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EPA

AN SAB REPORT: REVIEW OF THE RESEARCH PLAN FOR MICROBIAL PATHOGENS AND DISINFECTION BYPRODUCTS IN DRINKING WATER

REVIEW BY THE DRINKING WATER COMMITTEE (DWC) OF THE SCIENCE ADVISORY BOARD

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

February 28, 1997

OFFICE OF THE ADMINISTRATOR
SCIENCE ADVISORY BOARD

EPA-SAB-DWC-97-003

Honorable Carol M. Browner
Administrator
U.S. Environmental Protection Agency
401 M Street, SW
Washington, DC 20460

Subject: Review of the Research Plan for Microbial Pathogens and Disinfection Byproducts in Drinking Water

Dear Ms. Browner:

At the request of the Office of Research and Development (ORD), the Drinking Water Committee (DWC) of the Science Advisory Board reviewed the Agency's Research Plan for Microbial Pathogens and Disinfection Byproducts in Drinking Water. The Committee met to consider the plan during November 1995, March 1996, and July 1996. The DWC approved this report on December 30, 1996 and the Executive Committee approved this report on January 15, 1997.

The Agency charge to the Committee was to review the research plan and to provide advice on whether:

a) EPA had identified the correct research issues to support the development of the Interim and long term Enhanced Surface Water Treatment Rules, Ground Water Disinfection Rule, and Stage 2 Disinfectant/Disinfection Byproducts Rules;

b) The research topic areas or projects underway, or envisioned under the five-year plan, appear to adequately address the issues, and if not, should any other research topic area be funded in lieu of or in addition to those presented; and

c) EPA assigned appropriate priorities to the research?

The Plan was developed cooperatively between representatives of the Office of Research and Development and the Office of Water pursuant to the vision and general procedures contained in the Strategic Plan of the EPA Office of Research and Development. The Drinking Water Committee appreciates the opportunity to comment on this research plan. The Committee recognizes the magnitude of the effort and congratulates those within the Office of Research and Development and the Office of Water who have labored to create and coordinate this complex project. Their efforts have resulted in a plan that is much improved

over previous drafts which have been reviewed by the Drinking Water Committee.

Even though it notes the Agency's considerable progress with this research plan, the Committee is concerned that the short and long-term resources devoted to this plan will not be adequate to address all of the urgent needs for the development and promulgation of effective and efficient rules for drinking water protection and for the development of cost-effective technologies for the control of drinking water purity.

Two of the Committee's comments address overarching issues with the plan. First, the plan does not provide sufficient information on many of the proposed research projects to permit the Committee to fully understand what is intended, the need for the project, and why some projects indicated as being of lower priority are underway while others of higher priority are yet to be initiated. Second, the Plan does not provide information that reflects the critical path and flow of research components, information which is necessary to show project progression and help to ensure that projects of greatest uncertainty and importance are accorded appropriate attention and placed in realistic time frames.

A number of specific comments that the Committee wishes to bring to the Agency's attention are contained in the following paragraphs. An issue, that is of extreme importance to risk-based rulemaking, is the identification and quantification of the occurrence and distribution of pathogens, and the risks they present, in drinking water. This research deserves special emphasis. Without this effort, the Agency's ability to target the most important health risks associated with drinking water pathogens will be diminished.

The Committee also believes that it is important to develop a mechanism to identify emerging waterborne pathogens and to conduct intensive research on them as necessary. The Agency should be proactive in this area and should establish a program that anticipates these types of emerging pathogenic microorganisms. There is also a need for a microbial epidemiological study in ground water systems that should include efforts to identify the pathogens responsible for the measured health effects.

Research needs in the area of microbial risk management include: effectiveness of treatment processes for *Cryptosporidium*, treatment technologies appropriate for small systems, and identification and characterization of factors influencing microbial growth in distribution systems along with strategies for its control. In fact, research on microbial contamination in distribution systems must be regarded as a high priority component of this plan.

The Committee believes that a critical area that has been overlooked is the need for methods to assess the reliability of treatment plants and individual treatment processes. The Committee also believes that additional research is needed on the reliability of multiple barriers of treatment including: watershed protection and pathogen monitoring, multiple chemical inactivation steps, and filtration and/or sedimentation in addition to chemical inactivation.

In the area of disinfection byproducts, the proposed reevaluation of existing epidemiologic research, should be assigned the highest priority from among the group of health effects research projects, if it can be completed in a time frame relevant to the rule making process. In addition, in order to perform risk assessments for disinfection byproducts, there is an

absolute requirement for exposure data and knowledge of human health effects. Currently, exposure data are inadequate, primarily due to the lack of methods for proper measurement. This suggests that the highest priority should be placed on the acquisition of such methods for both Stage I and Stage II Disinfectant Byproduct Rules.

A critical component of the research plan is a discussion of which of the three risk management options the Agency and the industry will endorse for control of disinfection byproducts. The options discussed in the plan are: removal before disinfection, removal after disinfection, and changing the disinfection process to minimize the formation of related byproducts. Removal before, and changing the disinfection process, appear to be the most promising options.

A number of risk management projects of high priority include: analytical methods for viruses, protozoa, natural organic matter, and chemical contaminants; methods for control of byproducts formed during treatment with ozone, chloramines, and chlorine dioxide; and projects on disinfection byproduct control (e.g., such as granular activated carbon, coagulation, oxidation and biological filtration, membrane technology and ultraviolet methodology). The Committee has provided comments on other projects contained in the research plan which are not highlighted in this letter; however, they are available for your review in the enclosed report.

In summary, the Committee felt that the research issues identified to support the five rules, and the research questions to respond to the issues, were appropriate and that the current plan reflects considerable progress over past versions of the plan. Attention to the comments highlighted in this letter and detailed in the report should result in research results which will enhance the scientific support for your rule making in this important area. The Committee looks forward to the response from the Office of Research and Development and the Office of Water to its comments on this research plan.

Sincerely,

Genevieve M. Matanoski

Dr. Genevieve M. Matanoski, Chair
Executive Committee

Verne R. Ray

Dr. Verne Ray, Chair
Drinking Water Committee

ENCLOSURE

NOTICE

This report has been written as a part of the activities of the Science Advisory Board, a public advisory group providing extramural scientific information and advice to the Administrator and other officials of the Environmental Protection Agency. The Board is structured to provide balanced, expert assessment of scientific matters related to problems facing the Agency. This report has not been reviewed for approval by the Agency and, hence, the contents of this report do not necessarily represent the views and policies of the Environmental Protection Agency, nor of other agencies in the Executive Branch of the Federal government, nor does mention of trade names or commercial products constitute a recommendation for use.

ABSTRACT

The Science Advisory Board's (SAB) Drinking Water Committee (DWC) reviewed the draft *Research Plan for Microbial Pathogens and Disinfection By-Products in Drinking Water* which was prepared by the EPA Office of Research and Development (ORD) and the Office of Water (OW). The Plan presented information on knowledge gaps relative to pending policy determinations and discussed specific research projects for microbial pathogens and for disinfection byproducts that would provide information to fill these gaps. Research was also discussed in relation to the five major drinking water regulations it is intended to support. The charge to the DWC asked if EPA had identified the correct research issues to support rule making, whether research topic areas and projects adequately addressed the issues, and whether EPA had assigned appropriate priorities to the research?

The DWC recognized the complexity of the plan and complimented the Agency on its efforts which resulted in a substantially improved research plan. The DWC also agreed that, in general, the research issues identified to support the five rules and the questions proposed in the research plan were appropriate.

The Committee asked a number of questions about the plan. Among other things, they noted the large number of high priority projects and apparent insufficient resources to fund them all, and questioned how the Agency decided which ones to fund and why some medium priority projects were funded (i.e., already underway) while many high priority projects were not funded.

The Committee offered a number of comments and recommendations intended to help focus, augment, and supplement the Agency effort to plan the development of knowledge essential for informed and scientifically accurate rule making. The DWC suggested that the plan would be clearer if the discussion on the purpose of the research plan, presented in Section IV, was moved to the beginning of the plan. The Committee stated that many of the project discussions were unclear and did not provide complete information on the planned efforts. Further, the Committee stated that the Plan lacked information on a critical path of project progression that would ensure that research projects of greatest uncertainty and resource requirements were accorded appropriate and primary attention and placed in a realistic time frame for overall research progress.

The Committee noted a disconnect between the priority pathogens for health effects research (i.e., Norwalk virus and *Cryptosporidium*) and the priorities of the occurrence research and that not enough emphasis was being given to microbial identification and occurrence research. In addition, they suggested that a critical area had been overlooked on methods to assess the reliability of treatment plants and individual treatment processes and that additional research was needed on the reliability of multiple barriers of treatment. The Committee also noted the importance of the reevaluation of existing epidemiology studies to ensuring that appropriate additional DBP health effects research was relevant to planned rule making.

The Committee recommended that greater emphasis be given to identifying and quantifying the occurrence of the key pathogens and the health risks they pose in drinking water in order to support risk based management of the highest risks. They also stated that it was important for EPA to develop a mechanism to identify "new" waterborne pathogens as they emerge. The Committee recommended that data be developed on the concentration of viruses in groundwater sources and that the development of rapid, reliable monitoring methods for waterborne pathogens should receive a high priority.

The Committee also noted the importance of proper design and operation of water treatment facilities to reducing waterborne illness. In that regard, the Committee stated that it was important to know the percentage of epidemic waterborne illness attributed to treatment process upsets in comparison to the percentage of endemic waterborne disease caused by pathogens passing through well-operated treatment plants. The Committee suggested that it might be more cost effective to improve operational reliability of water treatment than to require increasingly higher logs of pathogen removal/inactivation.

The Committee noted that EPA chose to place a medium priority on research projects related to the growth of bacteria in distribution systems. They agreed that projects related to heterotrophic bacteria in distribution systems, should not be the highest priority. However, in light of the information being obtained in studies on the role of the distribution system in endemic microbial disease, the Committee believed that it would be appropriate to place a higher priority on research of microbial contamination in distribution systems. Besides characterizing the biofilms in the systems, research is needed on the integrity of distribution systems and their vulnerability to pathogen introduction from cross-connections, line breaks, pressure drops, etc.

The Committee also noted the absolute requirement for exposure data, and knowledge of human health effects, in order to perform risk assessments for disinfection byproducts (DBPs). Further, the Committee noted that the overall challenge was not merely in writing a regulation to balance the costs of more disinfection with the benefits of fewer microbes. They suggested that the bigger challenge is to write a regulation that sets tough microbial standards and allows goals to be met at the lowest cost without allowing new, significant risks from chemical byproducts, particularly if those risks are of greater importance than the microbial risk avoided.

