbaszadegan et al., 1998). Despite these advances and successes, a variety of strategic issues and technical problems must be further addressed in order for PCR and related nucleic acid amplification and detection methods to become practical and reliable for the direct detection of emerging pathogens in environmental samples.

There are several essential steps in the development and application of PCR, other related enzymatic amplification techniques, and nucleic acid hybridization techniques such as oligonucleotide probing for successful detection of human pathogens in environmental samples. These key steps are (1) identification and selection of oligonucleotide primers and hybridization probes for target genomic sequences; (2) testing of selected primers and probes for sensitivity, specificity and selectivity; (3) further purification and concentration of the pathogens in environmental sample concentrates to enable efficient and reliable enzymatic amplification of low numbers of target genomic sequences; (4) testing of the methods for their applicability to natural pathogen strains and actual field samples; and (5) verifying that PCR amplification and oligonucleotide probing detect human pathogens that are potentially infectious and therefore pose a risk to human health.

Selection of oligonucleotide primers and probes for target pathogens requires that sequence data be available. Such data are now available for some waterborne pathogens, and the database is increasing for a variety of emerging waterborne pathogens. However, these data are not comprehensive for all pathogens of concern, and they are still limited for some of the epidemiologically most important pathogens, such as the human caliciviruses and *Cryptosporidium parvum*. Proper selection of PCR primers and oligonucleotide probes requires detailed knowledge of the genomic organization and function and the nucleotide sequences of the target pathogens. Of particular importance are the type and

function of nucleic acid target (genome, chromosomal gene, extrachromosomal gene, rRNA, mRNA, etc.), its length (size), and location, and the extent to which **its** sequence is related to that of other, nontarget but genetically related microbes. It is essential to select oligonucleotide primers and probes having the following characteristics: (1) appropriate length, (2) desired sequence composition for specificity and selectivity, and (3) appropriate melting and annealing temperatures and other physical characteristics to prevent the formation of undesirable secondary structures, primer dimers, other primer interactions, and other artifacts that would interfere with RT, PCR, or nucleic acid hybridization.

Because of the large number of different waterborne pathogens, efforts have been made to amplify as many as possible using a single primer pair for those belonging to a genetically related taxonomic group. For the human enteric viruses, pan-specific primers and oligonucleotide probes have been developed for the human enteroviruses, group A rotaviruses, human caliciviruses, and adenoviruses. However, additional studies are needed to verify that these primers and probes do not amplify or detect similar or identical nucleotide sequences in the genomes of nonhuman animal viruses belonging to the same taxonomic groups. If so, alternative genomic sequences having greater specificity for the human pathogenic strains of these taxonomic groups must be selected. If this is not possible, additional analytical methods, such as RFLP or nucleotide sequencing, must be applied to the amplicons in order to conclusively identify them as being from the strain or type target microbe that infects and poses a health risk to humans.

PCR and RT-PCR detection of specific pathogens in a broader taxonomic group is achievable by several different methods. One method involves the use of additional primers internal to the group-specific primers that would amplify subsequently from the initially amplified cDNA ("nested amplification"). Another approach is hybridization using highly specific oligoprobes that would hybridize only with amplicons from a single pathogen type or strain. Selected oligonucleotide primers and probes must be tested for specificity and selectivity. It must be verified that primers have the ability to amplify a DNA of correct molecular weight and that the amplicon will hybridize with a specific nucleic acid probe (e.g., oligoprobe). Furthermore, it must be verified that the probes are nonreactive with the nucleic acid of nontarget microbes.

The sensitivities or lower detection limits of PCR or other nucleic acid amplification methods for target pathogens can be tested by determining the greatest dilution of a known quantified pathogen suspension that can be successfully amplified. The same sample is also quantified by infectivity, microscopic enumeration of the numbers of microbes or other methods so that the endpoint PCR titer can be compared to these other titers. Other approaches to quantifying nucleic acid amplification by PCR and RT-PCR have been described by Freeman et al. (1999). The quantification methods should include determining if there are materials in the sample interfering with PCR amplification and should estimate the concentration of target microbes in the sample. This can be done by measuring or quantifying the amount of amplicon (DNA product) produced under defined PCR or RT-PCR conditions using electrochemoluminescence, immunoassays, fluorescence signal increase (using a fluorescent primer that

incorporates into the amplicon), fluorescent signal decrease (by loss of fluorescent signal upon incorporation of the fluorescent primer into the amplicon), or other chemical methods. Also, the amount of target DNA amplified in the sample can be compared to the amount of target DNA amplified under the same conditions from a positive control sample containing a known amount of nucleic acid from the same target microbe suspended in a noninhibitory solution. Using this approach, however, it is not possible to determine if lack of or low amplification of the target is due to inhibition by sample constituents, to few target nucleic acids being present, or a combination of both.

Another approach to quantifying PCR or RT-PCR and determining the effects of sample-related inhibitors is to add a known amount of an internal nucleic acid standard as a positive control into the sample. Adding specific amounts of positive control nucleic acid sequences in the reaction mixture and determining the extent of amplification of this target (which differs from the true target) makes it possible to quantify both sample inhibition and the amount of actual target nucleic acid in the sample. This approach has been applied to the detection of human caliciviruses by RT-PCR (Schwab et al., 1997, 1998).

Sample Preparation for Pathogen Detection in Water by Nucleic Acid Methods

Typical environmental sample concentrates for pathogens are too large in volume (10 to 50 ml) and too contaminated with extraneous interfering constituents for reliable and sensitive enzymatic amplification of target pathogen genome sequences, especially at the low levels (low target nucleic acid numbers) typically found in most water samples. Therefore, in some previous studies target pathogen nucleic acid has been isolated from environmental samples by standard techniques of nucleic acid extraction, purification, and concentration, such as proteinase K digestion, phenol-chloroform extraction, and ethanol precipitation. However, these methods are cumbersome, laborious, and often inefficient, thus leading to poor recoveries and inadequate detection limits. Furthermore, disruption of pathogens to liberate target nucleic acid at an early stage of sample concentration and purification makes it impossible to compare pathogen detection by nucleic acid amplification to pathogen detection by other methods, such as infectivity or particle count.

Preferred sample cleanup and concentration strategies maintain pathogen integrity as long as possible prior to enzymatic amplification. The goal is to reduce the sample volume to <100 mL, remove interfering and inhibitory substances (e.g., particulates, salts, proteins, lipids, carbohydrates, and natural organic matter) and also place the pathogens in an aqueous medium compatible with enzymatic amplification as well as the other quantitation procedures, such as infectivity or particle count. For PCR or RT-PCR, the target nucleic acid is then liberated from the purified and concentrated pathogens by one or more of several physical methods, such as heat, freeze-thaw, sonication and bead beating, and/or

by other, chemical extraction methods as a final or near-final treatment step. This makes it possible to compare PCR endpoint titers with infectivity assay or particle count titers without intervening or additional purification and concentration steps that could cause differential losses.

Candidate chemical purification and concentration methods for subsequent nucleic acid amplification and some other pathogen detection methods include precipitation (e.g., polyethylene glycol for viruses); chromatography (e.g., Sephadex gels in spin-columns); chelation of metals (using EDTA, EGTA, "Chelex," etc.); ultrafiltration using high (e.g., 100,000 daltons) molecular weight cutoff filters; organic solvent (e.g., chloroform, fluorocarbon) extraction; detergent (e.g., Tweens and other nonionic detergents) treatment; enzymatic digestion (e.g., proteases, amylases, lipases, and nucleases); and antibody (immunoaffinity) capture on paramagnetic beads (immunomagnetic separation). Immunoaffinity capture and purification of pathogens as antigens is a cleanup and concentration option that has been successfully applied to some viruses, bacteria, and parasites. However, it is not applicable to some pathogens because of the lack of reagent quality antisera or the antigenic diversity of a large pathogen group lacking a common antigen (and hence requiring many antisera).

Overall, nucleic acid amplification by PCR or RT-PCR and hybridization using oligonucleotide probes is a specific, selective, and sensitive approach to the detection of pathogens in environmental samples. Oligonucleotide primers and probes can be selected to detect broad pathogen groups, such as the enteroviruses and Salmonella or specific pathogens, such as hepatitis A virus. In particular these methods can be used to detect fastidious pathogens, such as human caliciviruses and *Cyclospora cayatenensis*. Under optimized conditions method sensitivity or detection limit is less than one infectious unit and in principle as little as one target gene sequence. Methods have been developed and evaluated to concentrate and purify target pathogens from environmental samples such as water for successful detection by nucleic acid amplification and oligoprobe hybridization. These methods have been successfully applied to the detection of viral, bacterial, and protozoan pathogens in field samples of water. However, the inability of most of these nucleic acid methods to conclusively detect only the infectious pathogens is a limitation that remains to be overcome.

Microscopic and Analytical Imaging Methods to Detect Waterborne Pathogens

Microscopic methods include ordinary (light) microscopy (bright-field and dark-field), phase contrast, differential contrast, fluorescence, laser scanning, video, and other forms of microscopic and image analysis (Lawrence et al., 1997). These methods are not effective for viruses or other very small (ultra-small) agents, and some are not effective for very transparent agents unless the microbes are stained. The detection of internal and external structural features (e.g., organelles and reproductive units) is improved by various colored stains, fluorescent stains, advanced optical systems (phase contrast, Nomarski interference contrast, differential interference, and laser scanning), and the use of imaging by sensitive charge-coupled device cameras. For example, phase contrast and differential interference contrast microscopy are used to visualize

the internal structures of *Giardia lamblia and Cryptosporidium parvum* isolated from water. This helps distinguish them from algae and other particles of similar size and shape. Fluorescent (ultraviolet light) microscopy methods are useful for transparent cells or other cells or organelles that are difficult to detect. The cells are reacted with a fluorochrome that interacts with a cellular components or macromolecules, which are then detected by ultraviolet light microscopy. Capturing microscopic images by digital methods for image analysis using computers has greatly advanced the capabilities to detect, quantify, and characterize pathogens and other microbes in environmental samples. For example, computer-assisted laser scanning and video microscopy have been applied to the analysis of *Cryptosporidium parvum* oocysts in environmental samples (Anguish and Ghiorse, 1997). Another technology employing advanced image analyses to detect, quantify and characterize pathogens in water is laser-based flow cytometry plus fluorescent cell sorting, which are methods that have been previously described above.

Immunoassays to Detect Pathogens in Water

Immunofluorescent detection by microscopy or other methods is a specific and potentially powerful way to detect pathogens and other microbes in water if there are enough target pathogens in the sample for detection (McDermott, 1997). Antibodies directed against antigens of the target pathogen can be labeled (conjugated) with a fluorochrome or fluorescent dye (e.g., fluorescein isothiocyanate or another fluorochrome) for direct immunofluorescence. These fluorescent antibodies are reacted with the target microbe, and then the microbe preparation is washed to remove meted fluorescent antibody. The sample is then examined for the target microbe by ultraviolet light microscopy or another analytical method to detect the immunofluorescent signal (e.g., fluorometry). Alternatively, secondary fluorochrome-labeled antibodies directed against the primary antibodies (now serving as antigens) of the species of animal in which the antibodies against the microbe were raised can be used in an indirect immunofluorescence assay. The target microbial antigen is reacted initially with a specific antibody, and then the resulting antigen-antibody complex is reacted with fluorochrome-labeled antispecies antibody to provide the signal for immunofluorescent detection.

Enzyme immunoassays employ enzyme-conjugated antibodies directed against target pathogens. The antigen-antibody complex is detected and quantified by the ability of the enzyme to react with a substrate that typically produces either a colored product for colorimetry or emits light for luminometry. Enzyme immunoassays often are done on a solid phase to which the pathogen antigens have been applied, such as a membrane filter or the bottom of a microtiter plate well. To provide increased specificity and to facilitate separation of the target microbial antigen from other particles and solutes in the sample, the target antigen can be captured on the solid phase using a specific antibody

("sandwich" or immunocapture assay format). As with other immunoassays, enzyme immunoassays can be direct (enzyme-conjugated, primary antibody against antigens of the target microbe) or indirect (enzyme-conjugated, antispecies secondary antibody). Studies have repeatedly shown that solid-phase enzyme immunoassays generally are too insensitive for direct detection of microbial pathogens in water, as they require a minimum of 10,000 to 100,000 target microbes (or their antigens) for detection. In most situations drinking water and its sources rarely contain high enough levels of most target pathogens for direct immnoenzymatic detection. However, enzyme immunoassays also have been combined with methods to propagate target pathogens by various culture methods, thereby increasing their numbers for immnoenzymatic detection. For example, cell culture infectivity has been used to propagate noncytopathogenic viral pathogens and thereby enhance their detection (Payment, 1997).

Agglutination methods are used to detect pathogens by combining dispersed cells, viruses, or other forms of pathogen antigens with antibodies (on a slide, for example) and allowing for antigen-antibody reactions to produce agglutination (clumping) that can be scored as negative or various degrees of positive (strong, medium, or weak). One modification is latex bead agglutination in which antibodies against a specific microbial antigen (especially nonparticulate or "soluble" antigen) are attached to latex beads. The beads are reacted with the sample. If the sample contains the specific antigen, agglutination occurs by the reaction of antigens with antibodies on the beads resulting in the beads clumping together (agglutinating). As with enzyme immunoassays, agglutination tests are too insensitive to directly detect and quantify most waterborne pathogens in drinking water and other aquatic samples. The target microbes must first be propagated in order to obtain a sufficient number of them or a sufficient amount of antigen to detect and antigenically characterize them by agglutination methods.

Signature Biolipid and Other Biochemical Detection Methods

Some pathogens are detectable became they contain distinctive macromolecules or biochemicals that aid in their identification and detection. These include cell wall component assays for lipopolysaccharides, muramic acids, and assays for signature biolipids (White, 1995). Signature lipid biomarker analysis is based on the use of techniques such as liquid extraction and thin layer chromatography to separate and purify the microbial lipids from the microbes in the environmental sample. This is followed by quantitative analysis using gas chromatography/mass spectrometry, infrared spectroscopy, and nuclear magnetic resonance spectroscopy. Using these techniques it has been shown that *Cryptosporidium parvum* contains a characteristic phosphatidyl-ethanolamine, that may make it possible to detect this parasite in environmental samples (Schrum et al., 1997).

SUMMARY AND CONCLUSIONS

The identification and detection of microbial contaminants in drinking water must continue to be a high priority for assessing the risks from and managing the microbial quality of drinking water supplies. The essential information needs for quantitative microbial risk assessment can be applied to detecting, identifying, and characterizing microbial contaminants in drinking water supplies. The recognition of new waterborne pathogens as well as re-emerging ones posing increased risks due to newly acquired virulence properties and other traits requires further improvement of waterborne pathogen detection methods and better use of the advanced analytical methods now available. There must be continued efforts to improve and apply the methods for waterborne pathogen recovery, concentration, purification, separation from interfering materials, detection, isolation, assay, and characterization.

Methods for waterborne pathogen recovery and concentration by centrifugation, filtration and precipitation can be further improved and newly developed methods can be more widely applied. Purification and separation methods, such as immunomagnetic capture, chromatography (by ion exchange, adsorption, chelation, and size exclusion) and chemical treatment (with enzymes, detergents, and organic solvents) are advancing and becoming more widely used for waterborne pathogens.

Methods to assay, quantify, and characterize waterborne pathogens are advancing, but greater efforts are needed to determine pathogen infectivity and viability. Culture methods for viruses, bacteria, and parasites are preferred because they detect and quantify infectivity, which is the most relevant unit of measure in terms of health risk. For bacterial pathogens in water, better methods to detect infectivity are needed and existing methods to detect infectious bacteria must be more widely used. The detection of stressed, injured, and viable but nonculturable bacteria in water continues to be a technological challenge, and available methods to detect such bacterial pathogens in water continue to be underutilized. Detection and quantitation of waterborne vital pathogens by cell culture infectivity is possible for some of them, but many of the important waterborne enteric viruses are still not culturable. The combined use of cell culture and nucleic acid amplification (PCR, RT-PCR, etc.) and hybridization has improved the detection of some of the more fastidious waterborne viral pathogens, but these methods must become more widely used. Recently, it has become possible to detect and quantify the infectivity of some of the important waterborne parasites (*Cryptosporidium parvum* and some microsporidia) by cell culture methods. However, these methods require further refinement and verification and they have yet to be extensively applied in occurrence studies or exposure assessments.

Waterborne pathogen detection and quantitation by nucleic acid amplification and hybridization methods has advanced greatly in the last decade, has been successfully applied to pathogen detection in field samples, and appears to be a most promising technology for the future. However, further

improvements in these nucleic acid amplification and hybridization methods are needed to reliably distinguish infectious from non-infectious waterborne pathogens. The combination of these nucleic acid methods with culture methods appears to be the most promising approach for sensitive and specific detection and quantitation of infectious waterborne pathogens. The methods to purify and concentrate the target microbes and their nucleic acids from water by various physical and chemical means have advanced greatly in recent years. However, these methods need further improvement, consolidation, and simplification in order to achieve reliable, sensitive, and specific detection and quantitation of the target pathogens recovered and concentrated from water.

Viability and activity methods to detect and quantify waterborne pathogens also continue to improve, and they have been applied to field samples of water on a limited basis. However, there continues to be uncertainty about the ability of many of these methods to detect truly infectious waterborne pathogens, and many of the existing methods are cumbersome, tedious, and unable to detect low concentrations of target pathogens in water. Similarly, microscopy, analytical imaging, immunoassays, and biochemical analyses continue to advance as methods to detect, identify, and characterize pathogens in water. However, these methods lack sensitivity for direct detection and may not distinguish infectious from non-infectious organisms. The usefulness of these methods is improved when they are applied to pathogens that have been concentrated and purified from water or have been enriched in numbers by culture methods. Advances continue to be made in immunological, biochemical, nucleic acid, and bioassay methods to characterize potentially waterborne pathogens. The bases for and mechanisms of virulence and pathogenicity of these pathogens are becoming better understood at the biochemical, immunological, and genetic level. Such advances provide the needed tools for improved detection and identification of these microbes in water, understanding the role of the aquatic environment in their persistence, evolution, and selection, and better characterization of the human health risks from these waterborne pathogens.

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10

Biofilms in Drinking Water Distribution Systems: Significance and Control

Mark W. LeChevallier

A biofilm is a collection of organic and inorganic, living and dead material collected on a surface. It may be a complete film or, more commonly in water systems, small patches on pipe surfaces. Biofilms in drinking water pipe networks can be responsible for a wide range of water quality and operational problems. Biofilms can be responsible for loss of distribution system disinfectant residuals, increased bacterial levels, reduction of dissolved oxygen, taste and odor changes, red or black water problems due to iron or sulfate-reducing bacteria, microbial-influenced corrosion, hydraulic roughness, and reduced materials life (Characklis and Marshal, 1990).

Microorganisms in biofilms can include bacteria (including coccoid round, rod-shaped, filamentous, and appendaged bacteria), fungi, and higher organisms like nematodes, larvae, and Crustacea. Recently, researchers have shown that viruses and parasites like *Cryptosporidium can* be trapped in biofilms. Although viruses and *Cryptosporidium* do not grow in a biofilm, they can attach to biofilms after a contamination event. Therefore, it is important to thoroughly flush the distribution system to remove these organisms following a contamination event.

A primary reason that many water utilities become concerned with biofilms in drinking water systems is due to growth of coliform bacteria in the pipe network. In 1993 in the United States alone, nearly 4,400 water systems affecting 21 million people violated drinking water standards for total coliform bacteria (Pontius, 1995). Similar trends were noted for 1994 and 1995, with over 12,000 systems exceeding accepted coliform levels. Of concern are the nearly 2,000 systems every quarter that are significant noncompliers and repeatedly detect coliform bacteria in finished drinking water. Although some of these systems experience coliform occurrences due to cross connections and other operational defects, a large proportion of the systems can trace their problems to regrowth of the bacteria in distribution system biofilms.

FACTORS RELATED TO COLIFORM OCCURRENCES

Recent studies have examined data from over 90 water systems (see Figure 10-1) to determine the factors that contribute to the occurrence of coliform bacteria in drinking water (LeChevallier et al., 1996; Volk et al., 1996). These studies have shown that the occurrence of coliform bacteria can be related to the following factors: filtration, temperature, disinfectant type and residual, assimilable organic carbon (AOC) level, corrosion control, and pipe material selection.

Filtration

Four unfiltered surface water systems were included in one study (LeChevallier et al., 1996) and accounted for 26.6 percent of the total number of bacterial samples collected but 64.3 percent (1,013 of 1,576) of the positive coliform samples. Although the results do not suggest that treatment was inadequate (e.g., coliforms were not related to breakthrough of treatment barriers), the data suggested that filtration may be an important factor in preventing coliform regrowth. Following the study, one of the systems installed filtration and distribution system coliform levels were reduced by a factor of three over the following 18-month interval.

Temperature

On average, the occurrence of coliform bacteria was significantly higher when water temperatures were >15ºC (See Figure 10-2). However, the minimum temperature at which microbial activity was observed varied from system to system. Systems that typically experienced cold water had increases in coliform occurrences when water temperatures ranged near 10ºC. The strains of coliform bacteria in these systems may be better adapted to grow at lower temperatures (psychrophiles).

Disinfectant Residual and Disinfectant Level

For filtered systems there was a difference between systems that maintained a free chlorine residual and systems that used chloramines. For systems that used free chlorine, 0.97 percent of 33,196 samples contained coliform bacteria, while 0.51 percent of 35,159 samples from chloraminated systems contained coliform bacteria (statistically different at $p < .0001$). The average density of coliform bacteria was 35 times higher in free chlorinated systems as compared to chloraminated water (0.60 colony-forming units CFUs/100 ml for free chlorinated water, compared to 0.017 CFUs/100 ml for

Figure 10-1
Location of study sites.

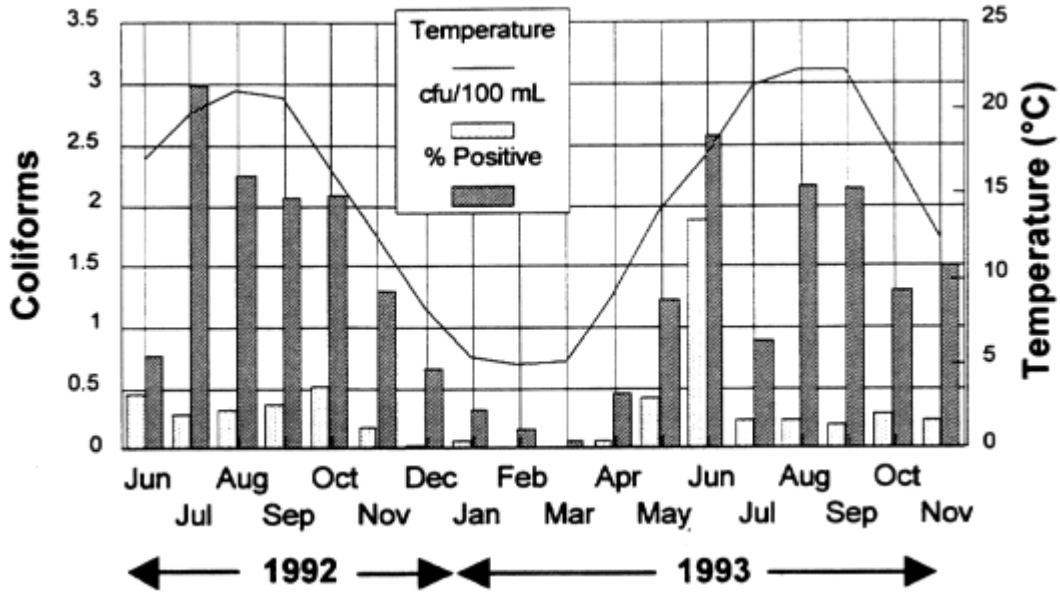

Figure 10-2
Relationship between monthly average water temperature and coliform occurrence.

chloraminated water). Previous research (LeChevallier et al., 1990; LeChevallier, 1991) has hypothesized that chloramines may be able to better penetrate into distribution system biofilms and inactivate attached bacteria. The fact that different disinfectants may interact differently with biofilms can be related to their different mechanisms of action. Free chlorine, for example, is known to react with natural organic matter to form trihalomethanes (Rook, 1974). Chloramines do not form these products to the same degree. Free chlorine attacks the cytoplasmic membrane of gram-negative bacteria to produce a cellular lesion (injury) that results in an increased sensitivity to surfactants (Zaske et al., 1980). Chloramines do not produce the same type of injury as free chlorine, and the chloramine lesion can be reversed with a reducing agent (sodium sulfite) (Watters et al., 1989). The penetration of free chlorine into a biofilm has been modeled and shown to be limited by its fast reaction rate (LeChevallier, 1991; DeBeer et al., 1994). Essentially free chlorine is consumed before it can react with the bacterial components of the film (Chen and Stewart, 1996). Chloramines, on the other hand, are slower reacting and can diffuse into the biofilm and eventually inactivate attached bacteria. This mechanism has been elegantly demonstrated by researchers at Montana State University using an alginate bead model (Chen and Stewart, 1996). Stewart and colleagues (in press) showed that free chlorine effectively did not penetrate alginate beads containing bacterial cells but that chloramines did penetrate into the alginate material and reduced bacterial levels nearly 1 million-fold over a 60-minute interval (2.5 mg/L chloramines, pH 8.9).

The effectiveness of a chloramine residual for controlling coliform occurrences suspected to be the result of biofilm growth in distribution pipelines is shown in Figure 10-3. The system experienced coliform occurrences even when free chlorine residuals averaged between 2 and 2.5 mg/L in the distribution system. Use of m-T7 medium, a technique that recovers injured bacteria (LeChevallier et al., 1983), showed coliform occurrence rates ranged between 10 and 40 percent even during months when coliforms were not recovered on the standard m-Endo medium. Conversion of the disinfectant to chloramines in June 1993 resulted in dramatic decreases in coliform occurrences measured by both m-Endo and m-T7 media, and the bacteria have not been detected in the finished drinking water for the three years following the change (Norton and LeChevallier, 1997).

In addition to the type of disinfectant used, the residual maintained at the end of the distribution system was also associated with coliform occurrences (LeChevallier et al., 1996). Systems that maintained dead-end free chlorine levels <0.2 mg/L, or monochloramine levels <0.5 mg/L, had substantially more coliform occurrences than systems maintaining higher disinfectant residuals. However, systems with high AOC levels needed to maintain high disinfectant residuals to control coliform occurrences (see Figure 10-4). Therefore, maintenance of a disinfectant residual alone did not ensure that treated waters would be free of coliform bacteria.

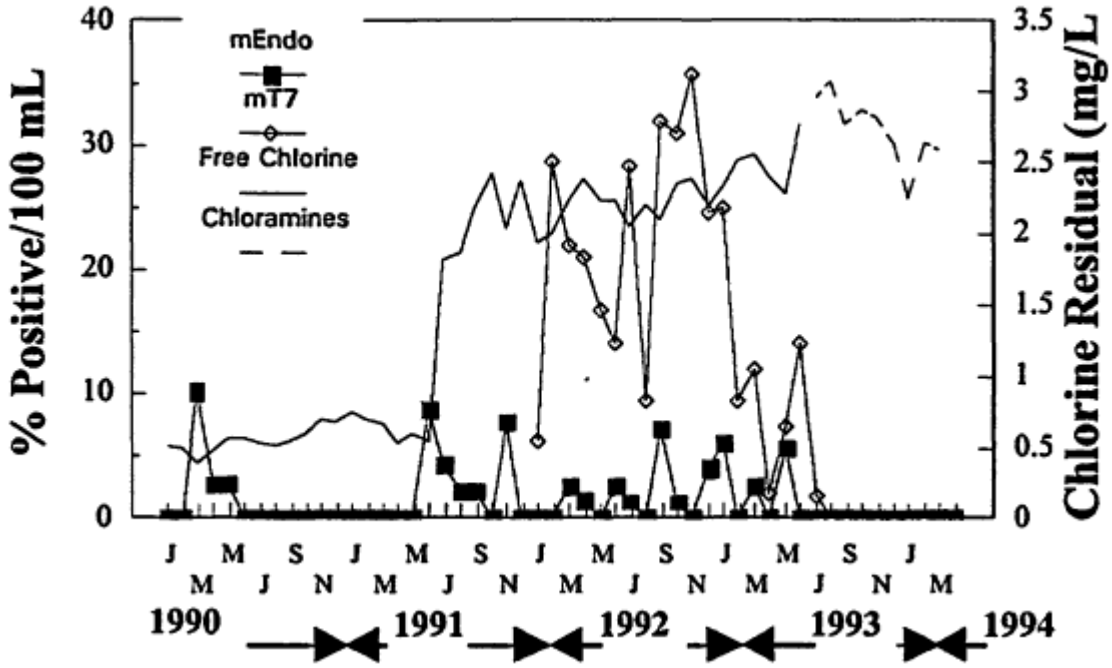

Figure 10-3
Coliform occurrence in a system before and after conversion from chlorine to chloramines.

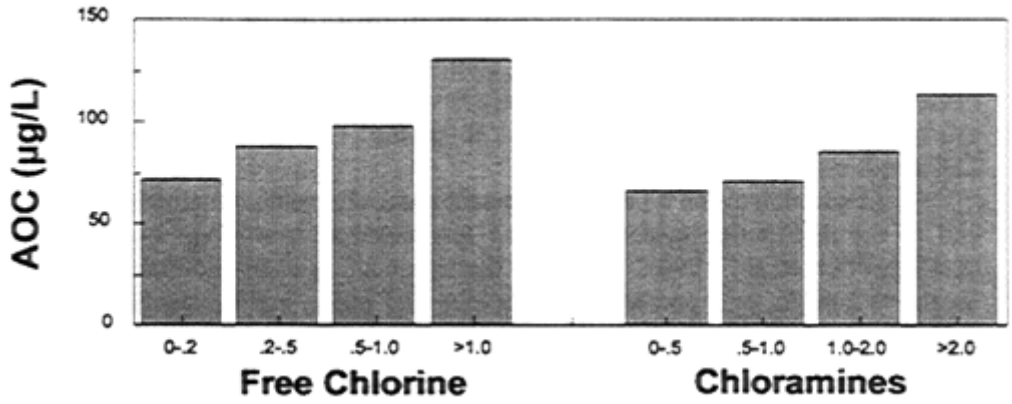

Figure 10-4
Relationship between AOC and distribution system disinfectant residuals.

AOC Level

The combined results from two surveys of AOC levels in North American drinking water systems (LeChevallier et al., 1996; Volk et al. 1996) are shown in Figure 10-5. The levels (summarized as the geometric mean based on 12 to 36 samples) range from 20 to 214 µg/L. The results also indicate that the majority of the total AOC results from the growth of the test organism, *Spirillum* sp. strain NOX. This AOC_{NOX} fraction is influenced by disinfection practices (chlorine, ozone, etc.) and suggests that changes in these practices (i.e., type of disinfectant, point of application, dose) can impact AOC levels in finished drinking water.

High levels of AOC can stimulate bacterial growth in distribution system biofilms (LeChevallier et al., 1996; Volk et al., 1996). On average, free chlorinated systems with AOC levels greater than 100 µg/L had 82 percent more coliform-positive samples, and the coliform densities were 19 times higher than free-chlorinated systems with average AOC levels less than 99 µg/L. However, high levels of AOC alone do not dictate the occurrence of coliform bacteria in drinking water but are only one factor. Figure 10-6 illustrates a decision tree that graphically depicts combinations of threshold values above which the probability of coliform occurrence is increased (Volk et al., 1996). As more of the threshold values are exceeded, the probability of coliform occurrences is increased. Data summarized in Table 10-1 show that the frequency of coliform occurrence was less than 2 percent when no threshold criteria were exceeded and increased to 16 percent when all three criteria were exceeded. The magnitude (number of positive samples per event) also increased with a greater exceedance of threshold criteria. Similar models developed for specific systems have yielded higher predictive probabilities (Volk and Joret, 1992).

TABLE 10-1 Relationship Between Threshold Criteria and Coliform Occurrence

No. Positive Criteria	Total No. of Events	Coliform-Positive Samples	No. of Coliform Episodes	Frequency of Coliform Observation (%)
0	160	3	3	1.9
I	292	18	15	5
2	191	24	16	8.4
3	62	26	10	16

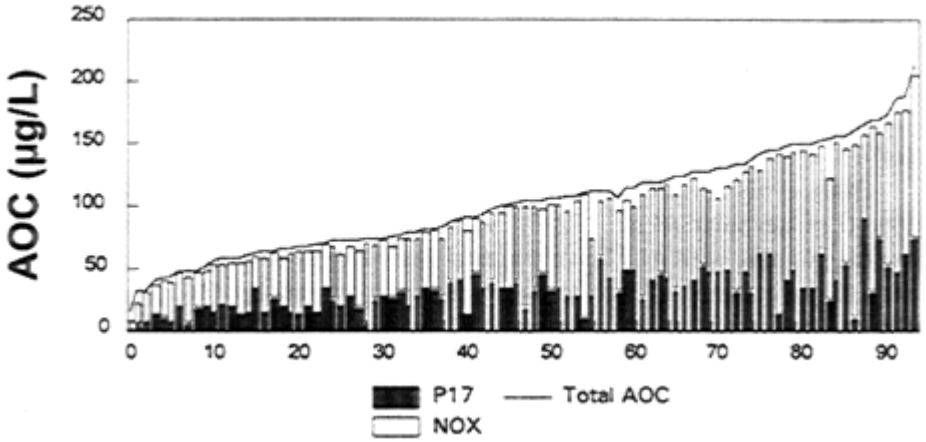

Figure 10-5
AOC levels in 94 North American water systems.