Key Words: Drinking water, disinfection, disinfection byproducts, microbial risk, pathogens

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Mrs. Mary Winston, Staff Secretary, Drinking Water Committee, Science Advisory Board (1400), U.S. EPA, 401 M Street, SW, Washington, DC 20460

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*Indicates consultant to the Drinking Water Committee.

GLOSSARY

AWWARF	American Water Works Association Research Foundation
BBDR	Biologically-based Dose Response
BM1	Benchmark Dose
EPA	US Environmental Protection Agency
DAA	Dichloracetic Acid
D/DBP	Disinfection/Disinfectant Byproducts
DWC	US EPA SAB Drinking Water Committee
ESWTR	Enhanced Surface Water Treatment Rule
EXD	Exposure Research, Disinfection/Disinfectant Byproducts Project
EXM	Exposure Research, Microbes Project
GAC	Granular Activated Carbon
GWDR	Ground Water Disinfection Rule
HAV	Hepatitis A Virus
HED	Health Effects Research, Disinfection/Disinfectant Byproducts Project
HEM	Health Effects Research, Microbes Project
ICR	Information Collection Rule
IESWTR	Interim Enhanced Surface Water Treatment Rule
NOM	Natural Organic Material
NWRI	National Water Research Institute
NOEL	No Observed Effect Level
ORD	US EPA/Office of Research and Development
OW	US EPA/Office of Water
PBPK	Physiologically-based Pharmacokinetic
PCR	Polymerase Chain Reaction
POE	Point of Entry
POU	Point of Use
QSAR	Quantitative Structure Activity Relationship
RAD	Risk Assessment Research, Disinfection/Disinfectant Byproducts Project
RAM	Risk Assessment Research, Microbes Project
RMD	Risk Management Research, Disinfection/Disinfectant Byproducts Project
RMM	Risk Management Research, Microbes Project
SAB	US EPA/Science Advisory Board
SWTR	Surface Water Treatment Rule
TOC	Total Organic Carbon

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1. EXECUTIVE SUMMARY

The EPA Office of Research and Development (ORD) and the Office of Water (OW) requested the Science Advisory Board's (SAB) Drinking Water Committee (DWC) to review a draft research plan for microbial pathogens and disinfection byproducts in drinking water. Following a series of preliminary presentations of the plan, a complete plan was presented in March, 1996. The DWC held a working session at a meeting in July, 1996.

The Drinking Water Committee appreciates the opportunity to comment on the Office of Research and Development's *Research Plan for Microbial Pathogens and Disinfection By-Products in Drinking Water*. Further, the Committee recognizes the magnitude of the effort and congratulates those within the Office of Research and Development and the Office of Water who have labored to create and coordinate a project of this complexity. The comments of the Drinking Water Committee are intended to help focus, augment, and supplement this effort that will have an important impact on the quality of U.S. drinking water by acquiring knowledge essential for a more informed and scientifically accurate implementation of the rule making process.

The Agency plan consists of four chapters, three appendices, and approximately 175 individual research projects that were intended to define the research needed to support EPA's development of drinking water regulations covering disinfectants, disinfection byproducts, and microbial pathogens. The regulations affected are the Stage I D/DBP rule, the Interim Enhanced Surface Water Treatment Rule (IESWTR), the Stage II DBP Rule, the Enhanced Surface Water Treatment Rule (ESWTR) and the Ground Water Disinfection Rule (GWDR). Another rule, the Information Collection Rule (ICR), that was promulgated during 1996, is intended to provide essential data on the occurrence and treatment for pathogens and DBPs in larger public drinking water systems. This Plan also includes projects that are sponsored by the American Water Works Association Research Foundation (AWWARF) and the National Water Research Institute (NWRI).

Chapter I of the Plan states the Agency's research needs that are linked to major policy questions that must be answered by research results. Chapter II focuses on research for microbial pathogens and Chapter III discusses research for disinfection byproducts. These projects are clustered under headings of Health Effects Research, Exposure Research, Risk Assessment Research, and Risk Management Research. The information provided includes the state of the science, specific research needs, and a short (in many cases too brief) explanatory statement on each of the selected research projects that address the research needs. This structure was intended to relate policy questions and major research questions to research needs and goals. In Chapter IV research projects are grouped into five major categories that show how the research is integrated within each of the specific drinking water regulations.

The Agency's charge to the DWC was composed of three major questions and a series of other questions specific to the separate components of the plan:

> **Charge Question I:** Has EPA identified the correct research issues to be addressed to support the development of the interim and long-term Enhanced Surface Water Treatment Rules, Ground Water Disinfection Rule and D/DBP Rules?
>
> **Charge Question II**: Do the research topic areas or projects underway or envisioned in the research plan appear to adequately address these issues?
>
> **Charge Question III**: Has EPA assigned appropriate priorities to the research?

The Committee recognizes the substantial efforts of the Agency to describe the research program for disinfectants, microbial agents and disinfection byproducts in a manner that reflects its relationship to research supported by the regulated community, and the cooperative approach to planning between the EPA office of Research and Development and the Office of Water. The Committee also recognizes the substantial effort made to relate specific research projects to research goals that must be met for human and environmental health purposes.

Response to Question I: In general, the research issues identified to support the five rules are appropriate. The Committee recognizes the complexity of the research plan with its multifactorial approach to both microbial and DBP research and acknowledges the considerable progress made by ORD and OW in comparison to previous versions of the plan. Also, in general, the questions proposed in the research plan are appropriate. However, the Plan lacks the identification of a critical path of project progression that would identify the rate limiting components. Such a critical path helps prioritize and plan the research projects so that those of greatest uncertainty and resource requirements are accorded appropriate and primary attention and placed in a realistic time frame for overall research progress. This would allow sequencing of data acquisition that satisfies requirements for interdependency of project data.

The purpose of the research plan is to provide EPA and others with information required to answer questions on the development of potentially significant research results to support drinking water regulations. The most meaningful discussion on the purpose of the research plan is presented in the last section (Section IV). Within this final section of the Plan, EPA presents the basis and foundations for the type of research needed to develop key regulations over the next five to ten years. EPA discusses the studies and why the information is needed. The driving force behind the development of the Plan would be clarified if Chapter IV was placed at the beginning of the Plan. Each portion of this section would then identify the types of studies needed to provide the necessary information.

Response to Question II: Because of the approach that is taken, the Committee questions whether some studies are included in the Plan because they are already underway, or if they are included because they provide critical information for the development of regulations. There is less than a clear statement of the information needs and the studies planned. The Committee suggests a process that EPA might have followed to identify the needed projects in section 3.1.2 of this report.

The Committee recommends that the microbial research goals statement put an even greater emphasis on identifying and quantifying the occurrence of the key pathogens and the health risks they pose in drinking water. This is necessary since the whole process of developing regulations for minimizing the human health risks of contaminants in drinking water requires identifying and specifying the contaminants posing the highest risks. If prioritization of contaminants for regulation is to be risk based, this approach must carry through to the identification and quantitation of the key pathogens and their health risks.

The Committee believes that it is important for EPA to develop a mechanism to identify "new" waterborne pathogens as they emerge. The current research program has placed the effort almost exclusively on one organism (*Cryptosporidium*) because it is currently believed to be the most resistant, worst-case organism. The Committee would be interested in knowing how a different organism, that might emerge next year, would be accommodated in the research plan?

The organisms of greatest health concern, as stated in the health effects portion of the microbial research plan are Norwalk type viruses and *Cryptosporidium*. Yet, the Information Collection Rule (ICR) will provide no information on Norwalk virus occurrence and the information on *Cryptosporidium* will be limited for risk assessment because the ICR method does not differentiate between infectious and non-infectious oocysts. The Committee believes that there is a potentially serious disconnect between the priority pathogens of the health effects research (i.e., Norwalk virus and *Cryptosporidium*) and the priorities of the occurrence research. These different priorities do not facilitate a coordinated pathogen risk assessment program.

The Committee is concerned about the absence of research projects examining the potential for surrogates to serve as indicators of virus or fecal contamination of groundwater. The Committee and other scientific panels have identified such indicators as critical research needs for the GWDR. EPA sponsored a national workshop to discuss the GWDR on July 10-11, 1996. Several research needs were identified at the workshop and the Committee recommends that these research needs be included and prioritized in a revised plan. Also, information about the concentration of viruses in a groundwater source must be known. Current surveys of viruses in groundwater are determining occurrence of viruses, but their densities are not being determined and the detection methods are inadequate. In addition, the EPA has stated that the focus must be on those viruses that occur most frequently, in the highest numbers and have the greatest health impacts. The Committee contends that the

research effort is not doing this. In order to achieve their stated goal, EPA should establish a mechanism whereby those viruses that are detected in groundwater are identified.

The Committee believes that a critical area that has been overlooked is the need for methods to assess the reliability of a treatment plant and individual treatment processes. The Committee also believes that additional research is needed on the reliability of multiple barriers of treatment to include: watershed protection and pathogen monitoring, multiple chemical inactivation steps, and filtration and/or sedimentation in addition to chemical inactivation.

In order to perform risk assessments for disinfection byproducts (DBPs) there is an absolute requirement for exposure data and knowledge of human health effects. Currently exposure data are inadequate primarily due to the lack of methods for proper measurement. This places the highest priority on the acquisition of such methods for both Stage I and Stage II Disinfectant Byproduct Rules. Until this component of the research plan is in place, adequate data for risk assessment will not be available.

The issues of epidemiological research, DBP mixtures research, and research on the toxicity of individual DBPs are appropriate, but the emphasis placed on each of them may not be. Much of the proposed DBP health effects research does not have direct impact either on the balance between controlling risks from pathogens and from DBPs in drinking water, or on the rule making process itself. This is partly because of the probable timing of the epidemiologic reevaluation, and studies that could have a major impact, and partly because the other studies are directed at providing the experimental foundation from which rational projections can be made in the future. This does not imply that the basic experimental toxicity studies are not important, but rather their accomplishment is less urgent. If the reevaluation of existing epidemiologic research can be completed in a time frame relevant to the rule making process, it should be assigned the highest priority from among this group of proposed projects. The evaluations and reanalysis of the epidemiologic studies should be paramount.

Response to Question III: EPA characterizes the research task as one of balancing the risk associated with disinfectants with the risks associated with microbial diseases, the idea being that, as disinfection is increased to reduce microbial risks, the risk of DBPs is inherently increased. This way of presenting the problem is not wholly accurate and it could easily lead to an erroneous identification of the research tasks that must be undertaken to produce the most effective regulation. In the view of the Committee, the challenge is not merely writing a regulation that balances the costs of more disinfection with the benefits of fewer microbes. In fact, the bigger part of the challenge is to write a regulation that sets tough microbial standards and allows this goal to be met at the lowest cost without allowing new, significant risks from chemical byproducts, particularly if those risks are of greater importance than the microbial risk avoided.

The Committee notes that there are many high priority projects and it is concerned with how they are ranked among themselves. There are obviously insufficient resources to fund all the high priority projects. How does the Agency decide which ones to fund? Also, why are some medium priority projects funded (i.e., already underway) when many high priority projects are not funded?

The development of rapid reliable monitoring methods for waterborne pathogens should receive a high priority. Also, proper design and operation of water treatment facilities is crucial to reducing waterborne illness. It would be extremely helpful to know what percentage of waterborne illness is caused by treatment process upsets resulting in epidemics versus the percentage of endemic waterborne disease caused by pathogens passing through well-operated treatment plants. It may be much more cost effective to improve operational reliability of water treatment than to require increasingly higher logs of pathogen removal/inactivation.

The EPA has chosen to place a medium priority on those research projects related to the growth of bacteria in distribution systems. The Committee agrees that projects related to heterotrophic bacteria in distribution systems should not be the highest priority. However, in light of the information that is being obtained in Payment's studies on the role of the distribution system in endemic microbial disease, the Committee believes that it would be appropriate to place a higher priority on microbial contamination in distribution systems. Besides characterizing the biofilms in the systems, research is needed on the integrity of distribution systems and their vulnerability to pathogen introduction from cross-connections, line breaks, pressure drops, etc.

Responses to specific issues in the Plan are contained in the appropriate sections of this report.

2. INTRODUCTION

2.1 Background

The U.S. Environmental Protection Agency (EPA or the Agency) is developing a series of drinking water regulations on disinfectants, disinfection by-products (DBPs) and microbial pathogens. The EPA Office of Research and Development (ORD) and the Office of Water (OW) prepared a draft *Research Plan for Microbial Pathogens and Disinfection By-products in Drinking Water* (the Plan)(EPA, 1995). The Plan is intended to define the research needed to support EPA's development of drinking water regulations covering disinfectants, disinfection byproducts, and microbial pathogens, to serve as a vehicle for facilitating and coordinating research with cooperators, and for communicating with those outside the agency who are interested in these regulations.

Disinfection and disinfection byproducts have been a recurring issue with the Science Advisory Board's (SAB) Drinking Water Committee (the Committee). Since 1990, the Committee has provided advice to the agency on at least seven occasions, including:

a) a report on recommendations for research on disinfectants and disinfection byproducts (SAB, 1990);
b) a review of the Office of Research and Development's drinking water microbiology research plan (SAB, 1991);
c) a commentary to the Administrator asking for adequate resource investments in disinfection byproduct research (SAB, 1992);
d) a commentary on the negotiated regulation for disinfectants and byproducts which highlighted the need for research in this area (SAB, 1993);
e) a report on the research program on disinfectants and disinfection byproducts in the Risk Reduction Research Laboratory (SAB, 1993a)
f) a report on the information collection rule (ICR) asserting the need for an overall plan to guide collection and analysis of data resulting from the ICR (SAB, 1994); and
g) an advisory on some near-term research proposals on DBPs along with a strong recommendation for a structured effort to coordinate EPA's DBP research program, including the use of formal scheduling and resource management (SAB, 1995).

The current review was initiated by a request from the Deputy Assistant Administrator for Science of the EPA Office of Research and Development (ORD). Portions of the draft *Research Plan for Microbial Pathogens and Disinfection By-products in Drinking Water* were forwarded to the Committee during October, 1995. Agency officials introduced the Plan to the Committee at a teleconference meeting on November 9, 1995. A follow up meeting was held in March, 1996 to discuss the Plan in detail. Additional information, in the form of

appendices to the plan, was delivered to the Committee just prior to its March, 1996 review meeting. The Committee held a working session on the Plan at a meeting during July, 1996.

2.2 The Charge

The Agency charge to the Committee was to review the research plan and to provide advice on whether:

a) EPA had identified the correct research issues to support the development of the Interim and long term Enhanced Surface Water Treatment Rules, Ground Water Disinfection Rule, and Stage 2 Disinfectant/Disinfection Byproducts Rules;

b) The research topic areas or projects underway, or envisioned under the five-year plan, appear to adequately address the issues, and if not, should any other research topic area be funded in lieu of or in addition to those presented; and

c) EPA assigned appropriate priorities to the research?

2.3 Overview of the Research Plan

The Agency's research plan consists of four chapters and three appendices. Chapter I introduces the Plan's purpose and the drinking water quality issues that the Plan and the regulations address; reviews EPA regulatory efforts; provides an overview of drinking water treatment; and describes the relationship among regulatory policy questions, research goals, research questions, and research needs.

Chapter I states that the Agency's research needs (pages I-6 through I-21) are linked to major **policy questions** that must be answered by research results (e.g., should drinking water disinfection by ozonation be encouraged in place of chlorination?). The Plan presents **major research questions** that are important to resolving the policy questions (e.g., What are the health risks caused by exposure to microbial pathogens?) and identifies **research goals** that, if attained, would provide useful data to address each question (e.g., To identify the health effects caused by microbial pathogens in drinking water.). Next, the Plan outlines more **focused research questions** (e.g., What are the health effects associated with exposure to waterborne pathogens?) and **research needs** which further identify the type of information that is needed (e.g., information on the pathobiology of infection and disease for waterborne pathogens.). The research goals have a one-for-one relationship to the four major elements in the environmental health risk assessment-risk management paradigm (health effects, exposure, risk assessment, and risk management).

Chapter I also presents an overview of the elements within this structure for the research plan and the criteria that the Agency applied in selecting research projects for each need.

Although all projects are high priorities, the Agency has assigned relative priorities (see Appendix A) within the population of projects using the following criteria:

a) High risk (research is likely to elucidate factors where preliminary information suggests significant public health impacts);
b) High uncertainty (results are likely to reduce significant uncertainties);
c) Regulatory relevance (high likelihood that results will lead to criteria which reduce risk in a cost-effective manner).

Other factors which the Agency considered in setting priorities included:

a) Short-term and long-term research needs balancing,
b) Linkage to other efforts (complements other research),
c) Anticipatory research (results will help anticipate future problems), and
d) Wider applicability (results may extend to other environmental issues)

Chapters II and III present information on the specific **research projects**. Chapter II focuses on research for microbial pathogens and Chapter III discusses research for disinfection byproducts. Both follow the same structure. For example, the microbial pathogen chapter (Chapter II) first discusses background information on waterborne infectious disease links to microbes and then repeats, in table form, the **research questions** that address each research goal (paradigm component). Then, information on specific projects clustered under the **categories** of Health Effects Research, Exposure Research, Risk Assessment Research, and Risk Management Research is given. This information includes the state of the science, specific research needs, and a short explanatory statement on each of the selected **research projects** that address the **research needs.** This structure was intended to relate policy questions and major research questions to research goals, questions, needs, and projects.

In Chapter IV, research projects are clustered into five major groups, which show how the research is integrated with each of the specific drinking water regulations. Within each cluster, the projects are further subdivided into either health effects, exposure, risk assessment, or risk management research. The regulatory clusters used to categorize research projects in the plan include:

a) **Stage 1 Disinfectant/Disinfection Byproduct** (D/DBP) Rule which addresses limits for a number of DBPs (THMs, haloacetic acids, bromate, chlorite, chlorine, chlorine dioxide, and chloramines) (proposed July 1994);
b) **Interim Enhanced Surface Water Treatment Rule** (IESWTR) which will enhance protection from pathogens while the Stage I DBP rule is being implemented (proposed July 1994);

c) **Long-term Enhanced Surface Water Treatment Rule** (ESWTR) which extends protection from pathogens for systems serving fewer persons than those addressed by the IEWSTR (not yet proposed);

d) **Stage 2 DBP Rule** which further reduces DBP levels addressed by the Stage 1 rule (proposed in part in July 1994); and the

e) **Ground Water Disinfection Rule** (GWDR) which enhances protection against pathogens in systems using ground water not under the influence of surface water (not yet proposed).

One additional rule that is relevant to these regulations is the **Information Collection Rule** (ICR) which will provide data on occurrence and treatment for pathogens and DBPs in larger public drinking water systems. This rule was proposed in February of 1994 and promulgated during 1996.

The Plan, and the DWC's review, also included projects that are sponsored by the American Water Works Association Research Foundation (AWWARF) and the National Water Research Institute (NWRI). These projects can also be grouped into these same categories. It is not clear to the Committee whether the Plan has been coordinated with research organizations other than the AWWARF. The Committee encourages the Agency to interact with the broadest possible group of organizations doing research in this area.

Chapter IV also presents information on how the research will be used to support estimation of national and local costs and benefits associated with each of the rules, and an approach to balancing the risk associated with regulatory decisions for microbial pathogens and DBPs.

A number of general characteristics are evident about the projects listed within the various categories. The interim ESWTR projects in health effects, exposure, and risk assessment are all focused on microbial studies as are the research projects in support of the long-term ESWTR and the ground water disinfection rule. Risk management research in support of both the interim and long-term ESWTR concentrates on either physical and biological removal of microbes or disinfection by single or multiple agents and also includes distribution system research. The Stage 1 and Stage 2 DBP rule associated research focuses on disease conditions that might result from chemical exposures and includes health effects related to cancer, tumor formation, reproductive effects, neurotoxicity, immunotoxicity, mutagenicity, and other toxic effects. Epidemiological feasibility studies on these disease states are part of the health effects research being conducted. All of the health effects projects in the Stage 1 DBP rule and all of the AWWARF exposure research projects are expected to be finished by the end of Calendar Year 1996. The projects on D/DBP methods, EXD 1 through EXD 6, will not be completed until 1998 and 1999. Risk assessment research activities are not identified in the research plan to support the Stage 1 DBP rule. Both risk assessment and risk management projects are concentrated on the Stage 2 DBP rule.