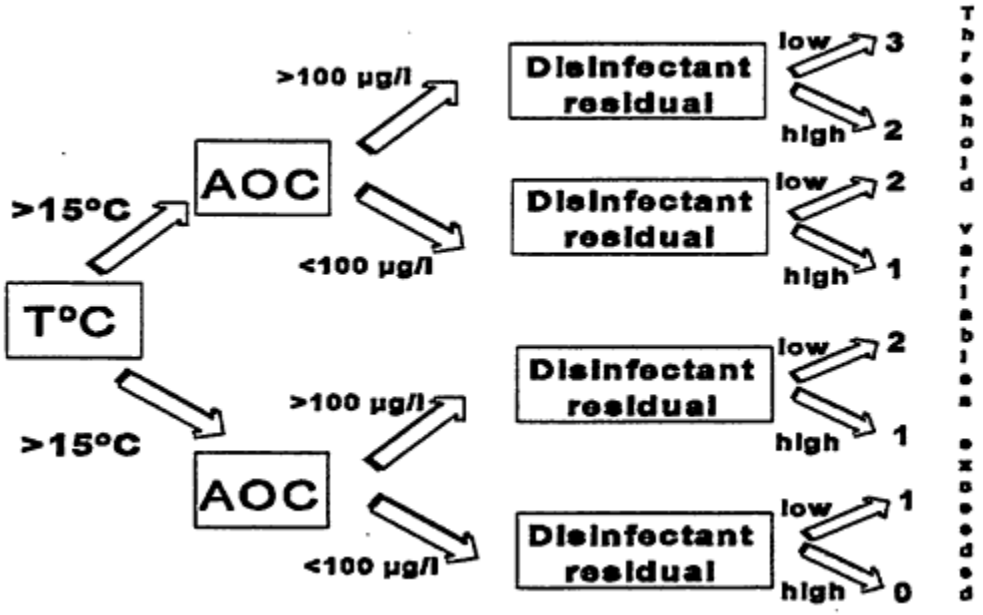

Figure 10-6
Decision tree for coliform occurrences in drinking water.

Corrosion Control and Pipe Materials

Most systems do not measure corrosion rates on a daily basis, so this parameter is difficult to evaluate full-scale. However, recent research has demonstrated that corrosion of iron pipes can influence the effectiveness of chlorine-based disinfectants for inactivation of biofilm bacteria (LeChevallier et al., 1990, 1993). Therefore, the choice of pipe material and the accumulation of corrosion products can dramatically impact the ability to control the effects of biofilms in drinking water systems.

Figure 10-7 shows average monthly corrosion rates (in milles "thousandth of an inch" per year) from a system in Illinois. The conventional plant effluent corrosion rate showed marked seasonal variations. Corrosion rates were the highest during the summer months when, traditionally, the incidence of coliform occurrences are the highest (Figure 10-2). Similar seasonal variations have been observed in other systems (Norton and LeChevallier, 1997).

This variation in corrosion rates is important because the corrosion products react with residual chlorine, preventing the biocide from penetrating the biofilm and controlling bacterial growth. Studies have shown that free chlorine is impacted to a greater extent that monochloramine, although the effectiveness of both disinfectants is impaired if corrosion rates are not controlled (LeChevallier et al., 1990, 1993). Increasing the phosphate-based corrosion inhibitor dose, especially during the summer months, can help reduce corrosion rates (Figure 10-7). In full-scale studies, systems that used a phosphate-based corrosion inhibitor had lower coliform levels than systems that did not practice corrosion control (LeChevallier et al., 1996). In addition to the level of generalized corrosion, localized pitting can provide a protective habitat for bacterial proliferation. The pitting of certain metal pipes can be accelerated by high levels of chloride and sulfate. The ratio of chloride and sulfate to bicarbonate levels is known as the Larson index and can indicate the propensity for pitting corrosion. Research has shown that consideration of the level of generalized corrosion, Larson index, corrosion inhibitor, and disinfectant residual is necessary to accurately predict the inactivation of biofilm bacteria (see Table 10-2) (LeChevallier et al., 1993).

Studies have shown that the Larson index can vary seasonally in drinking water systems, with the highest levels occurring during the summer months (LeChevallier et al., 1993). Factors that can influence the Larson index include anything that increases chloride levels (chlorine disinfection, aluminum or ferric salts) or that changes the alkalinity of the water (lime, soda ash, sodium bicarbonate have a positive influence; hydrofluosilicic acid, chlorine gas, certain coagulants depress alkalinity).

The pipe surface itself can influence the composition and activity of biofilm populations. Studies have shown that biofilms developed more quickly on iron pipe surfaces than on plastic PVC pipes, despite the fact that adequate corrosion control was applied, the water was biologically treated to reduce AOC levels, and chlorine residuals were consistently maintained (Haas et al., 1983; Camper, 1996). This

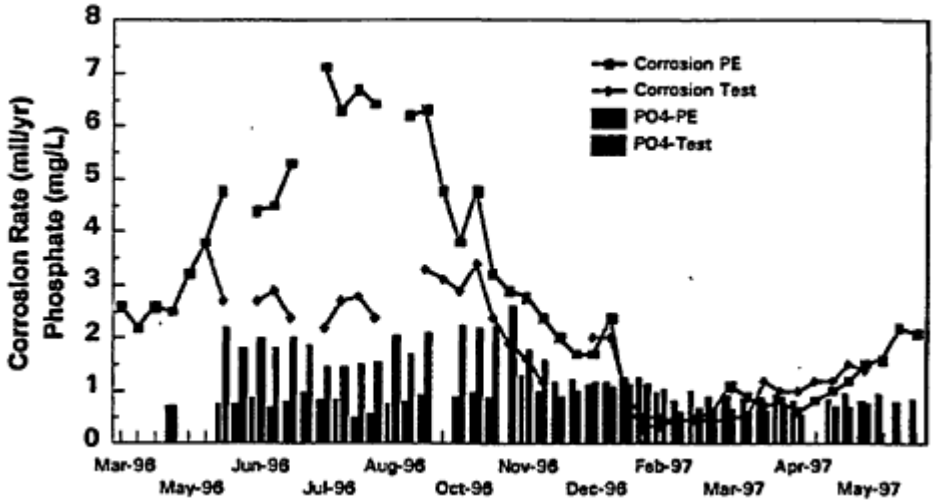

Figure 10-7
Increasing phosphate levels can reduce corrosion rates.

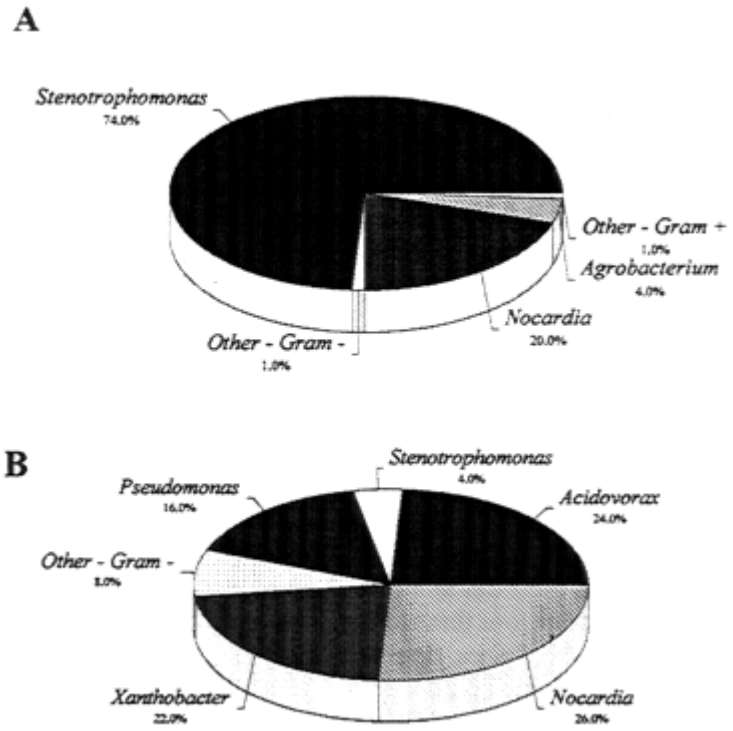

Figure 10-8
Microbial populations isolated from PVC (A) or iron pipe (B) surfaces.

TABLE 10-2 Multiple Linear Regression Modela for Monochloramine Disinfection of Biofilm Bacteria

Log Reduction Viable Counts	Coefficient	Standard Error	*t*-statistic	Significance Level
Intercept	-1.0734	0.5685	-1.888	0.0816
Log Larson index	-0.5808	0.1963	-2.958	0.0111
Log corrosion rate	-0.4820	0.3205	-1.504	0.1566
Log monochloramine	2.0086	0.9226	2.177	0.0485
Phosphate level	0.1445	0.0336	4.295	0.0009
Corrosion in Rsquared	0.746	F test:	13.474	

[a] Model is based on 18 observations.

TABLE 10-3 Detection Frequency of Slow-Growing Mycobacteria in Water Samples

		Percent Samples Containing Slow-Growing Mycobacteria			
Disinfectant Type	Nutrient Level	Raw	Plant/Well Effluent	Midpoint	Deadend
O_3/free	High	24	0	0	0
Free	Medium	6	0	0	6
Free	Low	11	0	0	6
Free	Groundwater	NA	0	29	24
Chloramine	High	47	6	6	12
Chloramine	Medium	39	11	0	33
Chloramine	Medium/low	39	17	11	50
Chloramine	Groundwater	NA	11	6	0

stimulation of microbial communities on iron pipes has been observed by other investigators.

In addition to influencing the development of biofilms, the pipe surface has also been shown to affect the composition of the microbial communities present in the biofilm (see Figure 10-8) (Haas et al., 1983). Iron pipes supported a more diverse microbial population than did PVC pipes. The purpose of these studies is not to indicate that certain pipe materials are preferred over another but to demonstrate the importance of considering the type of materials that come into contact with potable water.

PUBLIC HEALTH SIGNIFICANCE OF BIOFILM CONTROL

Growth of coliform bacteria in distribution system biofilms could be considered a nuisance if they had no public health significance. Coliform bacteria have traditionally been used to indicate the adequacy of drinking water treatment. A new interpretation of this indicator concept implies that drinking water is not adequately treated if coliform bacteria can proliferate in distribution system biofilms. One concern is whether opportunistic pathogens such as *Legionella pneunophila, Mycobacterium avium* complex (MAC), or other microbes can also proliferate.

Members of the *M. avium* complex (i.e., *M. avium* and *Mycobacterium intracellulare*) have been shown to occur in drinking water distribution systems with levels ranging between 0.08 and 4S,000 CFUs/ml (Haas et al., 1983; duMoulin and Stottmeier, 1986; duMoulin et al., 1988; Carson et al., 1988a; Fischeder et al., 1991; von Reyn et al., 1993, 1994; Glover et al., 1994). The greatest increase in *M. avium* complex infections has been with acquired immunodeficiency syndrome (AIDS) patients, approximately 25 to 50 percent of whom suffer debilitating and life-threatening MAC infections (Horsburgh, 1991; Nightingale et al., 1992). The organism infects the gastrointestinal or pulmonary tract, suggesting that food or water may be important routes of transmission for AIDS patients.

In an ongoing research study, examination of eight, well-characterized, drinking water systems showed that slow-growing mycobacteria were frequently detected in raw water and in distribution system samples using a chloramine residual (see Table 10-3). Either free-chlorine or ozone treatment appeared to be sufficient to eliminate mycobacteria to below detectable levels in plant effluent levels. The conclusion that chloramines provide a selective advantage for mycobacteria may be premature because of the higher rates of mycobacteria detection in raw water and possible elimination of bacteria that overgrow the selective medium. The reason for the frequent detection of slow-growing mycobacteria in the free-chlorinated groundwater site is unclear but may be due to the low chlorine residuals (average of 0.15 mg/L) observed at this location.

The levels of slow-growing mycobacteria detected in raw water samples and in distribution system samples are shown in Table 10-4. The results show that high levels were detected in a small number of samples. These levels could occur following flushing or other activities that could dislodge biofilm samples or resuspend distribution system sediments. Biofilm *Mycobacterium* levels ranged from nondetectable to >1,500 CFUs/cm^2.

Using a nested PCR method (Kulski et al., 1995), 304 of the 708 (43 percent) of the water isolates, and 337 of 747 (45 percent) biofilm were identified as members of the genus *Mycobacterium*. Using both the nested PCR method and a PCR-based technique involving amplification of the 65-kDa heat shock protein gene (*hsp-65*) followed by digestion of the PCR product with restriction endonucleases (PCR-RE) (Telenti et al., 1993; Steingrube et al., 1995), 20 percent of the water isolates and 64 percent of the biofilm isolates were identified as *M. avium* or *M. intracellulare*. Additionally, eight percent of the water isolates were identified as *M. kansasii*. Ongoing biofilm studies are examining the role of nutrients, pipe material, disinfectant species, and temperature in an effort to better control mycobacteria in drinking water.

TABLE 10-4 Average Density of Slow-Growing Mycobacteria in Water Samples

		Slow-Growing Mycobacteria/mL[a]			
Disinfectant Type	Nutrient Level	Raw	Plant Effluent	Midpoint	Deadend
O_3/free	High	0.46	<0.01	<0.01	<0.01
Free	Medium	<0.01	<0.01	<0.01	<0.01
Free	Low	2.44	<0.01	<0.01	3.41
Free	Ground	NA	<0.01	15.68	130.08
Chloramine	High	20.65	<0.01	812.70	33.65
Chloramine	Medium	4.94	0.52	<0.01	5.13
Chloramine	Medium/low	7.79	0.86	6.25	101.70
Chloramine	Ground	NA	13.08	7.28	<0.01

[a] For samples where slow-growing mycobacteria were detected.

CONCLUSION

The occurrence of coliform regrowth in distribution systems depends on a complex interaction of chemical, physical, operational, and engineering parameters. No single factor could account for all coliform occurrences, so the water utility operator must consider all of the above parameters in devising a solution to the regrowth problem. Even systems that do not experience coliform problems may want to more closely examine biofilm control strategies and a means of limiting the *occurrence* of opportunistic pathogens such as *Mycobacterium avium* complex in drinking water supplies.

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11

New and Emerging Drinking Water Treatment Technologies

Issam Najm and R. Rhodes Trussell

The development and implementation of water treatment technologies have been mostly driven by three primary factors: the discovery of new rarer contaminants, the promulgation of new water quality standards, and cost. For the first 75 years of this century, chemical clarification, granular media filtration, and chlorination were virtually the only treatment processes used in municipal water treatment. However, the past 20 years have seen a dramatic change in the water industry's approach to water treatment in which water utilities have started to seriously consider alternative treatment technologies to the traditional filtration/chlorination treatment approach. This paper identifies and discusses some of these "emerging" technologies.

TECHNOLOGY DEVELOPMENT AND IMPLEMENTATION PROCESS

For a new technology to be considered it must have advantages over traditional treatment processes. These can include lower capital and operations and maintenance costs, higher efficiency, easier operation, better effluent water quality, and lower waste production. Nevertheless, for a water treatment technology to be accepted and implemented at large municipal scale, it must be demonstrated in stages. Understanding this process is necessary in order to properly plan and introduce a new technology to municipal water treatment. A typical sequence of these stages might be summarized as follows:

Stage 1: Successful demonstration in another field.

Stage 2: Testing and development at bench- and pilot-scale levels (1 to 50 gpm).

Stage 3: Verification at demonstration-scale level (>100 gpm).

Stage 4: Multiple successful installations and operations at small full-scale level (0.5 to 5 MGD).

Stage 5: Implementation at a large-scale municipal water treatment plant.

Two important milestones must be achieved in parallel with the above stages: obtaining regulatory approval and reducing costs to competitive levels. Commonly, regulatory approval is necessary by the end of the demonstration-

scale Verification stage (stage 3) and prior to installation at small full-scale plants (stage 4). However, for a new technology to reach full acceptance (stage 5), its cost must be competitive with that of other more conventional processes that achieve the same objective.

The time duration for each of the above stages can vary greatly depending on the technology being considered, how urgent it is to have it implemented, how long it takes for its cost to reach competitive levels, and the significance of its role in the overall water treatment train. The last factor is different from the others in that it recognizes the difference between a technology that is proposed as an alternative to filtration, for example, which is an essential component of water treatment, versus a technology that is proposed to replace a less important component such as a pump, automation, chemical feed, taste-and-odor control, or preoxidation.

TECHNOLOGIES EVALUATED

A wide range of water treatment technologies have been developed or are currently in development. This paper focuses on technologies that can be applied in municipal water treatment plants. Such a technology should meet the following criteria:

- The technology can be scaled to large applications (i.e., > 5 MGD).
- The technology can be cost competitive with existing technologies at large scale.
- The technology can produce water that meets regulatory requirements.
- The technology has a high degree of reliability.