3. OVERARCHING COMMENTS

3.1 General Comments on the Charge

The Committee recognizes the substantial efforts of the Agency to describe the research program for disinfectants, microbial agents, and disinfection byproducts in a manner which reflects its relationship to the research supported by the regulated community, and the cooperative approach to planning the research between the EPA Office of Research and Development (ORD) and the Office of Water (OW). The Committee also recognizes the substantial effort made in relating specific research projects to research goals that must be met for human and environmental health purposes.

The general comments of the Committee are provided in this section in response to the three major elements of the charge from the Agency. Later sections of the report provide more detailed comments on components of the Plan.

3.1.1 Charge Question 1: Has EPA identified the correct research issues to support rulemaking?

In general, the research issues identified to support the five rules are appropriate. However, the committee is concerned that this plan, which is organized topically, does not provide research paths and schedules, and with few notable exceptions, does not convey a sense of research flow.

The purpose of the research plan is for EPA and others to coordinate development of research projects designed to answer questions about information needed to support drinking water regulations, as well as development of research projects designed to generate the significant research results needed. The most meaningful discussion on the purpose of the research plan is presented in the last section (Section IV--Balancing microbial and DBP risks: Integrating Research to Support Rule Development) in which the Agency attempts to tie all the pieces together. Within this final section of the Plan EPA presents the basis and foundation for the type of research needed to develop key regulations over the next five to ten years. EPA discusses the studies and why the information is needed. The driving force behind the development of the Plan would be clarified if Chapter IV was placed at the beginning of the Plan. Each portion of this section should identify the types of studies needed to provide the necessary information.

3.1.2 Charge Question 2: Do the research topic areas or projects underway or envisioned under the plan adequately address the issues?

Because of the approach that is taken, the Committee questions whether some studies are included in the Plan because they are already underway, or if they are included because

they provide critical information for the development of the regulations. There is less than a clear statement of the information needs and the studies planned.

The Committee believes that it would be helpful to look at the process that EPA might have gone through to identify the needed projects. The process could have included the following elements:

a) Definition of the regulatory objective: to coordinate the efforts to regulate microbial disease with the efforts to regulate disinfection byproducts so that neither regulation is done in the absence of satisfactory understanding of the impact it will have on the other.
b) Articulation of an understanding of the regulatory alternatives.
c) Articulation of an understanding of the impact of each alternative on both microbial and DBP issues. Note, the following relevant points: 1) models might be required; and 2) a strawman could be constructed to identify gaps in our understanding. Some can be filled by gathering data (e.g., how much dichloroacetic acid, DAA, is occurring); others can be filled by conducting some basic research (e.g., is there a threshold for the effects of bromate?); others gaps are unlikely to be filled in the coming decade; and filling still others may fall under questions of policy (comparing mortality and costs, identifying all the byproducts of each oxidant, etc.).
d) Development of a research plan to address the near term data gaps, a research plan to address the longer-term data gaps and white papers on the appropriate policy issues.
e) Review the research already being conducted by other parties to determine which data gaps remain.
f) Development of a schedule showing the relationships among all projects (EPA, others, near term data, long term data and policy issues). The schedule should show the resources required of EPA (manpower and funding).

It would also be helpful to provide a mechanism to review EPA's current list of projects. The following screening questions might be appropriate for this purpose:

a) Is this research essential to the current regulatory agenda? That is, what information need does it fill and what would be done differently if the research were not carried out now and in the future?
b) Does a good strawman exist that shows how this information could impact the regulatory outcome?
c) Ignoring funding, can this research be conducted before it is required for regulatory use?

3.1.3 Charge Question 3: Has EPA assigned appropriate priorities to the research?

EPA characterizes the task as one of balancing the risk associated with disinfectants with the risks associated with microbial disease, the idea being that, as disinfection is increased to reduce microbial risks, the risk of DBPs is inherently increased. This way of presenting the problem is not wholly accurate and it could easily lead to an erroneous identification of the research tasks that must be undertaken to produce the most effective regulation.

The Committee believes the question is one of reducing the risks associated with all drinking water practices as well as reducing the risk associated with microbial disease. All drinking water practices that reduce microbial risks do not necessarily result in increased health risks from chemical pollutants. One treatment practice, disinfection, which is particularly effective in controlling bacterial and viral agents, does produce a variety of chemical byproducts that are thought to present a health risk. This is particularly true of chlorine, the most common disinfectant. To date, water treatment practice, worldwide, has depended heavily on the effectiveness of chlorine, perhaps too much so. In the view of the Committee, the challenge is not merely writing a regulation that balances the costs of more disinfection with the benefits of fewer microbes. In fact, the bigger part of the challenge is to write a regulation that sets tough microbial standards and allows this goal to be met at the lowest cost without allowing new, significant risks from chemical byproducts, particularly if those risks are of greater importance than the microbial risk avoided.

The Committee notes that there are many "high" priority projects and it is concerned with how they are ranked among themselves since the resources are obviously insufficient to fund all of the "high" priority projects. How does the Agency decide which ones to fund? Also, why are some "medium" priority projects funded (i.e., they are already underway) when many "high" priority projects are not funded?

The Committee also notes that the evaluation and reanalysis of the epidemiologic studies are core components of this plan. The outcome of this broad component of disinfection byproduct research should help direct research activities in the other two areas (health effects and risk assessment related research). However, some highly focused and relatively isolated individual research projects are already in progress that have no apparent connection to human epidemiologic studies. Of the three main issues identified, the Committee thinks that the priority order should be: a) evaluation and reassessment of the epidemiologic studies, with feasibility studies if called for; b) research on DBP mixtures; and c) toxicologic research on individual DBPs. This order applies to the proposed risk assessment projects as well as to the health effects studies. It is also not clear that core microbiological issues are addressed adequately by epidemiologic studies. Priorities for individual research projects in these areas are discussed later in this report.

4. MICROBIAL RESEARCH

4.1 Overview

Microbial waterborne pathogens of concern include various bacteria, viruses, and protozoans that are the etiologic agents of human disease. Devastating, bacterial pathogens are largely under control with widely used disinfection measures. Therefore, the focus of concern for microbial pathogens in drinking water has been mostly directed to those pathogenic protozoans and viruses found as drinking water contaminants.

The research plan for microbial pathogens identifies key research issues for microbial pathogens and their health effects by stating major questions and research goals, and then presents research needs for more-specific research questions that respond to the research goals. In its presentation of microbial pathogen research, the Agency has made considerable progress in identifying key research issues as compared to the previous versions of the research plan. However, the Committee is concerned that the microbiological research questions and needs statements are perhaps not the key ones, or are not adequately articulated.

Research goals: Goals 1 and 3 are to identify the health effects and assess the risks caused by microbial pathogens (and DBPs) in drinking water. These statements are useful, but they do not specifically express the need to identify the important microbial pathogens and quantify their health effects in drinking water. Goal 2 is to determine the population distribution of exposure to microbial pathogens (and DBPs) in drinking water. This research statement is useful because it alludes to the need to quantitatively measure microbial pathogen exposure in drinking water. However, also equally important is the determination of the health effects of pathogen exposure on various segments of the population for a complete evaluation of the public health risk. Goal 4 is to evaluate the effectiveness of options for reducing risks from microbial pathogens (and DBPs). This goal also alludes to the quantitative aspects of pathogen exposures and their health effects by the need to reduce the risks through various options. The Committee recommends that the research goals statement put an even greater emphasis on identifying and quantifying the occurrence of key pathogens and the health risks they pose in drinking water. This is necessary since the whole process of developing regulations for minimizing the human health risks of contaminants in drinking water requires identifying and specifying the contaminants posing the highest risks. If prioritization of contaminants for regulation is to be risk based, this approach must carry through to the identification and quantitation of the key pathogens and their health risks.

4.1.1 Health Effects Research Needs for Microbial Pathogens.

The research question posed is: What are the health effects associated with exposure to waterborne pathogens? Based on the regulation of specific microbial pathogens or groups of

pathogens as contaminants, the Committee believes that this research question should be reframed as: What are the microbial agents that are causing health effects in drinking water? The reason for restating the question is to focus on hazard (microbial pathogen) identification, which is appropriate for a risk based approach to the regulations. The second research need in this section is epidemiology studies to characterize endemic and epidemic illness rates, to assess magnitude of risk, and to provide data for use in verifying risk models. The Committee believes that this research need should also include the phrase: "to determine etiologies of illness." The identification of the causative (etiologic) agents of waterborne illness is an essential part of the risk assessment process leading to contaminant regulation. Therefore, epidemiological studies lacking the identification of specific microbial pathogens (or immunological evidence of infections or illnesses attributable to them) will not provide the essential information for risk based regulation.

4.1.2 Exposure Research Needs for Microbial Pathogens

The Plan states that "little information is available on the levels of pathogens that occur in drinking water." Actually, little information is available on the types and levels of pathogens. Again, the Committee believes that pathogen (hazard) identification, that is, specifying particular pathogens, must be an essential part of the microbial research plan and deserves great emphasis. Research questions on page I-11 are:

a) What methods are needed to adequately measure or estimate occurrence of pathogens?,
b) What are frequencies of occurrence and densities of pathogens in source water, finished water, and distribution system water and what is the population distribution of exposure to the pathogens?, and
c) What are the factors affecting microbial contamination of ground water?

The Committee believes that the stated questions must put greater emphasis on the identification or specification of the microbial pathogens and the indicators or surrogates for them. The reasons for this have been stated previously: the criticality of the need for hazard (pathogen) identification in a risk based approach to the science in support of these drinking water regulations.

The first two research needs to address this question are: Analytical methods to detect and enumerate protozoa and viruses in water. The committee believes that these research needs should be expanded to include the identification of the pathogens. The research needs statements should be: analytical methods to detect, enumerate, and identify bacteria, protozoa, and viruses in water.

As will be elaborated later in this report, the Committee believes that the research Plan does not adequately address some of the important waterborne pathogens posing a high risk. In some of the proposed epidemiological studies, pathogen identification is lacking because

there is no effort to look for them or because the methods used to look for them (or evidence of infection with them) are inadequate.

4.1.3 Risk Assessment Research Needs for Microbial Pathogens

The research question posed in this section is: "How can the risks posed by pathogens in drinking water be characterized?" The identified research needs are: Modification of the risk assessment paradigm for microbial disease, development and application of dose-response models for microbiological disease, and methods to characterize risks from mixtures of pathogens, and mixtures of DBPs and pathogens.

The Committee agrees that these are the appropriate research questions and needs in the area of microbial risk assessment. However, the Committee is concerned about the need for balance in the levels of effort between microbial and DBP risk assessment research. Because both classes of contaminants are important and their risks must be balanced, there must also be a balanced level of effort in assessing their risks. In past communications, the Committee has noted that in the important area of hazard identification (contaminant selection), the approach for chemicals has been to conduct a separate analysis for each one, while the approach for microbes has been to focus on a single worst case pathogen (*Cryptosporidium* or a worst case virus) or to combine many of them into a into a single group (enteric viruses or culturable enteric viruses). Therefore the Committee recommends that greater emphasis be placed on a risk based approach to the identification and analysis of all human microbial pathogens, including bacteria, in drinking water. The proposed research plan has not taken this approach. Instead, it has focused on a few individual pathogens or large, heterogeneous groups of pathogens (e.g., enteric viruses) assumed (perhaps inappropriately) to represent the worst case. Further, the Committee believes that investments should be made according to risk, and that the risk associated with microbial agents merit greater investments.

4.2 *Specific Comments on Microbial Research*

4.2.1 Health Effects Research

In the following subsections, the Drinking Water Committee comments on the microbial research parts of the EPA Research Plan with emphasis on responding to the specific questions of its charge (Section 3.1).

a) Emphasis on characterizing the dose-response for Cryptosporidium and Norwalk virus.

The proposed research projects can be categorized into two groups: those related to quantifying the dose-response curve for pathogens, and those related to surveillance and investigation of waterborne disease outbreaks. Quantifying the dose-response relationships

for pathogenic microorganisms of concern is critical to the development of a risk based rule. All three of the microbiology-related rules (Interim Enhanced Surface Water Treatment Rule, Enhanced Surface Water Treatment Rule, and the Ground Water Disinfection Rule) are intended to be risk based; therefore, these projects should be given a high priority for funding. The two proposed dose-response projects are for *Cryptosporidium* and Norwalk virus. To our knowledge, the second phase of the Norwalk virus study, that will examine the low dose range, has not been funded. This project is crucial for the development of the three rules. In addition, there are other significant microorganisms for which dose-response data are needed. For example, Norwalk virus is one of a large group of human caliciviruses. It is unknown whether the dose-response relationship for Norwalk virus will be representative of the other members of the group. Therefore, investigating the dose-response of other viruses is necessary, in the Committee's opinion.

The Committee believes that it is important for EPA to develop a mechanism to identify emerging waterborne pathogens and undertake fast-track research on them as necessary. The current structure appears too rigid to identify and accommodate new waterborne pathogens as they emerge. The current research program has put the effort almost exclusively on one organism (*Cryptosporidium*) because it is currently believed to be the most resistant, worst-case organism. If a different organism is discovered to be the worst-case organism next year, how will this be accommodated in the research plan? The Agency needs to be proactive in this area and should establish a program that anticipates these types of emerging pathogenic microorganisms.

b) Specific pathogens and endemic/epidemic waterborne disease

Several projects (HEM 7-10) in the area of epidemiology are described. The Committee believes that, while this information is important to quantify the effects of drinking water contamination on public health, it is not essential for rule development unless it includes pathogen identification and quantitation.

The project to characterize endemic disease (HEM 7) plans to compare endemic illness in communities with different water treatment systems. While it is listed as a high priority project, the Committee questions whether this project will be completed in time to have an impact on the ESWTR. Furthermore, because the project has a very limited scope - only 4 communities will be involved - the Committee is concerned that this will not be sufficient to allow an extrapolation to the rest of the country. Having additional details about the proposed study, including the types of treatment processes being used in the communities, would help the Committee in its efforts to determine how representative these communities may be.

Although two epidemiological studies for surface water have been conducted, and others are proposed, no mention is made of an epidemiological study in ground water systems. The Committee believes that such a study would be as helpful in the development of the GWDR

as are the proposed epidemiological studies to the development of the IESWTR and the ESWTR. The Committee believes that such epidemiological studies should include efforts to identify the pathogens responsible for the measured health effects.

4.2.2 Exposure Research

a) Pathogens selected for study, analytical methods development

The EPA research plan proposes several research projects to develop methods to detect and quantify infectious pathogens. The Committee agrees that the ability to detect infectious pathogens is critical to the development of meaningful regulations that protect public health but do not pose an undue economic burden on the industry. A large number of these projects are focused on *Cryptosporidium*, and a few on Norwalk virus. Because a large number of projects to develop methods for *Cryptosporidium* are being funded by AWWARF, the Committee recommends that the EPA's efforts in this area be fully coordinated with those of AWWARF and other agencies. The Committee also recommends that research on methods for Norwalk virus detection be inclusive of the other Norwalk-like viruses (i.e., human caliciviruses) to the extent possible.

Research is needed to determine if Norwalk virus is the appropriate representative, or whether another human calicivirus would be a better representative of the group. Project EXM 9 is to develop culture methods for the detection of Norwalk virus. The Committee considers this an extremely high priority project, as Norwalk and related viruses may cause 25% of the waterborne disease in the U.S. The Committee asks whether this project is being conducted. We consider it to be particularly relevant to the GWDR, where viruses are the primary pathogens of concern. The Committee believes that the number of waterborne pathogens for which methods are developed needs to be increased.

The Committee recognizes that methods using viability assays to detect important waterborne pathogens are not yet available. Some of the proposed research projects (EMM 2, EXM 3, EXM 9) are attempting to develop such methods, which the Committee supports. However, the Committee believes that intensive efforts on such projects are needed in a time frame consistent with the time line of the proposed rules. This is needed in order to be able to do the risk assessment for these high priority pathogens. In addition, the Committee believes that greater emphasis should be placed on obtaining the best possible occurrence data for these important pathogens in drinking water systems using state of the science methods that attempt to measure viability or infectivity. The Committee also recommends that the Agency consider intensified efforts to obtain such occurrence data on these pathogens during future waterborne outbreaks. This would require better (more comprehensive and better coordinated) preparedness for timely investigative response to waterborne outbreaks. The Committee believes this to be achievable through the development of a coordinated, rapid response surveillance effort by the EPA, the Centers for Disease Control and Prevention, and the states and territories.

b) Approaches to estimate occurrence and exposure

The Committee believes that the current research plan has some important limitations and gaps in the area of microbial exposure assessment. These deficiencies are most critical for the long term ESWTR and the Ground Water Disinfection Rule. Too little emphasis is given to determining the occurrence of important waterborne pathogens in drinking water supplies to support the conduct of meaningful microbial risk assessments. If viable *Cryptosporidium*, Norwalk and other Norwalk-type viruses are truly the most important drinking water pathogens, because of their health effects, then greater emphasis is needed on obtaining exposure (occurrence) data. In addition, the Committee believes that current and proposed research on the occurrence of *Mycobacteria* (EXM 14), heterotrophic bacteria (EXM 17, 19, 20), and opportunistic pathogens (EXM 18) would be of limited or uncertain health significance in drinking water. Unless and until appropriate health effects research provides better and more direct evidence that they truly present significant health risks in drinking water, research on their occurrence should be given lower priority. Higher priority should be given to obtaining better occurrence and exposure data for those pathogens whose health effects in drinking water are clearly documented (e.g., Norwalk and other Norwalk-like viruses, rotaviruses and *Cryptosporidium parvum*).

The Committee is concerned that currently planned efforts to obtain data on occurrence of *Cryptosporidium* (ICR) and enteric viruses (ICR and ground water virus surveys) will not adequately address the research needs for exposure assessment. This is because the *Cryptosporidium* method does not determine viability and the enteric virus method detects only readily culturable (cytopathogenic) enteric viruses. The ICR virus detection method does not include hepatitis A virus (HAV), Norwalk, and the other Norwalk-type viruses judged most significant for health effects. The ground water virus survey attempts to detect Norwalk virus and HAV by polymerase chaing reaction (PCR), but the methods being used are inadequate. There are limitations of the PCR primers for Norwalk-type viruses and the method may detect the nucleic acid of inactivated viruses.

Project EXM 22 is described as a project to examine exposure to pathogens as a function of population distribution. It would be important to examine the health effects of the pathogens as a function of population distribution prior to examining the exposure. The Committee recommends that the Agency consider refocusing this project to examine how health effects may differ as a function of the population distribution. This information will assist in the risk assessment for vulnerable populations.

The EPA lists a number of projects (EXM 14 to 22) to examine the occurrence of several microorganisms in source water and distribution systems. The majority of these projects involve pathogenic and opportunistic bacteria in distribution systems. The Committee agrees that information on the occurrence of potential pathogens in distribution systems will be useful, but is concerned about the lack of projects on the occurrence of viral and parasitic pathogens. The Committee understands that the ICR is a massive effort to collect data on

the occurrence of *Cryptosporidium* and culturable cytopathogenic enteroviruses in source water, but considers this occurrence information inadequate for the development of risk-based regulations. The organisms of greatest health concern, as stated in the health effects portion of this research plan, are Norwalk type viruses and *Cryptosporidium*. The Committee agrees that these enteric virus and protozoan pathogens and others documented as causing waterborne disease, such as rotaviruses and *Giardia lamblia*, are the most important. Therefore, these pathogens of documented waterborne disease should be the highest priority for research on their occurrence in source water and distribution systems. The Committee believes that there is a serious disconnect or difference between the priority pathogens of the health effects research (such as Norwalk virus and *Cryptosporidium*), and the priority organisms of the occurrence research (*Mycobacteria*, heterotrophic bacteria, opportunistic pathogens, and certain newly emerging pathogens, such as *Aeromonas* and *Pseudomonas*). The Committee believes that these differences in the targeted organisms for research priorities in health effects and exposure (occurrence) should be resolved. Such differences in priority organisms do not provide the basis for a coordinated and integrated research program facilitating a risk-based approach to the microbial aspects of these regulations.

The Committee is concerned about the research projects on POU/POE devices (EXM 19-20). We believe that these projects should be low priority until there is documented evidence of health effects by the microbes associated with them from an articulated research program. Previous EPA studies have shown no such health effects. At the current time, these projects are not well designed, well focused, or justified as a part of an overall research plan. They could be redesigned and focused as treatment alternatives for small community and non-community systems.

c) Groundwater Research

The Committee perceives a disconnect between the research plan and the direction of development of the GWDR. The focus of the projects to support the development of a Ground Water Disinfection Rule is on the use of models to predict virus fate and transport. There is little or no credible evidence to support this modeling approach. It is unclear from the available information which of these projects (other than EXM 24b) is funded. Consistent with the data from waterborne disease outbreaks, it is clear that the emphasis for microbial research on ground water systems is correctly placed on viruses. However, the Committee believes that bacteria, and perhaps protozoans, should be included as potential concerns in these systems. Furthermore, the Committee is concerned about the absence of research projects examining the potential for surrogates to serve as indicators of virus or fecal contamination of ground water. The Committee and other scientific panels have identified such indicators as critical research needs for the GWDR. EPA sponsored a national workshop to discuss the GWDR on July 10-11, 1996. Several research needs were identified at the workshop and the Committee recommends that these research needs should be included and prioritized in a revised plan.