In this paper the following technologies are screened and evaluated: membrane filtration (low pressure and high pressure), ultraviolet irradiation, advanced oxidation, ion-exchange, and biological filtration. Many of these technologies are certainly not new to the water industry. However, either their application has been limited or they were introduced to the water industry so recently that many questions remain unanswered about their large-scale application.

Membrane Filtration Technology

There are two classes of membrane treatment systems that should be discussed: low-pressure membrane systems (such as microfiltration and ultrafiltration) and high-pressure membrane systems (such as nanofiltration and reverse osmosis). Low-pressure membranes, including microfiltration (MF) and ultrafiltration (UF), are operated at pressures ranging from 10 to 30 psi, whereas high-pressure membranes, including nanofiltration (NF) and reverse osmosis

(RO), are operated at pressures ranging from 75 to 250 psi. Figure 11-1 shows a schematic of the pore size of each membrane system as compared to the size of common water contaminants.

Low-Pressure Membranes

If there is a "Cinderella" story of a water treatment technology it is that of the application of low-pressure membranes for surface water treatment. The idea of using low-pressure membrane filtration for surface water treatment began developing in the early 1980s. At the time, low-pressure membranes had long been used in the food-processing industry as nonchemical disinfectants. During the latter half of the 1980s, several research projects were initiated by west coast water utilities (East Bay Municipal Utilities District and Contra Costa Water District), the American Water Works Association (AWWA) Research Foundation, and other organizations to evaluate MF and UF for municipal surface water treatment. The studies clearly showed that both MF membranes (with a nominal pore size of 0.2 mm and UF membranes (with a nominal pore size of 0.01 mm are highly capable of removing particulate matter (turbidity) and microorganisms. In fact, the research results showed that, when it came to these contaminants, membrane-treated water was of much better quality than that produced by the best conventional filtration plants. Figure 11-2 shows an example plot of turbidity removal by an MF membrane. The majority of treated-water samples had a turbidity level near the limit of the on-line turibidimeter (less than 0.05 Nephelometric Turbidity Units (NTU)). In addition, membrane filtration (both MF and UF) was proven to be an "absolute barrier" to *Giardia* cysts and *Cryptosporidium* oocysts when the membrane fibers and fittings were intact. Finally, the particular UF membranes tested by Jacangelo et al. (1995) were also proven to act as absolute barriers to viruses because of their nominal pore size of 0.01 mm.

As a surface water treatment technology, low-pressure membrane filtration has several advantages over conventional filtration and chlorination. These include smaller waste stream, lower chemical usage, smaller footprint, greater pathogen reduction, no disinfection byproduct formation, and more automation. For a while it was also believed that low-pressure membrane filtration is highly susceptible to excursions in raw water turbidity. However, pilot- and full-scale operational data have demonstrated that low-pressure membranes can treat turbidity excursions as high as several hundred NTUs with manageable impacts on process operation and efficiency (Yoo et al., 1995). All of the above advantages greatly favor membrane filtration over conventional filtration with chlorine.

On the other hand, because of their porous structure, low-pressure membranes are ineffective for the removal of dissolved organic matter. Therefore, color-causing organic matter, taste-and-odor-causing compounds such as Geosmin and methylisoborneol, and anthropogenic chemicals can pass through the membranes into treated water. This limits the applicability of low-pressure membrane filtration to surface water sources where the removal of organic matter is not required. One UF membrane system has overcome this

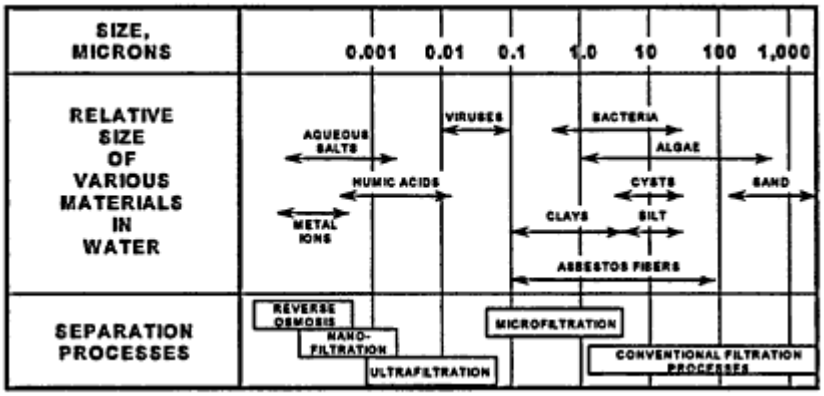

Figure 11-1
Pore size ranges of various membranes.

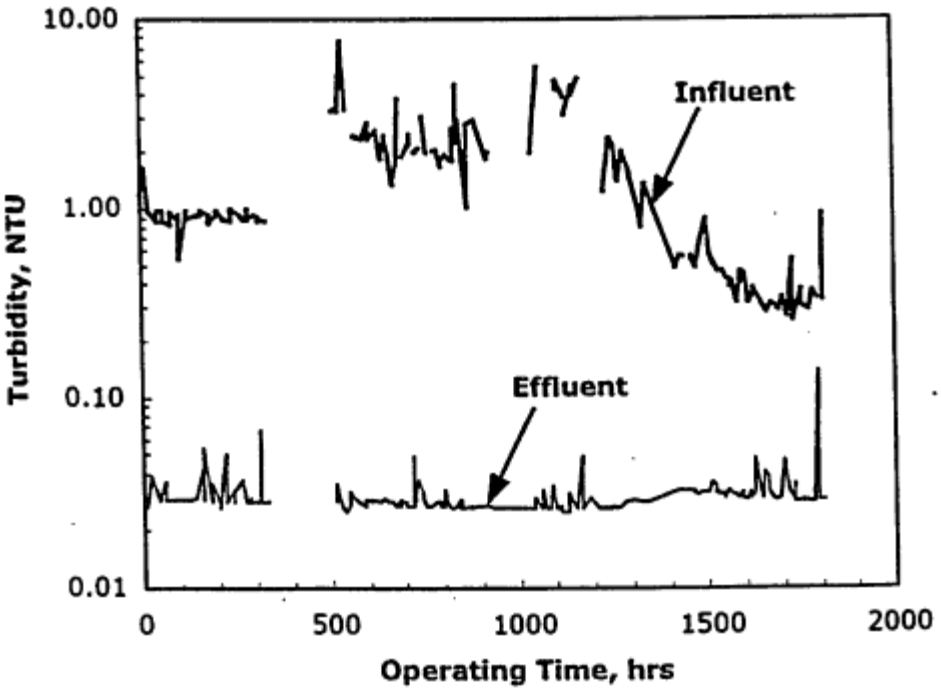

Figure 11-2
Example plot of turbidity reduction by MF membranes.

limitation by introducing powdered activated carbon (PAC) as part of the system. PAC injected into the influent water to the membrane is retained on the concentrate side of the membrane and disposed of with the waste stream. This approach is certain to expand the domain of low-pressure membrane applications in surface water treatment, especially at sites where organic removal is only occasionally required.

With all of these positive aspects, there were several obstacles that low-pressure membrane filtration had to overcome. First, for several years the cost of membrane filtration systems at "municipal" scale (i.e., greater than 1 MGD) was prohibitively high. Second, membrane filtration did not have regulatory acceptance and required extensive evaluation on a case-by-case basis. Third, information on its reliability in large-scale municipal applications was not available.

However, since the early 1990s, the cost of low-pressure membranes has decreased dramatically, which has made it more attractive to water utilities for full-scale implementation. In addition, a number of water utilities realized all the benefits that low-pressure membrane systems provided and decided to undergo the regulatory approval process to install these systems at relatively small and cost-effective scales. This has opened the door for the installation of increasingly larger low-pressure membrane plants. Until 1994, all MF or UF plants in the United States and around the world had capacities of less than 3 MGD. In 1994, the first large-scale MF plant (5 MGD) went on-line in San Jose, California, after undergoing significant testing to obtain California Department of Health Services approval. Since then the application of low-pressure membrane filtration has been on the rise. Figure 11-3 shows the recent profile of low-pressure membrane installation in North America in cumulative plant capacities. Today, membrane filtration is rapidly becoming accepted as a reliable water treatment technology. The California Department of Health Services has certified one MF membrane system for water treatment in the state, and has granted it 3-log *Giardia* removal credit and 0.5-log virus removal credit. It has also certified one UF membrane system and granted it 3-log *Giardia* removal credit and 4-log virus removal credit. Others are either being considered for certification or are actively undergoing the required testing. Membrane system construction costs are believed to be comparable to conventional plant construction costs up to a capacity of 20 MGD. However, this upper ceiling is rapidly rising. In fact, there are membrane plants being considered in the United States with capacities ranging from 30 to as high as 60 MGD.

High-Pressure Membranes

As noted earlier, included in this category are nanofiltration (NF) and reverse osmosis (RO) membranes. NF membranes are actually thin-film composite Re membranes that were developed specifically to cover the pore size between Re membranes (<1 nm) and UF membranes (>2 nm) (Matsuura, 1993)--hence the name nanofiltration. Thin-film composite (TFC) membranes are discussed later in this paper. The result was a type of membrane that operates

at higher flux and lower pressure than traditional cellulose acetate (CA) RO membranes. In fact, NF membranes are sometimes referred to as "loose" RO membranes and are typically used when high sodium rejection, which is achieved by RO membranes, is not required, but divalent ions (such as calcium and magnesium) are to be removed (Scott, 1995). Nevertheless, NF membranes are viewed by the water industry as a separate class of membranes than RO membranes and are discussed in this paper as such. NF membranes are commonly operated at pressures ranging from 75 to 150 psi (Lozier et al., 1997). NF membranes have been used successfully for groundwater softening since they achieve greater than 90 percent rejection of divalent ions such as calcium and magnesium. Several NF membrane-softening plants are currently in operation in the United States, with the first plant installed in Florida in 1977 (Conlon and McClellan, 1989). By 1996 the combined total capacity of NF plants in the United States was greater than 60 MGD, all in Florida (Bergman, 1996). It is estimated that approximately 150 NF membrane plants existed around the world by 1995, with a combined total capacity of approximately 160 MGD (Scott, 1995). Because most commercially available NF membranes have molecular weight cutoff values ranging from 200 to 500 daltons (Bergman, 1992; Scott, 1995), they are also capable of removing greater than 90 percent of natural

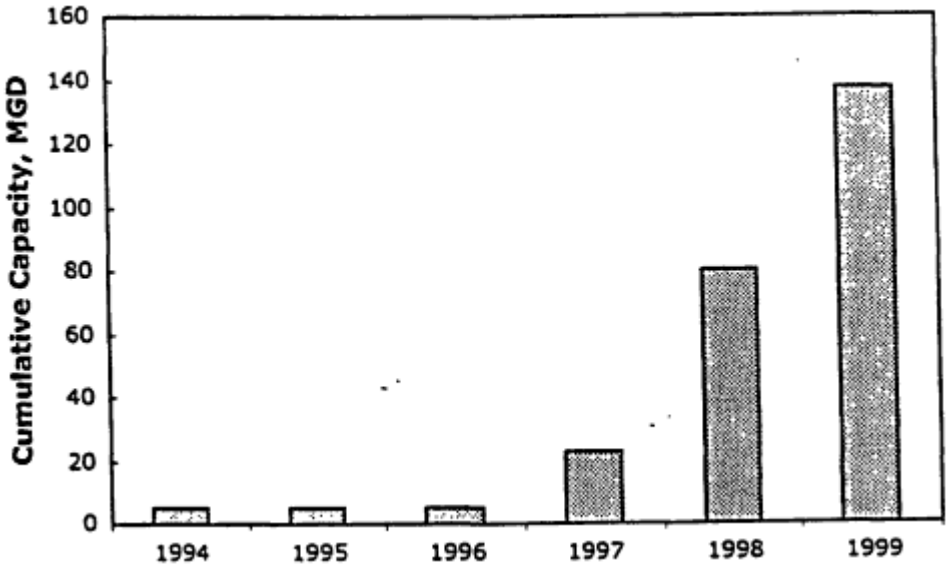

Figure 11-3
Profile of low-pressure membrane installations in North America.

organic matter present in the water. Therefore, they are also excellent candidates for the removal of color and, more importantly, disinfection byproduct (DBP) precursor material (Taylor et el., 1987; Tan and Amy, 1989; Bleu et el., 1992; Chellam et al., 1997).

Currently, NF membranes are being considered as a total organic carbon (TOC) removal technology in surface water treatment. The idea is to install NF membranes downstream of media filtration in order to maintain a very low solids-loading rate on the membranes. Although NF membranes have been designated by the U. S. Environmental Protection Agency (EPA) as one of two best available technologies (BATs) for meeting stage 2 of the Disinfectants/Disinfection Byproducts Rule, they have not been applied for surface water treatment at full scale. To date, pilot studies have been conducted to evaluate the applicability of NF membrane filtration downstream of media filtration during surface water treatment with mixed results (Reiss and Taylor, 1991; Tooker and Robinson, 1996; Chellam et al., 1997). The study reported by Chellam et al. (1997) clearly demonstrated that the fouling rate of NF membranes downstream of conventional filtration was two times higher than that of NF membranes downstream of MF or UF membranes. This was supported by the study of Reiss and Taylor (1991), which showed that conventional filtration pretreatment did not reduce the fouling rate of NF membranes to acceptable levels. Nevertheless, the Information Collection Rule includes data gathering on the applicability of NF membrane filtration for TOC removal from surface water sources. The majority of the data will be from bench-scale testing, which does not include information on long-term operational design and reliability, but some data will be obtained from pilot-testing programs. These data will provide additional input into the viability of NF membranes for surface water treatment.

RO membranes have long been used for desalination of seawater around the world. These membranes can consistently remove about 99 percent of the total dissolved solids (TDSs) present in the water, including monovalent ions such as chloride, bromide, and sodium. However, for a long time these membranes were predominantly made from CA and required operating pressures at or greater than 250 psi. Recent innovations in Re membrane manufacturing have developed a new class of Re membranes, called TFC membranes that can achieve higher rejection of inorganic and organic contaminants than CA Re membranes while operating at substantially lower pressures (100 to 150 psi). In addition, CA Re membranes commonly require acid addition to lower the pH of the water to a range of 5.5 to 6.0 to avoid hydrolysis of the membrane material. TFC RO membranes do not hydrolyze at neutral or high pH and therefore do not require pH depression with acid addition. It should be noted that the need for pH depression for preventing the precipitation of salts on the membrane surface (such as $CaCO_3$) may still be necessary in some cases depending on the quality of the water being treated and the availability of suitable antiscalents.

TFC RO membranes are currently being evaluated for water reclamation. Results from ongoing pilot studies have shown that TFC RO membranes can achieve greater than 90 to 95 percent rejection of nitrate and nitrite, compared to 50 to 70 percent removal with CA Re membranes. The same pilot studies also show that the TOC concentration in the effluent of TFC Re membranes can be as low as 25 to 50 g/L.

Because of their existing applications for water softening and seawater desalination, high-pressure membrane treatment is currently accepted by the regulatory community and the water industry as a reliable technology. The main obstacle to increased application of high-pressure membranes in municipal water treatment is their high cost. By nature of the current modular design of membrane systems, economies of scale are not recognized for large treatment plants. However, several membrane manufacturers are currently modifying their membrane system designs to make them economically attractive at large scale.

Two-Stage Membrane Filtration

From the above discussion it is apparent that low-pressure membranes are highly effective for particulate removal, while high-pressure membranes are effective for dissolved matter removal (both organic and inorganic). Conceptually, combination of the two membrane systems in series (MF or UF followed by NF or RO) would provide a comprehensive treatment process train that is capable of removing the vast majority of dissolved and suspended material present in water. Such a treatment train is commonly termed "two-stage membrane filtration." Other names include "integrated membrane systems" or "dual-stage membrane filtration." The only material that is believed to pass through such a treatment train includes low-molecular-weight organic chemicals. However, compared to existing treatment, a two-stage membrane filtration process (possibly coupled with PAC addition) would produce far superior water quality. The main concern about such highly treated water is that it may be more corrosive. Special corrosion inhibition measures for low-TDS waters of this kind require further development.

Several studies have been conducted to evaluate two-stage membrane systems for surface water treatment (Wiesner et al., 1994; Chellam et al., 1997; Kruithof et al., 1997; Vickers et al., 1997). The results of these studies have clearly shown that MF or UF membranes are excellent pretreatment processes to NF or RO membranes and that the combined particulate removal and organic removal capabilities of this treatment scheme produce excellent water quality that complies with existing and forthcoming regulatory requirements.

The primary obstacle that a two-stage membrane treatment system needs to overcome is its cost. Lozier et al. (1997) estimated the capital cost of a 40-gpm, two-membrane system at $4/gpd. The capital unit cost of a large-scale, two-stage membrane system may range from $2 to $3/gpd of capacity. This is still substantially higher than the cost of conventional treatment, which is estimated at $1 to $1.5/gpd.

Summary

Membrane filtration technology is rapidly becoming accepted in the water treatment industry. Low-pressure membrane filtration (MF and UF) is now replacing conventional filtration for surface water treatment at several locations in the United States. High-pressure membrane filtration (both NF and RO) is used primarily for softening and TDS reduction but is being evaluated for the removal of natural organic matter in water treatment. The main obstacle to large-scale implementation of membrane filtration is its capital cost. Ongoing innovations in the design of large-scale membrane systems are continually lowering their capital cost and making them increasingly cost competitive with conventional treatment processes.

Ultraviolet Irradiation Technology

Ultraviolet (UV) irradiation technology is primarily used in the water and wastewater treatment industry as a disinfection process that capitalizes on the germicidal effect of UV light in the wavelength range of 250 to 270 nm (EPA, 1996). The process is commonly designed such that water flows in a narrow region around a series of UV lamps. The microorganisms in the water are inactivated through exposure to the UV light. The process is compact since the time of exposure (which translates into hydraulic retention time) is commonly measured in seconds. The process works on the principle that UV energy disrupts the DNA of the microorganisms and prevents it from reproducing. UV irradiation technology has been used since the 1950s at approximately 500 drinking water facilities in the United States, and more than 1,500 facilities in Europe (Kruithof et al., 1992; Parrotta and Bekdash, 1998). However, the vast majority of the U.S. facilities are either transient-noncommunity groundwater systems or nontransient-noncommunity groundwater systems serving less than 3,000 people each. These are facilities that provide water to restaurants, highway rest areas, airports, schools, camps, factories, rest homes, and hospitals. In fact, UV disinfection technology in drinking water treatment is currently only promoted for small-scale groundwater systems. However, the process can certainly be scaled up to large-scale applications since it is currently applied at large-scale wastewater treatment plants for final effluent disinfection. The largest wastewater treatment UV system in the world is located in Edmonton, Alberta, Canada, with a peak design capacity of 265 MGD (Reed, 1998). For water treatment systems, a minimum UV dose is commonly set for UV systems. The National Sanitation Foundation (NSF) standard for Class A UV systems (i.e., those that can be used as point-of-use (POU) and point-of-entry (POE) treatment devices) requires that they emit a minimum UV dose of 38 mW-sec/cm^2, which is the dose determined to inactivate *Bacillus subtilis* spores (ANSI/NSF, 1991). Several states, including New Jersey and Wisconsin, have specific criteria for UV systems in the form of a minimum dose (Parrotta and Bekdash, 1998). Several European countries have also adopted minimum UV doses for pretreated drinking water (Norway at 16 mW-sec/cm^2 and Austria at 30 mW-sec/cm^2). All of these doses are based on the requirement to inactivate bacteria and viruses but not protozoans. There is limited information on the ability of UV irradiation to

inactivate *Giardia* cysts. Karanis et al. (1992) conducted a laboratory study to evaluate the UV inactivation of *Giardia lamblia* cysts obtained from infected humans and gerbils. The testing results conducted in distilled water are shown in Figure 11-4. The results show that a UV dose of approximately 40 mW-sec/cm^2 achieved 0.5-log inactivation of *Giardia lamblia*, whereas a UV dose of 180 mw-sec/cm^2 was required to achieve 2-log inactivation of *Giardia* cysts. Rice and Hoff (1981) also showed that a UV dose of 63 mW-sec/cm^2 achieved 0.5-log inactivation of *Giardia* cysts, also in distilled water. EPA has recently developed and published a guidance document for the application of UV technology for surface water treatment (EPA, 1997a). The California Department of Health Services has set a specific dose of 140 mW-sec/cm^2 as a requirement to meet the Title 22 criteria of 2.2 coliforms/100 ml in reclaimed water.

Published information on the cost of UV disinfection systems in drinking water treatment is limited to small systems. EPA has estimated the capital cost of a UV treatment system for a 1.5-MGD plant at $200,000 (at a UV dose of 16 to 30 mW-sec/cm^2). This translates into a capital unit cost of $0.13/gpd of capacity. The operations and maintenance cost of such a system is estimated at 1.5¢/1,000 gallons of water treated (Parrotta and Bekdash, 1998). On the other

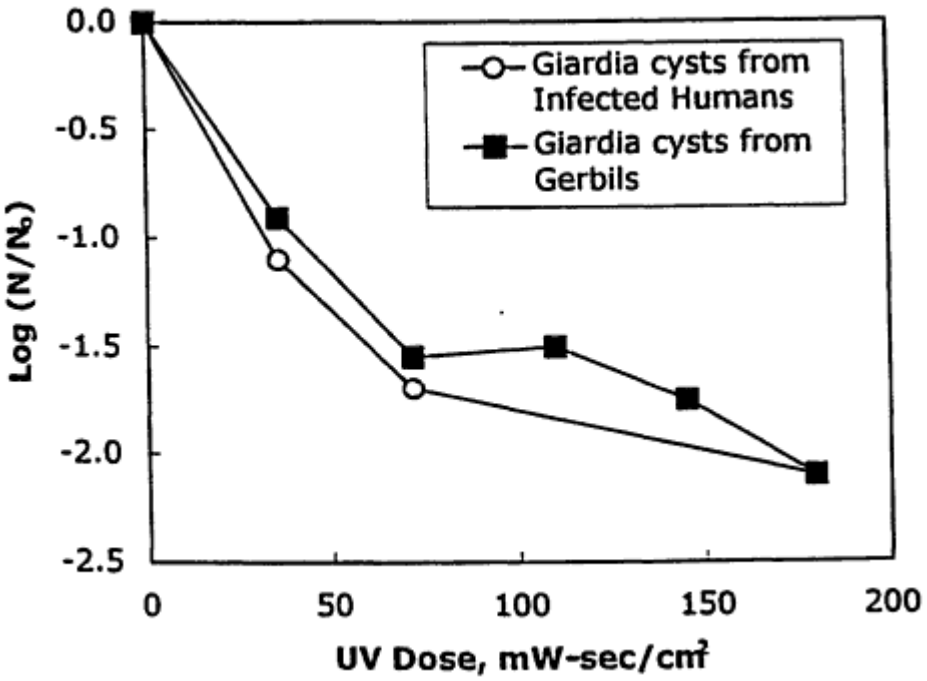

Figure 11-4
Inactivation of *Giardia lamblia* cysts with UV irradiation in distilled water.

hand, UV disinfection is commonly used in large-scale wastewater treatment plants. There, the cost of a 12-MGD UV treatment system designed to meet water reclamation standards is estimated at $1.5 million to $2 million. This estimate is for a medium-pressure UV system, treating water with a 55 percent transmittance (approximately 0.260 cm-1 UV-254 absorbance) and applying a dose of 140 mW-sec/cm ^{2}. This is equivalent to a cost range of $0.13 to $0.16/gpd of capacity. These cost values indicate that the application of UV technology to large-scale water treatment is cost competitive. If UV irradiation can be proven effective against *Cryptosporidium* at reasonable doses (<200 mW-sec/cm^2), it will become an attractive alternative to ozone, which is currently believed to be one of few effective disinfectants for inactivating *Cryptosporidium.*

There are four types of UV technologies of interest to the water industry: low-pressure, low-intensity (LP-LI) UV technology; low-pressure, medium-intensity (LP-MI) UV technology; medium-pressure, high-intensity (MP-HI) UV technology; and pulsed-UV (PUV) technology. Approximately 90 percent of the UV installations in North America have LP-LI UV technology, with some dating back to the 1970s. The power output of LP-LI UV lamps commonly varies from 40 to 85 W. Another unique characteristic of low-pressure lamps is that they emit a monochromatic light at a wavelength of 254 nm. EPA's design manual is specifically based on and tailored to LP-LI UV technology. The primary advantage of LP-LI UV lamps is their high efficiency. The primary disadvantage is their low power, which results in the need for a large number of lamps for a small plant. For example, a typical secondary wastewater effluent would require approximately 40 LP-LI UV lamps per MGD of peak capacity. Considering that a significant labor effort is required to clean and maintain UV lamps, the application of LP-LI UV technology at large scale is not desirable.

LP-MI UV lamps are identical to LP-LI UV lamps with the exception of a higher power output--170 W compared to 40 to 85 W. Therefore, a typical secondary wastewater effluent would now require only 20 to 24 lamps per MGD of capacity. This makes LP-MI UV technology more applicable for medium-size water treatment facilities than LP-LI UV technology.

MP-HI UV lamps operate at substantially higher gas pressure inside the lamps compared to low-pressure UV lamps and are characterized by a power output that varies from 5 to 30 KW. Contrary to low-pressure lamps that produce all of their light at approximately 254 nm, medium-pressure lamps produce a polychromatic light, of which only 25 percent is in the germicidal wavelength range of 200 to 300 nm. However, because of the higher power output of MP-HI UV lamps, UV disinfection systems using this technology are substantially smaller than those using LP-LI UV technology, simply because of the need for significantly fewer lamps. This technology has been used in small-scale water treatment and industrial applications since the 1980s. However, it was not introduced to the municipal wastewater market until 1994. Currently, more than 270 MP-HI UV systems are in operation, with 70 of them operating at municipal wastewater treatment plants. One drawback of MP-LI UV technology is its low power efficiency compared to low-pressure technology. Another drawback is its high capital cost. Typically, a low-pressure UV lamp costs about $500, whereas a medium-pressure UV lamp costs about $5,000. Nevertheless, considering the substantial savings in the number of lamps, both capital and operations and main

tenance costs of large-scale MP-HI UV systems are lower than those of LP-LI UV systems. In fact, the general assumption in the industry is that UV systems with peak flow greater than 10 MGD should utilize MP-HI UV technology in order to keep the number of UV lamps at a manageable level.

Low- and medium-pressure UV technologies are past the research stage and have been accepted as reliable disinfection technologies. In fact, specific LP-LI UV doses are listed in the Surface Water Treatment Rule (SWTR) *Guidance Manual* (EPA, 1991) for the inactivation of viruses in water. The cost of UV systems is also not prohibitive since the technology is less expensive than ozone and many other disinfection processes.

The new UV technology under development is pulsed UV technology. In this process the energy is stored in a capacitor and then released to the lamp in a short, high-intensity pulse. The duration between pulses is approximately 30 milliseconds, and each pulse lasts for less than 1 millisecond. The intensity of each pulse is believed to be about 107 mW/cm^2. One manufacturer of this technology claims that the high energy emitted with each pulse is far more effective for the inactivation of microorganisms compared to the same level of energy emitted over an extended period of time. Figure 11-5 shows a plot of the inactivation rate of MS2 bacterial virus with pulsed UV and LP-LI UV systems. The results suggest that, for the same UV dose, pulsed UV systems may achieve approximately one log additional kill of MS2 virus compared to that achieved by traditional LP-LI UV. However, questions remain about the ability to accurately measure the UV dose emitted by a pulsed UV system. Regardless of the type of UV technology used, the obstacles against application of this technology in municipal water treatment can be summarized as follows.

Limited Information on Giardia and Cryptosporidium Inactivation Capability

As noted above, there is limited data on the inactivation of *Giardia* with UV technology. Two studies have shown that a UV dose of 40 to 65 mW-sec/cm^2 is required to achieve a 0.5-log inactivation of *Giardia lamblia* and that 180 mW-sec/cm^2 is required to achieve 2-log inactivation of *Giardia lamblia*. Data on UV inactivation of *Cryptosporidium* oocysts is even more sparse than that of *Giardia* cysts. Recent data presented at the 1998 AWWA Water Quality Technology Conference in San Diego, California, suggested that, using a mouse-infectivity model, a UV dose of 20 mW-sec/cm^2 is sufficient to achieve 4-log inactivation of *Cryptosporidium* oocysts. However, using excystation to measure oocyst viability, the results indicate that only 1-log inactivation of *Cryptosporidium* oocysts was achieved with UV doses as high as 170 mW-sec/cm^2. If these results can be validated by others, they seem to emphasize the notion that UV irradiation does not kill an organism but only limits its ability to reproduce and thus infect a host organism.

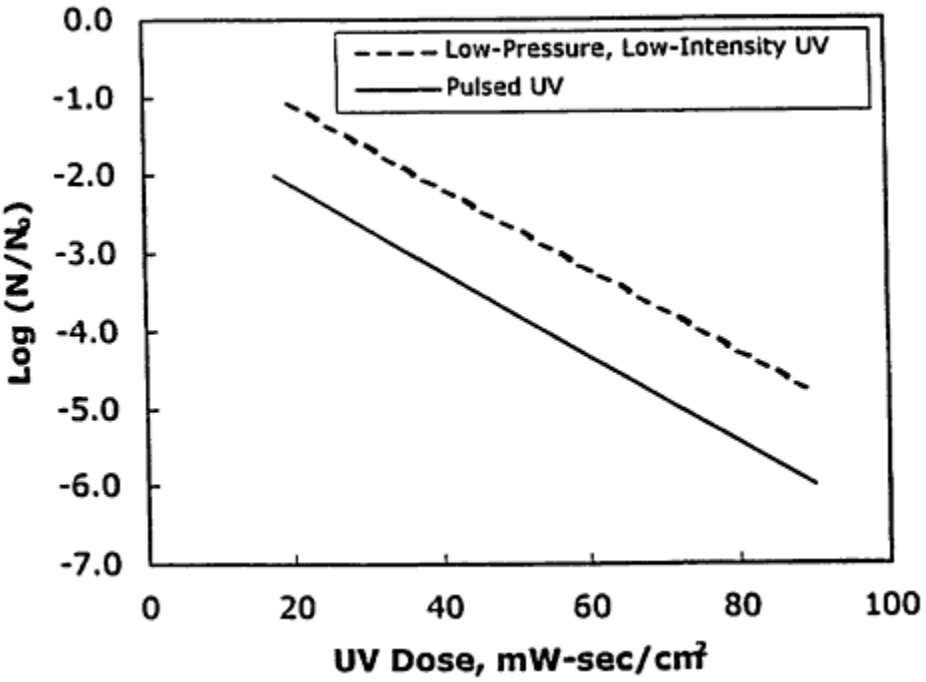

Figure 11-5
Inactivation rate of MS2 bacterial virus with pulsed UV and low-pressure UV systems.

No Significant Oxidation Capability

One of the added benefits of disinfection with ozone, chlorine, or chlorine dioxide is the ability of each to also act as an oxidant for color, taste, and odor control. Unfortunately, disinfection with UV irradiation does not provide this added benefit because UV light, even with hydrogen peroxide addition, is not a strong oxidant As such, even if *Giardia* inactivation with UV light is proven to be feasible, the process will be limited to water systems that do not rely on the disinfectant for any color, taste, or odor oxidation.

Operational Challenges

A UV treatment process is comprised of a series of UV lamps enclosed inside a quartz sleeve. UV light passes through the quartz and into the water. Because of the high energy emitted by the UV lamps, the temperature of the quartz sleeve can rise substantially, causing precipitation of various scales on the surface of the sleeve, thus blocking the passage of the UV light into the water and dramatically reducing the efficiency of the process. The scales are commonly caused by the precipitation of calcium, iron, or magnesium salts. Several UV light manufacturers have developed continuous cleaning mechanisms to prevent scale buildup. However, this problem still plagues the majority of UV systems. Considering that natural waters can greatly vary in calcium, iron, and magnesium

content, this issue may be a significant obstacle to widespread implementation of UV irradiation technology in water treatment.

Severely Impaired by Particulate Matter

UV treatment systems rely on the ability of UV light to reach and inactivate the target microorganism. However, if particulate matter is present in the water, it can shield the microorganism from the UV light and thus render the process ineffective. There is no documented correlation that the authors are aware of between suspended solids content and process efficiency. Until such correlation is developed and accepted, UV application in surface water treatment is confined to postfiltration, where the solids content is negligible.

Limited Process Reliability

Despite claims of UV manufacturers, field-scale UV systems commonly experience failures in various components. Their high reliance on sensitive electrical components, such as capacitors and ballasts makes them vulnerable to high incidences of failure.

In summary, UV irradiation is a promising disinfection technology for large-scale water treatment applications. It is compact and cost effective. More *Giardia and Cryptosporidium* UV-inactivation information is required before it is considered a reliable process for meeting current and upcoming water disinfection requirements.

Advanced Oxidation Technology

The term "advanced oxidation processes" (AOPs) was first used by Glaze et al. (1987) and Aieta et al. (1988) to describe a process that produces hydroxyl radicals (OH) for the oxidation of organic and inorganic water impurities. AOPs include a number of processes. However, three main AOPs are discussed herein: ozone, ozone with hydrogen peroxide addition, and UV irradiation with hydrogen peroxide addition. AOPs can have multiple uses in water treatment. Examples include oxidation of synthetic organic chemicals, color, taste-and-odor-causing compounds, sulfide, iron, and manganese and destruction of DBP precursors prior to the addition of chlorine. However, Trussell and Najm (in press) have demonstrated that AOPs may not be good candidates (i.e., cost effective) for DBP precursor de destruction. In this paper the application of each of the above processes in municipal water treatment is briefly discussed, and some of the challenges facing each process are presented.