Monitoring for indicators or even pathogens may be an important aspect of the GWDR, yet there is little research to support this approach. There are no projects designed to determine which indicators to use and the manner in which they would be used (e.g., when to monitor, what sample volume to collect, etc.).

Project EXM 23 (virus survival in the subsurface) is clearly important because information on virus survival in the subsurface is vital to determining a system's vulnerability to contamination. Therefore, the Committee encourages such research. A project in this area is being funded by AWWARF, but more information will be necessary to obtain an adequate picture of the important factors controlling virus survival. The Committee is concerned about the proposed project's reliance on bacteriophages. This is because bacteriophages are indicator viruses, and ultimately, it will be necessary to provide findings from similar research on human enteric viruses.

Projects EXM 25-27 focus on the use of mathematical models to predict virus fate and transport, and this may be a long-term goal of the Agency. However, the Committee believes that this goal will not be achieved in the time frame of the GWDR. Therefore, the Committee questions the priority of these projects relative to other potential projects. In particular, the Committee believes that high priority research projects are needed to characterize and quantify the factors affecting virus survival and transport in groundwater, and to develop methods for assessing fecal contamination of ground water using reliable indicators.

4.2.3 Risk Assessment Research

a) Development of quantitative microbiological extrapolation model accounting for thresholds, severity, and duration of exposure

The Committee is concerned that the level of effort in the critical area of microbial risk assessment is inadequate. The resource investment proposed for this research is appears to be inadequate for the research needed to develop risk-based regulations. Microbial risk assessment is a relatively new area compared to chemical risk assessment and additional effort is needed before adequate comparative risk assessment is possible. The Committee believes that additional areas that need to be addressed include: 1) the effects of mixtures of microorganisms (there is evidence that co-infection with enteric viruses and bacteria may result in infections with more severe health effects); 2) the effects of multiple exposures over time; 3) multiple routes of exposure (i.e., ingestion and inhalation); 4) model validation by the use of epidemiological data or other approaches; 5) the effects of immunity of the exposed individual and population on susceptibility to infection; and 6) evaluation of secondary spread of infectious agents. The Committee also believes that end points of infection in addition to diarrhea (e.g., meningitis, myocarditis, respiratory disease, diabetes) need to be assessed and quantified.

The Committee is pleased to see that the Agency has developed a risk assessment paradigm for use in these regulations. However, the Committee is concerned that the data needed for the risk assessment model are not available nor are there projects proposed to obtain the needed information.

Projects RAM 2 and 3 propose to conduct research on important topics such as severity of the exposure endpoint and mixtures of pathogens. It is unclear from the research plan who will conduct these projects and whether they will be funded. Lack of details on these projects makes it difficult for the Committee to evaluate them. The Committee has some concerns about the efforts to develop a threshold model. Existing data on dose-response in human feeding studies do not preclude threshold or non-threshold models. A non-threshold response seems likely for microorganisms for which multiplication within the host results in infection. For this reason, the Committee believes that a threshold for microorganisms would have to be demonstrated experimentally.

4.2.4 Risk Management Research-Microbial Pathogens

a) Overview

1) Risk management research for Microbial Pathogens

The key research questions in this section of the Plan are: "How effective are various treatment processes in removing pathogens?", and "How can the quality of treated water be maintained in the distribution system?" The Committee agrees that these are appropriate and important research questions. However, the Committee also believes that another critical research question is: "How can the microbial quality of source water be protected and evaluated to insure that it is consistent with finished water quality of acceptable microbial risk after appropriate treatment?" The research needs in the area of risk management include: Effectiveness of treatment processes for *Cryptosporidium*; treatment technologies appropriate for small systems; and identification and characterization of factors influencing microbial growth in distribution systems and strategies for its control.

Furthermore, the Committee also believes that there are additional research needs in the area of risk management for microbial pathogens. A focus on treatment for *Cryptosporidium* is reasonable, based on current information of its health risks and resistance to disinfection. However, other waterborne microbial pathogens may emerge that are highly resistant to treatment and of significant health risk. However, *Cryptosporidium* only recently supplanted *Giardia* as the worst case waterborne protozoan pathogen to date. With the continued discovery of new, potentially waterborne protozoan parasites, such as *Cyclospora cayetanensis* and the *Microsporidia*, the research needs for treatment processes should extend to additional waterborne pathogens as their existence and significance is recognized. The Committee also believes that the research needs on factors influencing microbial growth

in distribution systems and strategies for control should be expanded to include microbial intrusion as well. This is because the extent of cross connections, water line breaks and repair practices, and other conditions causing microbially contaminated water to enter distribution systems is not adequately known at present.

b) Specific Comments

The October 1995 SAB Review Draft of the EPA's Research Plan for Microbial Pathogens and Disinfection Byproducts in Drinking Water contains the following statement (page II-30): "For example, in the United States the waterborne disease outbreak rate for communities using surface sources without filtration is eight fold greater than communities with filtered water systems. Properly designed and operated water treatment systems that include filtration and disinfection can greatly reduce the risk of waterborne disease." This statement raises several important points regarding reducing waterborne illnesses in the U.S. They are: 1) Improved watershed protection and better pathogen monitoring systems that provide early warning of increased pathogen loading to treatment plants is needed. Storm events and other activities on watersheds often lead to highly increased concentrations of pathogens in raw waters entering water treatment facilities. Watershed control programs and rapid, reliable pathogen monitoring systems for both raw and treated waters would be extremely effective in reducing waterborne epidemics. The development of rapid, reliable monitoring methods for waterborne pathogens should receive a high priority; 2) Proper design and reliable operation of water treatment facilities is critical to reducing waterborne illness. It would be extremely helpful to know what percentage of waterborne illness is caused by treatment process upsets resulting in epidemics versus the percentage of endemic waterborne disease caused by pathogens passing through well operated treatment plants. It may be much more cost effective to improve the operational reliability of water treatment plants than to require increasingly higher logs of pathogen removal/inactivation. The Committee believes that another critical area that has been overlooked is the need for methods to assess the reliability of a treatment plant and individual treatment processes. The questions that need to be answered include a) how reliable are these processes in continually achieving the required level of pathogen reduction?; b) how often do these processes fail and how often do they achieve less than the required level of reduction?; c) What are acceptable levels of failure and sub-optimal treatment?; and d) Should item 'c' be based on the quality of the source water? The Committee believes that field studies are needed on individual treatment processes and plants to answer these questions, as this information is needed for the ESWTR and future regulations; and 3) the Committee believes that additional research is needed on the reliability of multiple barriers of treatment, to include: watershed protection and pathogen monitoring, multiple chemical inactivation steps, and filtration and /or sedimentation in addition to chemical inactivation. The issue of multiple independent treatment barriers relates closely to improved reliability of operations described above. For example, physical-chemical treatment steps for surface water supplies can efficiently remove most pathogens, so an upset in one of the barrier(s) is less likely to generate a waterborne disease outbreak.

Microbiological population densities in the watershed vary over several orders of magnitude over a period of time and the events that result in their transport to the water plant intake are also highly variable. Moreover, where microbiological pathogens are concerned substantial health impacts can occur from high concentrations in drinking water for only a short time. Hence, in this area, treatment systems must be fail-safe. Adequate public health protection is not achieved just by providing a certain number of logs of removal. It is important that significant portions of the removal are performed by independent treatment barriers, where the performance of one barrier is not entirely dependent on the success of the other. A treatment plant with filtration and chlorination does have independent barriers for bacteria and virus removal, but not for the control of *Cryptosporidium*.

There are two ways microbiological risks can be viewed. First in terms of catastrophic events, outbreaks, epidemics, etc. Second as a more or less continuous, low level endemic event occurring at low density throughout the population. The first sort of risk is a well-known fact and many examples can be cited. The second is the result of a reasonable hypothesis which epidemiological studies are presently struggling to confirm. The Committee feels that EPA's efforts should be designed to effectively address both of these types of risks.

The risk of endemic disease can be addressed by requiring treatment process trains that can be expected, over the long haul, to achieve more effective pathogen removal. This appears to be the course EPA has presently set. The risk of catastrophic events requires that watershed protection be addressed and that treatment trains include greater reliability. One way to achieve that reliability is to provide the sort of independent treatment barriers mentioned earlier, so that, if one treatment barrier fails, chances are another is still in place.

1) Alternative treatment processes development and emphasis on *Cryptosporidium*.

The focus on treatment alternatives for *Cryptosporidium* inactivation in surface water systems seems appropriate, although the Committee is concerned about this approach of choosing a single "worst-case" pathogen. However, the Committee believes that there is a lack of research on those pathogens of greatest health concern in ground water, especially the enteric viruses. Systems using ground waters will need information on treatment alternatives that are effective against viruses. More information is needed on poorly-characterized viral pathogens, such as Norwalk virus and the other human enteric viruses. While the need for projects of this type is described in the Plan, the Committee is concerned that no specific projects on this topic are listed in the FY 95-96 Plan.