Ozone

There are numerous published books, peer-reviewed articles, and proceedings papers on the application of ozonation in drinking water treatment. The reader is referred to AWWARF and CGE (1991) to obtain information on the fundamental chemical principles of ozone reactions in water to produce hydroxyl radicals, general ozone applications in water treatment, and the design of ozone treatment systems.

Since the early 1980s the application of ozone in water treatment has increased, especially for color removal, taste-and-odor control, and/or disinfection. With the increased pressure to reduce chlorination byproduct formation and the need to inactivate increasingly resistant pathogens, many utilities are looking to ozone as their primary disinfection process. Ozone also has unique benefits over most other disinfectants including taste-and-odor control and the ability to inactivate of *Cryptosporidium*. Promulgation of the SWTR resulted in a dramatic increase in the development, design, and construction of ozonation processes in new and existing plants across the United States. In 1990 approximately 40 ozone water treatment plants were in operation in this country (AWWARF and CGE, 1991). In 1998, the number of ozone plants having greater than 1-MGD capacity was estimated at 114 (Rice and Overbeck, 1998).

It is fair to assume that ozone is no longer considered an "emerging" water treatment technology since it has been applied in large municipal treatment plants such as the city of Los Angeles' 600-MGD Aqueduct Filtration Plant (12,000 pounds/day ozone capacity) and the city of Dallas' 300-MGD Elm-Fork water treatment plant (15,000 pounds/day ozone capacity). However, the design of ozone systems for water disinfection is currently undergoing a noticeable change. For the past 10 years, ozone disinfection systems have been designed to achieve low levels of *Giardia* inactivation. This required ozone contactors with "conventional" design criteria, including an average hydraulic retention time of 8 to 12 minutes and ozone doses ranging from 0.5 to 2 mg/L for an average water quality. For such low doses the ozone-residual concentration is virtually nondetectable in the effluent of the ozone contactor. However, with utilities planning to use ozone for *Cryptosporidium* inactivation, process engineers need to consider redesigning the ozone systems to accommodate the requirement for a far higher contact time (CT) requirement, which translates into higher ozone doses and/or longer contact times. Optimization of ozone system designs for *Cryptosporidium* inactivation can help maintain ozone application in water treatment at cost-effective levels. In addition, testing done at pilot and demonstration levels is showing that ozone application to conventionally designed contactors at doses required for *Cryptosporidium* inactivation result in substantially high ozone-residual levels in the effluent water from the contactor. This residual ozone quickly volatilizes into the atmosphere as it exits the closed ozone-contactor environment to the open downstream environment.

Therefore, quenching of this residual ozone before the water exits the contactor is necessary in order to minimize operator exposure to unhealthy levels of ozone in the atmosphere. This task appears to be more challenging than earlier thought. Options to quench the ozone residual include air stripping the ozone in the last chamber of the ozone contactor and quenching the ozone residual with a reducing agent to the last chamber of the contactor (these include

hydrogen peroxide, thiosulfate, and bisulfite). Air stripping the ozone in the last chamber requires installation of a separate air-stripping system. It is also not clear what air-to-water ratios are required to achieve effective stripping of ozone residual. Studies have shown that quenching the ozone residual with hydrogen peroxide is not always effective. Preliminary results seem to indicate that the reaction between ozone residual and hydrogen peroxide is substantially slower in lower-alkalinity waters. There is limited information on the effectiveness of thiosulfate or bisulfite for quenching ozone residuals in water.

It should be noted that one of the main obstacles to wider use of ozonation in municipal drinking water treatment is the potential formation of bromate (BrO_3-), a possible human carcinogen, when the water being treated contains bromide. In general, bromide concentrations greater than 50 g/L may result in bromate formation at levels greater than the maximum contaminant level (MCL) of 10 g/L. At this time the only demonstrated bromate formation control strategy is to depress the water pH in the ozone contactor to less than 6.5 to 7. Additional work is needed to control bromate formation during ozonation of bromide-containing waters.

Rule-of-thumb costs for ozone systems are currently estimated at $2,000 to $3,000 per pound per day of ozone capacity. Therefore, for a 12-MGD treatment plant requiring an ozone dose of 5 mg/L, the capital cost of the ozone treatment system is estimated at $1 million to $1.5 million. This includes the ozone equipment and the concrete ozone contactor. This cost range is equivalent to a unit capital cost of $0.08 to $0.12/gpd of capacity.

Ozone with Hydrogen Peroxide Addition

When hydrogen peroxide (H_2O_2) is added to ozonated water, it reacts with the molecular ozone, which accelerates the formation of hydroxyl radicals. Therefore, in an ozone-H_2O_2 process the goal is to increase the concentration of hydroxyl radicals, which is a stronger oxidizer than molecular ozone, and consequently rapidly reduce the concentration of molecular ozone. Therefore, hydrogen peroxide is added to an ozone process if it is used as an oxidation process but not as a disinfection process, which relies on the prevalence of a high concentration of molecular ozone.

The ozone-H_2O_2 process is used for the destruction of taste-and-odor-causing compounds, color removal, and destruction of micropollutants, such as volatile organic compounds (Karimi et al., 1997), pesticides, and herbicides. Stoichiometric analysis suggests that the optimum H_2O_2-to-ozone ratio is approximately 0.3:1 (mg/mg). However, pilot-and full-scale studies have shown that the optimum ratio is more on the order of 0.5:1 to 0.6:1 mg/mg (Karimi et al., 1997; Najm et al., in press).

Currently, the conventional design of an ozone-H_2O_2 treatment process is one in which hydrogen peroxide is fed as a liquid to the influent water and an ozone-rich gas is fed through fine-bubble diffusers at the bottom of a contactor.

Considering the complexity of the reaction chemistry between ozone, hydrogen peroxide, natural organic matter, and other water constituents, it is not clear whether such a conventional design is the optimum design for an ozone-H_2O_2 treatment system. Innovations in engineering design may be able to improve the efficiency of the process at lower ozone and/or hydrogen peroxide doses.

UV Irradiation with Hydrogen Peroxide Addition

In the presence of UV light, hydrogen peroxide decomposes to form hydroxyl radicals. Addition of hydrogen peroxide to the influent of a UV irradiation process is currently being used for the destruction of micropollutants from groundwater, but it can also be used for the same purposes as other AOPs, which include the destruction of taste-and-odor-causing compounds and the removal of color. The reaction between UV and hydrogen peroxide to form hydroxyl radicals is substantially slower than that between ozone and hydrogen peroxide. However, in many groundwater remediation efforts, the simplicity of a UV irradiation system has been favored over the complexity of an ozone generation and feed system. However, owing to the slow hydroxyl-radical formation reaction in UV-H_2O_2 systems, the process must be operated with an excess of high concentration of hydrogen peroxide (5 to 20 mg/L hydrogen peroxide residual). Therefore, for this process to be used in drinking water treatment, either the process should be modified to utilize less hydrogen peroxide or a treatment process should be installed downstream to quench the hydrogen peroxide residual to acceptable levels (<0.5 mg/L) before the water is put into the distribution system. The various options available for quenching the hydrogen peroxide residual include chlorine, thiosulfate, sulfite, or granular-activated carbon.

Ion Exchange Technology

Ion exchange (IX) technology has been used in the chemical and environmental engineering fields for a long time. However, its use has been mostly limited to water softening (Ca^2+ and Mg^2+ removal), either at the water treatment plant or as a point-of-use treatment process and for industrial applications, such as the production of fully demineralized water. However, with new limits being set on several inorganic chemicals, IX technology is finding new applications in water treatment. Some of the primary candidates for removal with IX include nitrate, arsenic, selenium, barium, radium, lead, fluoride, and chromate. Surveys conducted in the early 1980s showed that 400 communities exceeded the nitrate MCL of 10 mg/L as nitrogen (AWWA, 1985) and 400 communities exceeded the fluoride MCL of 4 mg/L (EPA, 1985). A new contaminant recently discovered in groundwater is perchlorate ($C1O_4$-), which is a component of solid-rocket fuel. The California Department of Health Services has adopted a perchlorate action level of 18 g/L. IX technology is ideal for the removal of perchlorate ion from contaminated groundwater.

The technology is commonly designed as a fixed-bed process in which a synthetic resin is packed. As water passes through the resin bed, contaminant

ions present in the water are exchanged with ions on the resin surface, thus removing the contaminant ions from the water and concentrating them on the resin. The resin is frequently regenerated to remove the contaminant from the resin surface and replenish it with the original exchange ion. There are four primary types of IX resins: strong acid cationic (SAC) resin, weak acid cationic (WAC) resin, strong base anionic (SBA) resin, and weak base anionic (WBA) resin.

Table 11-1 lists the various ions that can be removed by each type of resin, the resin regeneration requirements, and some of the operating pH ranges for each resin type (Clifford, 1990). As their names indicate, SAC and WAC resins are used to remove cations from water (e.g., Ca^{2+}, Mg^{2+}, Ra^{2+}, Ba^{2+}, Pb^{2+}), while SBA and WBA resins are used to remove anions from water (e.g., NO_3^-, SO_4^{2-}, $C1O_4^-$, $HAsO_4^{2-}$, SeO_3^{2-}, etc.). SAC resins operate over a wide range of pH values (1 to 14), whereas WAC resins can only operate at pH values greater than 7. During water softening, SAC resins can remove both carbonate and noncarbonate hardness, whereas WAC resins can only remove carbonate hardness. On the other hand, WAC resins are easier to regenerate than SAC resins and do not result in sodium concentration increases as SAC resins do.

TABLE 11-1 Types and Characteristics of IX Resins

Resin Type	Functional Group	Ions Removed	Regeneration	Operating pH Range
Strong acid cationic (SAC) resin	Sulfonate RSO_3^-	Total hardness, Mg^{2+}, Ra^{2+}, Ba^{2+} Pb^{2+}, etc.	Regenerated with HCl or NaCl	1 to 14
Weak acid cationic (WAC) resin	Carboxylate $RCOO^-$	Carbonate hardness, Mg^{2+}, Ra^{2+}, Ba^{2+}, Pb^{2+}, etc.	Regenerated with HCl	>7
Strong base anionic (SBA) resin	Quaternary amine $RN(CH_3)_3^+$	NO_3^-, SO_4^{2-}, $C1O_4^-$, $HAsO_4^{2-}$, SeO_3^{2-}, etc.	Regenerated with NaOH or NaCl	1 to 13
Weak base anionic (WBA) resin	Tertiary amine $RN(CH_3)_2H^+$	NO_3^-, SO_4^{2-}, $C1O_4^-$, $HAsO_4^{2-}$, SeO_3^{2-}, etc.	Regenerated with NaOH, or Ca(OH)2	<6

The cost of IX technology is competitive with that of other inorganics removal processes, such as lime softening, high-pH precipitation, and high-pressure membranes (e.g., RO membranes). For example, the capital cost of IX

treatment for nitrate removal from groundwater is estimated at $0.4 to $0.5/gpd. However, application of IX technology large-scale is problematic because of the waste stream produced by the process. The volume of the waste stream is not large and can amount to only 2 to 5 percent of the water volume treated; however, the waste stream contains a high concentration of acid (HCl), base (NaOH), or salt (NaCl), ranging from 1 to 3 M. In addition, the waste stream contains a high concentration of the contaminant removed from the water (e.g., NO_3^-, $HAsO_4^{2-}$, Pb^{2+}, etc.). The disposal of a waste stream containing these components is the primary obstacle to widespread implementation of IX technology at large-scale water treatment plants. Plants in coastal areas may have the option of disposing of this stream into the ocean. However, no cost-effective disposal options exist for inland plants.

Biological Filtration

All of the technologies discussed above are physical and/or chemical processes. In fact, the water treatment industry depends solely on physical and/or chemical processes to meet water quality goals. Utilization of biological processes in water treatment has been frowned on by the industry because of concern about the introduction of microorganisms to water. However, this barrier has been broken by the introduction of biological filtration as the most effective process for the production of biologically stable water. This was specifically driven by concern about the increase in the concentration of biodegradable organic matter (BOM) as a result of ozonating natural waters. There is concern that higher BOM levels may result in increased potential for biological regrowth in the distribution system. Therefore, implementing biological filtration in the water treatment plant reduces BOM concentrations in the water before it is introduced into the distribution system. Several plants in the United States currently use biological filtration after ozonation. In fact, Stage 1 of the D/DBP Rule, which became final in December 1998, requires water utilities to implement biological filtration for BOM removal if ozone is used at the treatment plant (EPA, 1997b).

There are several unanswered questions about the design and operation of biological filtration, such as what filter media type and size to use and what minimum empty bed contact time (EBCT) can be used while maintaining satisfactory BOM removal.

Pilot studies conducted by various researchers have concluded that either granular-activated carbon (GAC) or anthracite, compared to sand, is required as the attachment medium for the biofilm. Clearly, anthracite is substantially less expensive than GAC. Anthracite has been shown to be equivalent to GAC as a biological filtration medium when used in warm climates (Montgomery Watson, 1992). However, it may not be satisfactory in cold climates, as studies have shown that a higher GAC surface area, compared to that of anthracite, is required to maintain an active biofilm when treating cold water. Wang et al. (1995) showed that the concentration of biomass on the surface of biologically active GAC filters was approximately three to eight times greater than that on the surface of biologically active anthracite filters. Figures 11-6 and 11-7 show examples of the impact of media type, temperature, and EBCT on the

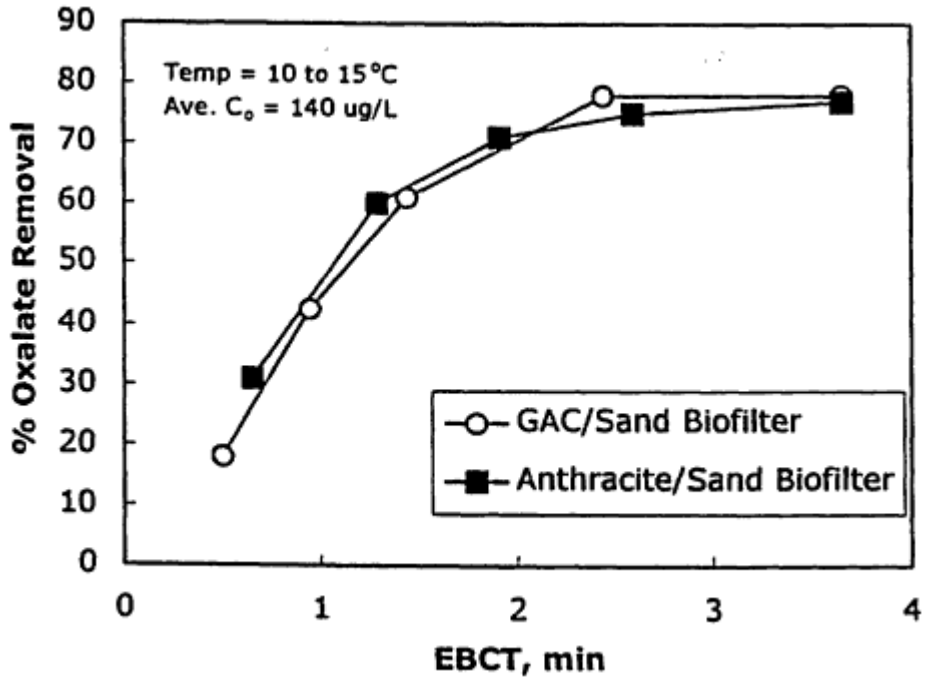

Figure 11-6
Impact of media type and EBCT on the removal of oxalate by biological filtration

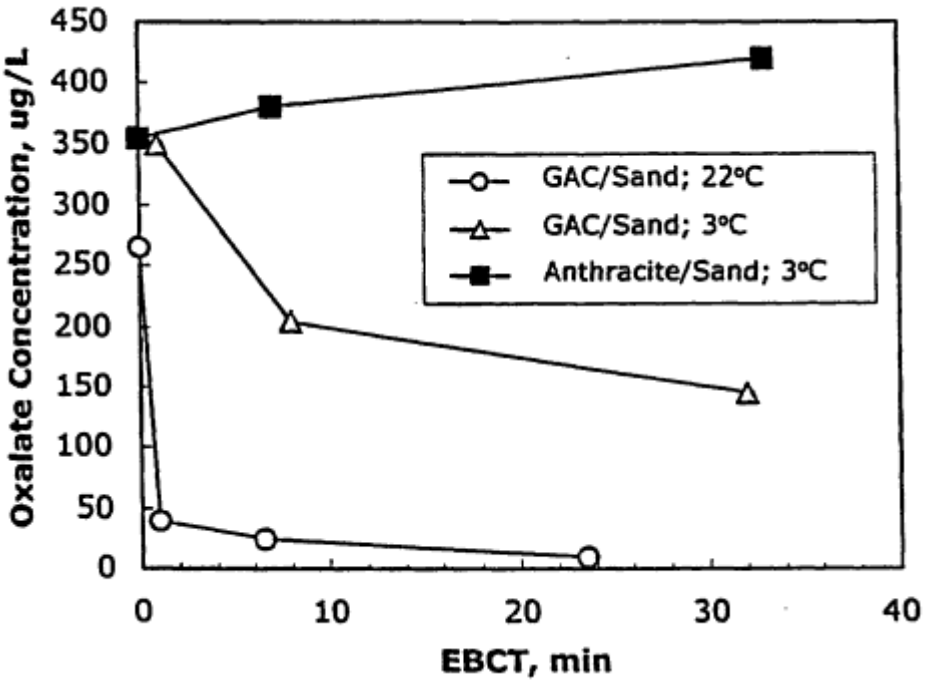

Figure 11-7
Impact of water temperature and EBCT on the removal of oxalate by biological filtration.

performance of biological filtration (Coffey et al., 1997; Emelko et al., 1997). Figure 11-6 shows that under warm-temperature conditions (10 to 15°C), the biological removal of oxalate (a byproduct of ozonating natural water) by GAC or anthracite filters is virtually identical. Figure 11-6 also shows that under warm-temperature conditions the majority of the oxalate removal occurs within two minutes of EBCT. Figure 11-7 shows that only under cold-water temperature conditions (1 to 3°C) was the biological removal of oxalate by GAC filters substantially higher than that by anthracite filters. Figure 11-7 also shows that under cold-water temperature conditions an EBCT in excess of 10 minutes may be required to achieve high removal of oxalate. The general trend in the design of biological filters is to include a shallow sand layer (6 to 12 inches) under the GAC or anthracite media. This sand layer serves as a partial barrier against the breakthrough of biomass into the filter-effluent water. Biological filters are operated the same as conventional dual-media filters, with the exception that no chlorine or chloramine is present in the influent water to the filter. However, there are unanswered questions about the proper backwashing procedure for biofilters. Some plants have determined that intermittent addition of 4 to 5 mg/L of chlorine to the backwash water (about once every third backwashing) can help control the biological culture in the filter, prevent the growth of multicellular organisms in the filter, and increase filter run lengths by reducing the headless buildup rate (S. Teefy, Alameda County Water District, Fremont, Calif., personal communication, 1998). Additional work is required to address operational issues of biofiltration processes.

The use of biofiltration in drinking water treatment opens the door to new and innovative applications of this process. Biofiltration can be used for the biological reduction of various inorganic contaminants such as nitrate, bromate, perchlorate, chlorate, and selenate. However, its use for these applications still requires a substantial amount of research and engineering and is far from being ready for implementation at large municipal scale.

CONCLUDING REMARKS

Historically, the water industry has adapted to new technologies at a slow, incremental pace. In the past 20 years there has been a rapid entry of new technologies that continue to be developed, tested, demonstrated, and introduced into the municipal water treatment market. Some of these technologies are membrane filtration, UV irradiation, advanced oxidation, ion exchange, and biological filtration. These are certainly not the only technologies being considered by the water treatment industry. However, they have come a long way toward demonstrating their reliability and applicability to large-scale municipal water treatment plants. As the cost of these technologies continues to decrease, their applicability will steadily increase.

There is almost no contaminant that cannot be removed from water. The question becomes that of cost. As alternative water resources become increasingly less available, the need for innovative and cost-effective treatment technologies will rise steadily.

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12

Emerging Drinking Water Contaminant Databases: A European Perspective

Walter Jülich

Drinking water production in Western and Central Europe has its similarities and dissimilarities compared with the situation in North America. Groundwater is heavily utilized in certain regions, whereas others depend on the availability of surface water from lakes and rivers. Chlorination is avoided as far as possible; slow sand filtration or bank filtration is the method of choice, followed by advanced treatment such as activated carbon, ozonization, and at some places membrane filtration.

Groundwater, if unpolluted, is preferred. Lake water is often remarkably free of chemical pollutants but has its own biological problems (growth of microalgae or cyanobacteria), whereas river water is often quite heavily polluted and in need of various treatment steps.

The quality of drinking water and the number of contaminants that might be encountered in it strongly depend on the quality of the raw water (except for disinfection byproducts). The quality of the raw water in turn depends not only on chemical and biological properties (which are influenced by industrial activities, effluents of municipalities or runoff from agriculture) but also recreational activities, shipping routes, river bank structures and so forth. So, at least in Western Europe, databases are rarely used for drinking water parameters only but invariably contain millions of data on raw water too. That is the reason I would like to concentrate here on both aspects, since most contaminants that we encounter in raw water can find their way to drinking water, at least if treatment fails.

BACKGROUND

As secretary of the International Association of Waterworks (IAWR) in the Rhine basin and director of the Dutch-Belgian Association of Waterworks, I am particularly familiar with the situation in Western and Central Europe and base this paper on my experiences in these regions. It can safely be stated that the most advanced treatment of surface water for the production of drinking water can be found in this part of Europe (Switzerland, Germany, France, and the Netherlands). Also, there is probably no other river in Europe that for decades

has been so intensely monitored for hundreds of parameters. According to a recent list of the Association of Rhine and Meuse Waterworks (RIWA), more than 1,200 chemical substances have been detected in Rhine water and/or drinking water. Not surprisingly, database structure and development are important for those waterworks associations and follows modem lines of thinking.

The Rhine Catchment Area

Reasons for this preoccupation with the Rhine is the special situation of its basin. The Rhine River is not only one of the major rivers of Europe, but its river basin is also the most densely populated and most heavily industrialized area in Europe. The catchment area of the Rhine belongs to eight different countries.

After World War H when industrial activities started again and wastewater treatment was almost unknown, the waterworks in the Rhine basin became worried. Since they did not expect fast results from governmental activities, they decided to start their own monitoring programs along the Rhine and Meuse rivers and the important lakes and tributaries. The intention of the waterworks was not only to measure the extent of the pollution but also to confront industries and governments with the data and to demand the elimination of toxic or other relevant substances, especially those that are not biodegradable.

Out of necessity, the 120 waterworks in the Rhine basin, belonging to eight different countries, created an international association (the IAWR) specifically for the catchment area of the Rhine. All waterworks are also members of their national waterworks association, but they needed a second, more specialized, association for the problems of their own river basins. Nowadays it is modem to speak about policies based on river basins, but 40 years ago this was quite unique.

Governments were and are of course important because of the regulations and laws that are issued, but they were not very active in finding and inhibiting pollution. The waterworks associations were much more active in this field: apart from monitoring water quality at many places, staff members also went by boat to relevant emission points of industries or communities to find the sources of pollution. And they could do what no government institution could: cross the border and take water samples in a neighboring country.

This would in itself not be enough because detecting the source of pollution and filling the database is one thing but eliminating the pollution is another matter. Discussions with industries or governments could take days or weeks but were always successful if the polluting substances could be traced in drinking water and were toxic. The reason for success was that in such a densely populated area the general public is very sensitive about the purity of its drinking water. The pressure on industries and governments would have been enormous, if the waterworks associations had to publish in the newspapers that their

demands were refused. Thanks to the efforts of the international associations of waterworks of this area, the International Rhine Commission, and numerous discussions with industries and governments, the water quality of the Rhine has improved dramatically.

Drinking Water Production in Western and Central Europe

One short remark concerning the possibility for drinking water contaminants may be useful. When the Romans conquered part of the Rhine valley (nearly 2,000 years ago) they had the problem of finding drinking water. They never used river water directly; they also did not like to dig wells near rivers but preferred to build aqueducts that carried water from the mountains to the valley. Also nowadays, large cities to small villages all use either deep groundwater (about 50 to 300 m deep) or riverbank filtration. Numerous studies have shown that even severe accidents of chemical industries will not make the bank filtration water useless, since normally not more than one percent of the pollutant or even much less will be found in the wells. What hurts are high constant levels of pollution.

Thus, large cities like Cologne or Dusseldorf, producing drinking water for one million inhabitants each, use bank filtration, while cities such as Bonn derive their water from reservoirs in the mountains. Also in the Netherlands, river water is not directly used. The city of Amsterdam, for example, pumps Rhine water from the center of the country via a 60-kin-long pipeline to the dunes near Amsterdam, where it is infiltrated and passes through thick layers of sand; after about three months the water is pumped up again and treated. All larger waterworks in the Rhine catchment area use rapid and slow sand filtration, activated carbon, and ozone for disinfection. Chlorine as a disinfectant is avoided and cities such as Amsterdam have not used it for at least 10 years.

Monitoring and Databases in Western Europe

Since almost SO years we find a parallel development as far as the monitoring efforts and the development of databases are concerned. The waterworks associations concentrated on raw water and drinking water, the governments concentrated on raw water, sediments, and many other aspects that concern water from rivers, lakes, or groundwater. As a result, monitoring programs of the governments contain many more aspects but analyze fewer contaminants in raw water and nothing in drinking water. Databases of waterworks are often more specialized for water parameters and more flexible and less cluttered with other datasets.

In recent years, collaboration between waterworks associations and government institutions has improved, particularly in the Netherlands, where according to an agreement between RIWA (waterworks) and RIZA (government), relevant water contaminants are analyzed by only one of both organizations, depending on the monitoring station. A free exchange of data ensures that both sides can utilize the results in their publications.

THE STRATEGIC POSITION OF DATABASES

A database with records concerning water quality should not be established without a purpose. It is an important part in a sequence of events, from questions to meaningful answers, but not an endpoint:

- Question: Usually the process starts with a question about water quality at a given location. If a river is concerned, the answer would be insufficient if only the water quality at the spot were analyzed because a second question would then inquire about the source of the pollutant, which is probably farther upstream.
- Monitoring: A monitoring program must therefore be specified that contains the strategic position of the monitoring points (e.g., at the border of a country or near emissions pipes of industries or bigger cities), the frequency of monitoring and the possibility of seasonal influences (such as climate, seasonal use of pesticides, or batch production in industries), the parameters that should be analyzed, and the appropriate analytical methods.
- Database: The data shall be placed in a database in such a way that they remain meaningful and are easily extracted. Since the structures of databases are not easily changed, the definition of fields, possible ways of input, connection with other programs and output by way of tables, graphs, and so forth must be thoroughly discussed. A database is nothing but a tool that stores datasets and keeps them available. Often, the analytical data alone do not give an answer to the original question because they must be interpreted and discussed together with other factors.
- Interpretation: Interpretation of data is the next step, taking into account the detection limit of the analytical method, the recovery rate, plausibility of the result, and so forth.
- Integration: This is followed by integration with other facts or factors, such as limiting values concerning human health or ecotoxicology, presence of other contaminants with similar or antagonistic behavior, biological or chemical degradation, and the influence of radiation. A given contaminant is not regarded as being isolated from the rest of the waterborne pollutants but is part of a much larger group of substances or organisms.
- Answer: Finally, an answer is given that (under ideal conditions) not only contains the concentration of a certain substance in water but gives an interpretation of the data as far as the methods are concerned and places these data in a broader context of health-related information and possible synergistic or antagonistic effects.

A DATABASE FOR WHOM?

Water quality monitoring and storage of data depend on who is interested. Most decision makers in governments are chiefly interested in information that determines whether a policy and the subsequent management program are actually achieving the desired results. Waterworks, on the other hand, may only be interested in those parameters for which limiting values exist. Also, politicians may find other parameters important but sometimes not for a long time. Interest can shift from one legislation period to another, depending on scientific insight, changing requirements, or pressure by action groups.

Thus, in the Netherlands, interest is shitting from contaminants in water to those in sediments, and ecological and ecotoxicological studies are now high on the priority list. In former years government institutions in the Netherlands studied roughly the same parameters as the waterworks (such as chloride, nitrogen, phosphate, heavy metals, and pesticides); now they concentrate more on substances in sediments (and try to use mathematical modeling to enable them to calculate the concentration of a substance in the water phase). Biotests or the study of contaminants in biota or the food chain gain more and more importance.

Growing costs and shifting priorities make the work with mathematical models more important. Based on the concentration of a contaminant in sediments, the concentration in water is calculated. The results will also be stored in databases under the name of the parameter. In this case it is important to make a reference to the mathematical model that has been used and also to the sediment data, in case a better model can produce more accurate predictions of the concentrations.

CONTENTS AND USES OF DATABASES

Databases have several purposes: they are filled with relevant information on physical properties, chemical substances, (micro)biological data, limiting values, etc.; a query makes it possible to obtain the raw data; connections between parameters or monitoring points should be possible; calculations and statistical operations should be possible; and output in form of tables or graphs is standard. Databases are used to check the status quo (e.g., the drinking water quality at a certain moment); for operational purposes (how water treatment is performing); to determine trends over months or years; to show the parallel development of certain parameters (e.g., orthophosphate and total phosphate) or the interdependency between parameters (e.g., oxygen concentration and dissolved organic carbon); and to check whether regulations (e.g., concerning waste water treatment or nitrogen removal) are effective.

Depending on the interests of a person who asks a question, a database must contain different sets of data: for a trend analysis over decades, one analysis per week or month can be sufficient (depending on the parameter); for operational purposes, continuous measurements every 10 minutes or every hour might be necessary; and in other cases the mere presence or absence of a parameter (perhaps above a limiting value) might already be sufficient.

"DECISION MAKERS" AND THEIR RESPONSIBILITY

An old-style decision maker simply wanted to know "everything" because he felt responsible. In those days hundreds of pages were filled with tables containing thousands of data. More often than not a good decision was not really possible. A well-filled database was the basis for these reports.

A modern-style decision maker has no time, hates voluminous reports, and wants the information preferably on one page, accompanied by a graph and a few figures enabling a "yes" or "no" answer. How many data are necessary for such a report? Can a database give an complete answer? Here, I think, interpretation of data and integration with other aspects gains importance; a database report in itself may not be sufficient.

Formerly, a report consisted of datasheets listing the analytical data of all parameters that had been analyzed. The database had to produce these reports based either on actual measurements or statistical data such as monthly averages, minima and maxima, percentiles, and so forth. It was hoped that these reports fulfilled a need.

Nowadays a decision maker is not interested in all data of all parameters; there are only some general questions and a request for an answer, based of course also on the contents of databases. Questions such as these require an answer:

- Is this country safe, now and in the future, or are there problematic spots on the map?
- Can drinking water be produced from surface water or groundwater? Is this water safe and healthy? What is the relationship between the costs of treatment and pollution? Are there dangerous substances in water and what are the health risks? Who is producing these contaminants and why?
- Will the natural environment be the same for future generations? Will it improve or deteriorate and why? Can this process be stopped?
- Can people swim in waters without health risks?
- What is the effect of climate changes of longer periods? How does it effect water availability and quality? Is drinking water safe?
- Will there be enough water of sufficient quality for people, shipping purposes, power plants, industries, and agriculture? Which sector has priority?

For a politician these are important questions and a thorough answer is expected. This should be easy, one assumes, because databases contain the results of monitoring efforts for which millions have been paid.

FORM DATA TO INFORMATION

To get information, you need data. For every piece of information the right number of data is required. Less data would make the information fragmentary or would produce perhaps no information at all. A huge number of data might, on the other hand, not produce more information; it would simply be a waste of time and money. Thus, a question about the water temperature of a certain place, date, and time could be based on one analytical record in the database, whereas a comparison of the average water temperature of two years would be based on two statistical operations, which use a dataset of perhaps only 12 measurements per year (one per month) or literally thousands of data per year.

The number of analytical data thus depends obviously on the precision that is required and the situation in the area. To measure the water temperature of the Congo River every 10 minutes would be nonsense, since it doesn't change much in that country. To measure the temperature of the Rhine every 10 minutes would also be nonsense for most questions, although it differs considerably during the seasons, but we know already that the pattern doesn't change much over the years or decades. On the other hand, if contaminants must be detected that are released in batches by unknown industries, much more data may be required.

Accordingly, there is no general rule concerning the amount of data required for meaningful information. It depends on the country, the situation, the contaminants, and the questions that are likely being asked. As far as a database is concerned, it should be able to harbor a large number of records (on the order of millions), respond in a flexible way to the information needs of today and tomorrow, and connect well to other software programs.

Short- and Long-Term Questions

Short-term questions are related to everyday decisions: these concern either questions about the status quo of a water source or comparisons between conditions of recent years. Long-term questions concern, for example, predictions of the water flow of a river (depending on all possible criteria such as water usage by industries or agriculture up to discussions about climate changes); trends in water quality and future impacts (e.g., concerning population growth, higher demands, new scientific results concerning toxicology); trends in biological species composition, population growth of water biota, indication of adverse factors; development of riverbeds and riverbanks in time, influence of sea-level rising; rivers and lakes as commercial shipping routes; and development of recreational shipping and its influence on water quality, biological diversity, and structure of riverbanks and bank vegetation.

Data Collection: Systematic or Pragmatic Approach

A systematic approach covering all kinds of aspects would require a database that has been structured in such a way that it can contain a wide variety of data for which questions have actually been asked or might be asked in the

future. It would contain billions of data, most of which will never be extracted, but it hopefully will contain some data for most questions.

The pragmatic approach will not gather all data. Instead, it mainly concentrates on present needs and expectations. Many inquiries that are now of interest (e.g., concerning ecology, endocrine disruptors, etc., were not asked 20 years ago; consequently, our dataset is very limited. Also, many questions have only been possible because of the advancement of analytical methods, and also in this case older data are lacking.