2) Assignment of medium priority to projects related to microbial quality

The EPA has chosen to place a medium priority on those research projects related to the growth of bacteria in distribution systems. The Committee agrees that projects related to heterotrophic bacteria in distribution systems should not be the highest priority. However, in

light of the information that is being obtained in Payment's studies on the role of the distribution system in endemic microbial disease, the Committee believes that it would be appropriate to place a higher priority on microbial contamination in distribution systems. Besides characterizing the biofilms in these systems, research is needed on the integrity of distribution systems and their vulnerability to pathogen introduction from cross-connections, line breaks, pressure drops, etc.

c) Comments on Chapter IV, Balancing Microbial and DBP Risks

1) Interim and Long-Term ESWTR

EPA states that because the long-term ESWTR will apply to small systems, very simple and inexpensive methods must become available for measuring or estimating (through surrogates) *Cryptosporidium* in water. Several research projects are underway, by both EPA and AWWARF, to develop more efficient and reliable methods for the detection of *Cryptosporidium* in water. The Committee does not feel additional efforts to find biological indicators for *Cryptosporidium* will be fruitful. Instead, EPA should consider other suitable approaches to assessing the exposure of small systems to this and other pathogens. (IV-6, line 15)

EPA will likely require that some level of disinfection, in addition to physical removal, be required to ensure that virus levels are adequately reduced. There is a need to assess how much virus removal is actually achieved through physical removal processes. This will enable EPA to determine exactly what level of removal through disinfection will be required, so that the total virus removal is adequate. The Committee believes that the contributions of physical and chemical removal and inactivation by disinfection must be quantified for viruses. It is not possible to quantify chemical risks of disinfectants and their byproducts without specifying treatment trains for effective reductions of viruses and other pathogens. (IV-6, line 20)

It is stated that the ICR data will be used to validate gross assumptions on treatment effectiveness. It is not clear how the data obtained from the ICR will be used to accomplish this. Finished water monitoring will occur, presumably, at a limited number of sites. Whether these data will be reflective of treatment systems nationwide is unknown. (IV-7, line 26)

EPA proposes to test the validity of risk estimates based on dose-response curves using epidemiolgical data. It is not clear how the projects listed to accomplish this will provide the necessary information. For example, waterborne disease outbreak surveillance is unlikely to provide epidemiological evidence in a form that will allow an evaluation of dose-response. This is because current surveillance is too slow to respond to outbreaks to get good samples for pathogen analysis. Furthermore, such pathogen analysis is rarely done or is done using inadequate recovery and detection methods. (IV-12, line 8)

Several projects are listed to examine the health significance of bacteria growing in biofilms in the distribution system. This is certainly an important area of research. However, a more comprehensive need is the issue of distribution system integrity. There is growing evidence that endemic and epidemic waterborne disease is associated with breaks in the distribution lines, cross-connections and other breaches of distribution system integrity. Greater research effort should be expended in the area of design, construction, operation, and maintenance of distribution system integrity. (IV-12, line 14)

2) Ground-Water Disinfection Rule

One of the key issues identified by EPA is to determine the level of disinfection to require for systems that are vulnerable to fecal contamination. In order to determine the level of disinfection required, target disinfection requirements must be determined based on an acceptable level of risk of infections per year. Additionally, information about the concentration of viruses in the source water must also be known. Current surveys of viruses in ground water are determining occurrence of viruses, but their densities are not being determined and the detection methods are inadequate. In addition (line 25), EPA states that the focus must be on those viruses that occur most frequently, in the highest numbers, and have the greatest health impacts. The Committee contends that the research effort is not doing this. In order to achieve their stated goal, EPA must establish a mechanism whereby those viruses that are detected in ground water are identified. (IV-21, line 7)

The GWDR will have a major impact on non-community systems, thus the approach used in this Rule will of necessity be much different than that used in the SWTR and ESWTR. From the current research plan, it is not clear to the Committee that the needs of non-community systems are going to be addressed. (IV-22, line 22)

EPA has listed projects to define the public health significance of microorganisms in ground water systems. However, no epidemiological study for ground-water systems is proposed, so it is difficult to see how risks of endemic disease will be determined. It is also stated that indicator occurrence in source waters and distribution systems will be determined. Yet, no projects are listed to study indicator occurrence in any ground water system. In a previous section of this report, the Committee noted that this information will be critical to the development of the rule, which is likely to require monitoring for indicators. (IV-23, line 5)

The Committee notes that a survey on disinfection practices currently in use by ground-water systems by industry is mentioned but details of the study are not provided. Therefore, it is not possible for the Committee to judge or comment on the merits of this study in terms of its objectives and design. The Committee believes surveys of this nature can only be helpful in measuring process effectiveness. (IV-23, line 12)

Approaches for monitoring for coliphages are stated as being investigated. But no projects on this topic are listed in the research plan. The Committee has already expressed

its concern about the lack of research to identify and utilize coliphages or other appropriate indicators of virus pathogens and fecal contamination in general. (IV-23, line 30)

5. DISINFECTANT/BYPRODUCTS RESEARCH

5.1 Overview

In order to perform risk assessments for disinfection byproducts (DBPs) there is an absolute requirement for exposure data and knowledge of human health effects. Currently, exposure data are inadequate primarily due to the lack of methods for proper measurement. This places the highest priority on the acquisition of such methods for both Stage 1 and Stage 2 Disinfectant Byproduct Rules (e.g., projects EXD 1, EXD 2, and EXD 3). Until this component of the research plan is in place, adequate data for risk assessment will not be available. As such, risk assessments conducted on current data will have high degrees of uncertainty (health effects research is dealt with in section 5.2).

Another critical component of the research plan is a discussion on control of disinfection byproducts by one of three options:

a) Removal of natural organic materials before disinfection;
b) Changes in the disinfection process that will minimize the formation of related byproducts; and
c) Removal of disinfection byproducts after they are formed.

The Committee believes that a combination of options 'a' and 'b' listed above will be the most effective way to concurrently meet the need to control microbiological contaminants while also avoiding undesirable chemical byproducts.

The issue is not one of byproducts of disinfection, but of byproducts of oxidation. At the present time, the use of strong chemical oxidants, particularly chlorine, is probably the most important single tool for controlling microorganisms in drinking water. In that role oxidants are called disinfectants. But these same oxidants are also used for certain other treatment objectives, such as oxidation of sulfide, oxidation of iron and manganese, odor control, etc. Whenever they are used, strong oxidants are likely to react with natural organic matter (NOM) in the water to produce chemical byproducts. Chlorine is noteworthy because it reacts not only by oxidation, but by other mechanisms such as addition and substitution. As a result, evidence suggests that chlorine produces a greater number of chemical byproducts.

Disinfection with chemical oxidants is attractive because evidence suggests it is more effective in removal or inactivation of many microorganisms than are traditional physiochemical treatment processes alone. It is doubtful if some drinking water supplies currently in use could be made safe from bacterial disease using traditional treatment technologies, were it not for the use of chemical oxidants as disinfectants.

Nevertheless, alternatives are appearing on the horizon that offer the promise of removing or inactivating microorganisms without the formation of such extensive chemical byproducts. Examples are ultraviolet light, microfiltration, ultrafiltration, and reverse osmosis. Research in the use of these technologies is of critical importance, especially for small systems.

Moreover, there are also some strong chemical oxidants that are seeing wide use outside the U.S., such as chlorine dioxide and ozone, which produce a more limited number of chemical byproducts, and where control of byproduct formation may be feasible under certain conditions. Chlorine dioxide and ozone are also found to be effective in inactivating a wider variety of microorganisms than chlorine. It does not make sense to abandon the search for alternatives to disinfection when chlorine itself is not effective with *Cryptosporidium* and some of the alternatives are.

Nevertheless, conditions in the distribution system must be controlled. Today it is U.S. practice to do this by maintaining the presence of a chemical oxidant in the system (that is also known as a disinfectant) usually free or combined chlorine. So long as utilities elect to use a free chlorine residual as a means for maintaining acceptable conditions in the distribution system, they must also seriously consider controlling the level of natural organic material (precursor material) in the water entering the distribution system as well.

Evidence suggests that chloramines, properly administered, result in far fewer chemical byproducts, allowing their use to maintain distribution systems with much higher levels of NOM present. On the other hand there is also some indication that, under certain conditions, particularly warm temperatures, chloramine residuals may become unstable, resulting in nitrite formation. Finally in Europe today, particularly in Holland and Switzerland, some success is being achieved in maintaining distribution systems with no residual at all.

The Committee urges the EPA to probe deeper into the need for distribution system residuals and into the alternatives for achieving them. What role does the disinfectant residual play in protecting the distribution system? How important is the disinfection residual in the overall context of actions effective in protecting the distribution system? If methods for removing pathogens from the water supply are found that do not require that the bulk of the NOM be removed as well, the problem of the distribution system will remain to confound success unless these issues are more seriously addressed.

Still another decision that must be made in prioritizing or orienting treatment processes is whether to use an enhanced softening process in removing total organic carbon (TOC). This process is tied to the removal of precursor materials. Research in the use of membrane technology for small systems is another critical area. Operator education and capability are important components of membrane technology use.

Alternate disinfectant research, e.g., EXD 10, EXD 11, and EXD 12 are of the highest priority along with treatment research projects such as RMD 1, RMD 2, RMD 3, RMD 4, RMD 6 and RMD 7. Appendix A contains the table of EPA research projects that support rules for Enhanced Surface Water Treatment, Disinfection Byproducts, and Ground Water Disinfection. The projects have been arranged in the risk assessment/risk management paradigm to facilitate the review on scope, their applicability, and comprehensiveness in satisfying the risk characterization process. Also, the Committee's priority recommendations for these projects are indicated.

5.2 Specific Comments on DBP Research

5.2.1 Health Effects Research

The issues (epidemiologic research, DBP mixtures research, and research on the toxicity of individual DBPs) are appropriate, but the emphasis placed on each of them may not be. Much of the proposed health effects research does not have direct impact either on the balance between controlling risks from pathogens and from DBPs in drinking water, or on the rulemaking process itself. This is partly because of the probable timing of the epidemiologic reevaluation, and studies that could have a major impact, and partly because the other studies are directed at providing the experimental foundation from which rational projections can be made in the future. This does not imply that the basic experimental toxicity studies are not important, but rather that their accomplishment is less urgent.

If the reevaluation of existing epidemiologic data and completion of any feasibility or larger epidemiologic research can be completed within a time frame relevant to the rulemaking process, it should be assigned the highest priority from among this group of proposed projects. The evaluation and reanalysis of the epidemiologic studies should be paramount; the outcome of this broad project should inform research activities in other health effects-related areas, and in risk assessment-related research. However, individual research projects in the areas of health effects and risk assessment, some of them highly focused and relatively isolated, are already in progress without the benefit of any insight to be gained from the human epidemiologic studies. Of the three main issues identified, the priority order should be (a) evaluation and reassessment of the epidemiologic studies, with feasibility studies if called for; (b) research on DBP mixtures; and (c) toxicologic research on individual DBPs. This order applies to the proposed risk assessment projects as well as to the health effects studies. Committee advice on the priorities for individual projects are listed in Appendix B. Comments on specific studies are given in the following paragraphs.

Epidemiology studies on the residual DBP are limited because of unknown exposure. Therefore, improving estimates of residual DBP exposure are needed. This aim has a high priority, and has already been funded. However, these data will not be useful for immediate regulatory purposes (HED 1). A search for biomarkers in the field is very unlikely to be productive, given the multiplicity of exposures that might be associated with any identified

health effect and the near impossibility of teasing out any single exposure from among the many (HED 2). Little information is available on the reproductive effects of DBP. The use of geographic information systems (DBP in relation to distance from water plant) and birth weight has the possibility of providing epidemiological data on reproductive effects of DBP in humans (HED 3).