That is the reason why a more pragmatic approach gains ground: the problem-oriented approach. In river systems such as the Rhine, where water quality has improved considerably over the past two decades, water quality still is the daily bread for waterworks but not for governments. The latter are nowadays more interested in the quality of river sediments, since the sediments act like a sink containing all kinds of undesirable chemical substances of the past, which are slowly released into the environment—effects that are all the more noticeable because of the much improved water quality. Thus, interest is gradually switching to new matrices, and the study of older parameters or former matrices is reduced.

DESIGN OF DATABASES: HISTORY AND MODERN DEVELOPMENTS

Old-Style Database Design

Years ago—and here I speak of personal experience in our waterworks associations—a database was programmed by a specialist who often belonged to the computer department of an institute or came from a company specializing in databases. During that time, computer departments were powerful parts of the institute; they decided which hardware and software had to be used and often had a preference for programming the database entirely themselves.

Often a tailor-made database was created for the special needs of that time. More often than not, only the programmer knew the details, and he was often the only person who could change or adjust the database. Generally, a precise description of the structure was missing or was not adjusted in subsequent years, and the source code was usually not available for other specialists. Frequently, additional parts of the database program were written in different programming languages, depending on the knowledge of the programmer at the time and the availability of new programming languages over time.

Mainframes or minicomputers were bought, running under Unix or similar systems, and installed in special air-conditioned rooms and could be operated only by specialists. Queries had to be written in SQL, a language normally not mastered by a decision maker. The production of tables, graphs, or other forms of output also required a specialist.

New-Style Database Design

Changes took place that affected the well-being of the computer departments and could only be brought about after years of heated discussions. The important questions centered not so much on the design and integrity of the new-style database but on the users. In our case it was mandatory that even a secretary be able to extract data without the help of a specialist.

A modem database should be user friendly (can be utilized by all authorized persons, from secretary to director); flexible (can be easily adjusted or rebuilt, depending on future demands); based (preferably) on powerful PCs (no longer minicomputers or mainframes); available in a PC network or on standalone PCs; able to insert new data automatically via modem or from disks (no specialist required); and able to produce tables or graphs via query by example.

The database of the RIWA-IAWR is a modem example: it works on powerful PCs under Windows 95 or NT; its structure is modular, consisting of a core database for raw data, surrounded by a variable number of specialized modules (e.g., for production of tables or graphs, calculations, statistical methods, trends, detection of extreme values, monitoring schemes); it is based entirely on existing programs such as Access for the database and parts of the graphs, Word for texts, Excel for tables and other graphs, statistics programs, and so forth; programming was only necessary to interconnect the commercially available software; the structure of the database and its modules is documented, and the documentation is constantly kept up to date; and the source code is available.

DATABASE OF THE ASSOCIATIONS OF RHINE AND MEUSE WATERWORKS (RIWA)

The databases of the waterworks associations in Amsterdam (RIWA) and Karlsruhe (TZW, Germany) have similar structures and philosophies. The database at TZW is still being developed; therefore, I shall give some comments based on the RIWA database, which has existed for several years:

- Number of parameters: there are about 1,500 parameters in the database, and the number is constantly growing.
- Code: all parameters have a four-digit number for the concentrations of a chemical substance (e.g., 0230 for chloride in µg/L) or for the numbers of biological entities per 100 µ/L (e.g., bacteria, oocysts of *Cryptosporidium*); other laboratories use five digits.
- Entity: the entity is an integral part of the parameter; thus, arsenic in micrograms per liter would be another parameter than arsenic in ng/L; entities are not uniform in laboratory information management systems (LIMS)—at least not in Europe; confusion can thus easily be avoided by treating them as different parameters; if necessary, automatic calculation is switched on to transfer data from the nanograms per liter to the micrograms per liter parameters.
- Control: Find extreme (and probably faulty) values; this is either done by a special module that produces a report or visually by controlling the graphs of

all parameters for all monitoring places in a certain year, a graph-module produced all necessary graphs during the night, which are then placed on the screen in intervals of 5 seconds; about 700 graphs can be checked visually per hour. The complete monitoring network can thus be checked within one or two days.

- Validation: After validation of the data at the end of the year, the dataset for the year is closed and changes in the dataset can only be inserted by a few authorized persons.
- Statistics: After validation the normal statistical calculations are carried out (e.g., minimum, average, maximum, means, percentiles). The resulting data are preserved in the database and are thus quickly available.
- Reports: For reporting purposes the report module produces the tables of our yearbooks. Several other formats are already fixed, and every user can easily build his or her own format (query by example).
- Graphics: Graphs can contain the data of one or several years, with or without the relevant limiting values. Boxplots are built in and so is the possibility for combining datasets of one parameter but from different places or datasets of different parameters from the same location.
- Export: Datasets, tables, and graphs can be exported as comma or tab delimited ASCII-file or as Word or Excel-file for use in other programs.

Delivery of Raw Data

Since data are coming from about 20 different laboratories or institutions, using many different LIMS or database engines, we had two choices: (1) either ask that the requested data be delivered in a certain format that we would define, or (2) allow the data to be delivered in the default format of their system and create a conversion program for each data format at our place. The first option would have been easier for us, but it did not work. So we decided to adapt ourselves and accept all kinds of formats provided the format of a lab remains the same for at least one year and we are notified about format changes. To everyone's satisfaction, this works perfectly.

NEW DEMANDS FOR DATABASES

For New Contaminants

Most databases have been built for chemical parameters but often include colony counts of bacteria. Our database is no exception. This poses the question whether new contaminants can be incorporated or not. As long as the presence of these contaminants is reported in concentration per volume or number per volume, there should not be a problem. This is probably the case for the majority of new contaminants, whether they are new chemical substances, medicinal drugs

in water, chemicals acting as endocrine disruptors, or the counts of *Cryptosporidium* and *Giardia* in water. Also, parameters such as the mutagenicity of water pose no problem if expressed in revertants per volume.

Other characterizations of raw water or drinking water are often not preserved in the computer but are kept in a graphical way: the movements of daphnia or mussels are recorded as graphs and are usually kept in this way only. It would nevertheless be possible to keep the underlying data in the computer and to produce the graph anew if necessary. Many other biotests that produce a yes/no answer can also be stored in the database. However, the use of computers in storing data from biotests is often not regarded as necessary. If performed on a more regular basis it would make one problem very clear: the almost complete lack of standardization, which does not allow the biotest results to be compared—at least not in the way it is done with chemical parameters. But this may be merely a matter of time and agreement.

Biological Databases

Biological data in the classical sense of the word are often placed in specialized databases, not together with chemical parameters. The reasons for this are that thousands of names can be involved if algae and invertebrates are studied; synonyms should be inserted and kept up to date, since in older literature different names are often used for the same taxon; and a hierarchical structure is wanted that shows the relationship between taxa (not only an alphabetical list of unrelated names); the systematics must be updated.

Databases for Screening Purposes

Another specialized part concerns the screening of water sources using either gas chromatography/mass spectroscopy (GC/MS) or liquid chromatography/mass spectroscopy (LC/MS) fingerprint methods. GC/MS produces a spectrum of many peaks of substances. Depending on the source, some or many of the more prominent peaks can be identified; others belong to unknown substances. With the amazing progress in analytical methods, some of these peaks will be identified in later years, and it would be valuable to compare the new results with older GC/MS spectra.

To facilitate this study, the Dutch organization of waterworks has built a database (called Infospec) that can hold all of the relevant data of the GC/MS spectra and can (retroactively) attach a name to them if the underlying substance is recognized. This program works independently but can be connected to the normal database. The program was developed by KIWA for PCs under DOS. The new version will run under Windows and is a joint effort of KIWA (for the Dutch waterworks) and RIZA (for the Dutch government). It will be used in the whole Rhine catchment area and will also be available worldwide.

How Many Databases Are Necessary?

In former days, and many government institutions still work the same way, there was one single database to hold all the data that were thought to be valuable or necessary. These were very complicated databases indeed and not at all flexible. Nowadays, at least as far as the waterworks associations in Western and Central Europe are concerned, smaller, more specialized, databases are preferred. Based on PCs under Windows, with a modular structure they are user friendly and easy to maintain. Classical databases (containing chemical and microbiological parameters), biological databases, and the so-called Infospec database for GC/MS screening can easily be combined in a network if the structure (modular concept) and the interface are properly designed.

FROM DATA TO INFORMATION

As noted earlier, information is a much advanced stage and is reached after evaluation of datasets and integration with other aspects. Modem decision makers rely on information, whereas tables with raw data (the original product of a database) are relevant on the working floor and in the hands of specialists.

Information is not easily obtained. Many different databases and a lot of expertise are necessary. The information, once given, may be sufficient for a politician, but for a scientist it is often useless since no reference is made to the data that have been used. Many of the modem reports of governmental institutions are therefore difficult to follow: the message may be clear but not the underlying. That may be the reason that in Europe data must be available on a much broader scale. Some countries (such as Germany) are very reluctant to put raw data on disks, CDs, or the Internet; others (e.g., the Netherlands) prefer to open the databases to the public.

The waterworks in the Netherlands, for instance, always had a policy to publish all data. Nothing was kept secret, even disturbing facts. As a consequence people trust their waterworks. They know the waterworks associations are active and alert and will do everything in their power to change the situation for the better.

All countries, however, regardless of their policies concerning the availability of data, fear that raw data can be interpreted in a very different (and sometimes wrong) way by an average citizen in the streets. They are therefore trying to find better ways of communication. At present, many different graphical ways are explored that could deliver meaningful information, not just of raw data, and of course in dealing with Europe each country does it in a different way.

SUMMARY

The old graveyards of data, held in mainframes or minicomputers, are a chapter of the past. Specialized databases—for instance, for chemical, biological, or GC/MS-data—are developed under Windows and kept in local networks. The structures must be as flexible as possible, based on specialized modules surrounding a database core. Reporting facilities have become a matter of utmost concern, and the information to the general public must follow the modern lines: from reports to disks, CD-ROM, and the Internet.

Appendix

Biographical Sketches of Committee Members and Staff

Warren R. Muir, Chair, is president of Hampshire Research Institute, Inc., a nonprofit organization in Alexandria, Virginia, and Hampshire Research Associates, Inc., a scientific and engineering consulting firm. Both organizations study issues relating to pollution prevention, risk assessment, and the use of data and information to promote environmental goals. He has held positions as senior staff member for environmental health for the Executive Office of the President, Council on Environmental Quality; deputy assistant administrator for testing and evaluation at the U.S. Environmental Protection Agency; and director of EPA's Office of Toxic Substances. Dr. Muir chaired the NRC Toxicology Information Committee, currently serves as a member of BEST, and has served on several other committees. He received a B.A. in chemistry from Amherst College and M.S. and Ph.D. in chemistry from Northwestern University.

R. Rhodes Trussell, Vice-Chair, is the lead drinking water technologist and director for corporate development at Montgomery Watson, Inc. Dr. Trussell serves on the EPA Science Advisory Board's Committee on Drinking Water. He has served on several NRC committees and is a member of the National Academy of Engineering. Dr. Trussell received his B.S. in civil engineering and his M.S. and Ph.D. in sanitary engineering from the University of California, Berkeley.

Frank J. Bove is a senior epidemiologist for the Epidemiology and Surveillance Branch of the Division of Health Studies, Agency for Toxic Substances and Disease Registry. Dr. Bove has published several papers and reports on the epidemiology of exposure to drinking water contaminants and related adverse health effects. He received a B.A. in political science and philosophy from the University of Pennsylvania and an M.S. in environmental health science and an Sc.D. in epidemiology from the Harvard School of Public Health.

Lawrence J. Fischer is a professor in the Department of Pharmacology and Toxicology and is the director of the Institute for Environmental Toxicology at Michigan State University. His primary research interest is biochemical toxicology. Specific research includes absorption, distribution, metabolism, and excretion of drugs and chemicals and toxicity of chemicals to the endocrine pancreas (gland). Dr. Fischer received his B.S. and

M.S. in pharmacology from the University of Illinois and his Ph.D. in pharmaceutical chemistry from the University of California, San Francisco.

Walter Giger is a professor and senior scientist in the Chemistry Department at the Swiss Federal Institute of Environmental Science and Technology. His research, teaching, and consulting activities focus on organic compounds in the environment and in the geosphere. Research topics include development of analytical techniques for identification of organic pollutants in drinking water, wastewater, and natural waters; investigation of sources, occurrences, and fate of organic pollutants in wastewater and drinking water, and evaluation of chemical, physical, and biological processes that determine the environmental fate of chemicals. Dr. Giger received his B.S. and Ph.D. in chemistry from ETH Zurich.

Branden B. Johnson is a research scientist in the Division of Science and Research at the New Jersey Department of Environmental Protection. His research interests and work activities include broad areas of risk communication, risk perception, natural and technological hazard management, and environmental policy. Dr. Johnson is currently involved in research related to the Consumer Confidence Report requirements of the Safe Drinking Water Act Amendments of 1996 and public reaction to information on *Cryptosporidium* in drinking water. He received a B.A. in environmental values and behavior from the University of Hawaii, Manoa, and an M.A. in environmental affairs (water resources) and a Ph.D. in geography from Clark University.

Nancy K. Kim is director of the Division of Environmental Health Assessment of the New York State Department of Health and is an associate professor in the School of Public Health at the State University of New York, Albany. Her research interests include chemical risk assessment, exposure assessment, toxicological evaluations, structural activity relationships, and quantitative relationships among toxicological parameters. She received her B.A. in chemistry from the University of Delaware and her M.S. and Ph.D. in chemistry from Northwestern University.

Michael J. McGuire is president and founder of McGuire Environmental Consultants, Inc., in Santa Monica, California. The firm provides consulting services to public water utilities and industries in the areas of Safe Drinking Water Act compliance and water treatment optimization. Prior to forming his own corporation, he was assistant general manager of the Metropolitan Water District of Southern California. Dr. McGuire received his B.S. in civil engineering from the University of Pennsylvania and his M.S. and Ph.D. in environmental engineering from Drexel University.

David M. Ozonoff is a professor in and chair of the Department of Environmental Health in Boston University's School of Public Health. His research work centers on health effects to communities of various kinds of exposures to toxic chemicals; new approaches to understanding the results of small case-control studies; and the effects of exposure misclassification in environmental epidemiology. He has studied public health effects resulting from exposure to a number of contaminated sites. Dr. Ozonoff received his M.D. from Cornell University in 1967 and his M.P.H. from The Johns Hopkins School of Hygiene and Public Health in 1968.

Catherine A. Peters is an assistant professor in the Program of Environmental Engineering and Water Resources in the Department of Civil

Engineering and Operations Research at Princeton University. Her research interests include the behavior of multicomponent organic contaminants in the environment, with particular emphasis on non-aqueous phase liquids (NAPLs); innovative mathematical modeling approaches for characterization of chemical heterogeneity of pollutants; and risk-based decision making for complex multicomponent contaminants. She received her B.S.E. in chemical engineering from the University of Michigan and her M.S. in civil engineering and Ph.D. in civil engineering/engineering and public policy from Carnegie Mellon University.

Joan B. Rose is a professor in the Marine Science Department at the University of South Florida. Her research interests include methods for detection of pathogens in wastewater and the environment; water treatment for removal of pathogens; wastewater reuse; and occurrence of viruses and parasites in wastewater sludge. Dr. Rose served on NRC's Committee on Wastewater Management for Coastal Urban Areas and the Committee on Potable Water Reuse. She received a B.S. in microbiology from the University of Arizona, an M.S. in microbiology from the University of Wyoming, and a Ph.D. in microbiology from the University of Arizona.

Philip C. Singer is a professor in and director of the Water Resources Engineering Program at the University of North Carolina, Chapel Hill. Dr. Singer was formerly a member of NRC's Water Science and Technology Board and served on the Committee on U.S. Geological Survey Water Resources Research. A member of the National Academy of Engineering, he has published dozens of papers and reports principally concerned with aspects of water chemistry and drinking water quality. He received his M.S. and Ph.D. in environmental sciences and engineering from Harvard University.

Deborah L. Swackhamer is an associate professor in the Division of Environmental and Occupational Health in the School of Public Health at the University of Minnesota. Her research involves assessment of contaminants in the environment and associated risks to public health and the environment. She has published dozens of papers on topics ranging from inventories of xenobiotic organic compounds in the Great Lakes, to analytical methods for contaminant detection, to bioaccumulation of organochlorine compounds in fish and multimedia approaches for modeling human exposure. She has served on the executive committee of the Division of Environmental Chemistry of the American Chemical Society, the Board of Directors of the International Association for Great Lakes Research, and the Science Advisory Committee of EPA's Great Waters program. She was a member of the National Research Council's Committee on Coastal Oceans. Dr. Swackhamer received her M.S. in water chemistry and her Ph.D. in oceanography and limnology from the University of Wisconsin, Madison.

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