Implementation of either or both of the feasibility studies HED 4 and HED 5 is dependent on completion of reassessments of existing epidemiologic data, and on completion of epidemiologic studies underway. We are hampered in this evaluation by lack of information concerning which of the data reanalyses, which we understood might have been undertaken shortly after our initial briefing in the spring of 1995, may in fact have been undertaken, nor have we been given the results of any of the current epidemiological studies. However, particularly in view of the new carcinogen risk assessment guidelines proposed and shortly to be promulgated by the EPA, it is clear that reassessment of existing epidemiologic data is a prerequisite to the determination whether either these feasibility studies or the related full epidemiologic study, HED 6, should be carried out. It is probable that a thoughtful data reanalysis will reduce the range of estimates of excess cancer risk for the U.S. population as a result of consumption of chlorinated water. The results of the data reanalysis likely will also direct the design of feasibility studies. While we endorse the high priority assigned to these three proposals, it is not clear whether even the feasibility studies, if they are deemed to be warranted, can be completed within a time frame that would allow their outcomes to influence the rule making process significantly. It is certainly unlikely (although not impossible) that HED 6 could be completed within that time frame. With respect to policy questions and research goals, these three proposals are correctly assigned the highest priority. The results of the proposed studies would help greatly to reduce the uncertainty associated with assessments of current health risks (HED 4, 5, and 6).

We strongly discourage the conduct of standard two-year bioassays. Of considerably greater utility would be chronic studies at lower dose rates (lower, that is, than the maximum tolerated dose), incorporating other toxicity endpoints in addition to carcinogenicity and having pharmacokinetic and mechanistic components. In other words, the best use of resources would be a well-planned study designed to generate as much relevant information as possible at dose rates somewhat in excess of intake rates in drinking water, but not ludicrously so. Parts of other proposed projects would be subsumed in a general chronic study of this kind (HED 7).

Screening of reproductive and developmental effects is needed for DBPs. The EPA and NTP have superb capabilities for performing these studies (HED 8). There is little indication that either neurotoxicity or immunotoxicity is a likely endpoint of toxicity for DBPs. Other, more immediate issues should be addressed first (HED 9).

Successful development and validation of physiologically-based pharmacokinetic (PBPK) and biologically-based dose-response (BBDR) models for DBPs are laudable proposals and

would greatly facilitate extrapolation of animal dose-response data to humans. The likelihood is high that they would significantly improve utilization of animal dose-response data in human health risk assessment for specific DBPs, reducing the risk to public health in a cost-effective manner. The two proposals are not independent, since, as noted, every BBDR model has a PBPK model at its core. They should be combined and addressed as a unit. Further, developing a BBDR or PBPK model, adequately validated for extrapolation applications, is not a light undertaking. The list of potential DBPs to be modeled (bromate, trihalomethanes, and haloacids) is too large. Some economy could be achieved by utilizing generic physiologic models that would accommodate the kinetic characteristics of specific chemicals, but nonetheless some selections must be made. Achievement of a BBDR model, utilizable in practice, will require 18 months to two years for each chemical modeled. It is unlikely that this work would have broad impact on the rulemaking process itself (HED 11, 12).

EPA scientists have shown that haloacetic acids have toxic effects on the male reproductive system in rodents. To determine if this effect occurs in humans as well as if other DBPs are likely to produce this effect, one needs to understand the mechanism. By understanding the mechanism, biomarkers can also be developed (HED 13). However, while we encourage mechanistic research on DBPs, rationales should be provided for undertaking specific research projects with individual chemicals. Why were the haloacetic acids chosen for mechanistic research, while other DBPs were not?

The mixtures workshop has been conducted. A report of the workshop should be provided to the SAB (HED 14A). The toxicity of mixtures of DBPs is of extreme importance. However, the scientific community is not convinced how to best perform these studies. Information from the workshop and details of the studies to be performed are necessary to adequately evaluate this proposal (HED 14B). Interaction studies that are likely to be of most value are of known mixtures. The EPA has been performing good studies in this area and they should be continued (HED 17).

Many chemical carcinogens are mutagens however, many are not. Most of the "weak" carcinogens in drinking water are not thought to produce tumors by mutagenic mechanisms. Other mutagenic mixture studies have not been overly revealing (HED 16).

5.2.2 Exposure Research

The Committee agrees with methods development for bromate, haloacetic acids, and expanding quality control for TOC as high priority projects (EXD 1, 2, 3). Also methods for peroxides and aldehydes (EXD 7 and 9) are high priority. The identification of new disinfection byproducts from alternate disinfectants, methods for non-volatile DBPs (EXD 10 and 11) also rank high. The Committee considers DBP changes in distribution systems to be a high priority project (EXD 12). Without these methods for exposure and the concomitant health effects research, risk assessments are not possible. Further, these methods are

needed to obtain information on occurrence and population exposure to these byproducts. On the other hand, there are no significant projects that address capturing exposure information to contaminants or byproducts. The exposure modeling attempt is inadequate in the absence of good exposure monitoring to validate models that are employed. Without quality exposure information, the risk assessment would have significant uncertainties, and would not be useful or reliable in risk management decisions. Quality risk assessments on contaminants byproducts are needed for making balanced risk management decisions between byproducts and microbes.

5.2.3 Risk Assessment Research

a) General Comments

In general, the research projects, when successfully completed, can be expected to generate very useful information. However, there seem to be some inconsistencies in the expected completion dates for some of the projects based on two US EPA documents. The dates are expected completion dates based on the Revised EPA Research Plan Chapter 4 Tables, dated April 8, 1996. Accordingly, most of the projects are expected to have started as of today. It is not clear whether the completion dates would include the completion of the final reports (after peer reviews) or just the active research. The funding appropriations do not show resource allocations (e.g., number of person years, equipment, etc.). Such information would be useful. There is no information provided on the qualifications of the investigators or detailed description of the research projects, thus precluding an adequate evaluation.

In summary, the research projects aim at providing more accurate risk estimates, reducing uncertainties and developing methodologies to evaluate more complicated issues. All of these would be very useful in determining how to use experimental information most appropriately and most effectively for regulatory purposes. It is important that these are coordinated with the health effects research projects which generate data and information for risk assessment. In turn, the health research components need to be planned to generate data that will be useful for risk assessment. However, the schedules for the risk assessment projects and health effects studies do not seem to be coordinated. For example, the peer-reviewed papers describing the results of cancer dose-response studies will be prepared in FY'96-99, and the ones for trihalomethanes and bromate will be prepared in FY'96-99, whereas the final reports for the risk assessment are expected in FY'97. It would be useful for a timeline to be constructed to show how the different projects relate to each other in content and time sequence. The US EPA can also form partnerships with state water programs that have the expertise and capabilities to conduct work related to the research activities, especially in coordination with state level drinking water programs which share the same interest in regulating the same chemicals. This will contribute to more efficient use of resources.

Quantitative risk assessment models are to be applied to human and animal data to characterize the risks associated with exposure to disinfectants and DBPs. It is important to start using the recently revised Agency cancer risk assessment guidelines with available new studies, new data analysis and improved dose response models. Therefore RAD 1 is very appropriate. As an initiation, two to four chemicals can be assessed using the guidelines, and then the assessment can be completed with the other chemicals as appropriate. These risk assessments must continue and they should use new available data or analyses which provide new risk parameters (e.g., cancer potencies). This project is essential for generating new assessments so that no resources will be wasted on using the old risk assessment guidelines. USEPA is soliciting public comments on selecting priority chemicals for risk characterization also using new guidelines. DBPs are high priority chemicals in this regard and RAD 1 should be integrated with RAD 4. (RAD 1: Cancer risk assessments, completion date 1997) The comment on RAD 1 also applies to other research projects, especially RAD 2,3, and 4.

One project examines the validity of combining data sets prior to modeling and calculating a pooled slope factor. From this project, RAD 2, two studies and a final report and a case study have been published. It would be necessary for the Committee to see the results of this work in order to evaluate its potential applicability to the rule making process. On the other hand, while bromate is a DBP of potentially great concern, no broad rationale is provided for combining bromate data sets to estimate a pooled slope factor. Meta-analysis can be justified in some cases, and its statistical advantages can be real; but no justification for combining data sets is given here. This project is well underway, but it is not relevant to immediate rulemaking needs (RAD 2; Cancer combination study for bromates, completion date 1997).

Another project uses a benchmark dose (BM1) and/or categorical regression approach for estimating references doses. Development of these potentially useful new approaches, versus the traditional NOEL and margin of safety approaches, should be strongly supported. It would be necessary to compare results with the traditional approach. Benchmark doses were indicated to have been completed for methyl mercury and boron. The Committee members should be provided with these reports. In addition, non-cancer risk assessments need to continue and be combined with cancer risk assessments for a complete assessment (RAD 3: Non-cancer risk assessments, completion date 1998).

The project to develop case studies, with development of models for estimating variances in uncertainty factors for both cancer and non-cancer endpoints, will be useful for comparing cancer estimates. It involves the implementation of the agency's recently released risk characterization policy that addresses the need for informative and consistent approaches for communicating risk assessments to the public and decision makers. This is essential in order that risk assessment be appropriately understood and will contribute toward the trust and credibility given to the Agency performing the risk assessments. As noted above, RAD 4 should be integrated with RAD 1. However, application of the new EPA guidelines to DBP

risk characterization is less immediate in the context of standard setting and rule making than reanalysis of the epidemiologic studies, RAD 5 to 7. (RAD 4: Risk characterization, completion date 1998).

Three studies (RAD 5 to 7) set the stage for all other health effects research on DBPs by defining clearly what is known and what is not. RAD 5 will evaluate the newer epidemiologic studies (completion date 1997). This project applies a meta-analysis approach to earlier studies and evaluates new studies on adverse health outcomes associated with drinking water conducted in Canada and Colorado. This will provide a better understanding of actual risks and it is essential that the newer epidemiology data be reviewed. RAD 6 will assess previously conducted studies (completion date1997). This project will develop consistent statistical tools and improved methods for analyzing epidemiologic data to address confounding factors. Meta-analysis will be conducted on bladder and rectal cancers. RAD 7 will identify ongoing cancer studies (completion date 1996). The project identifies dietary cohort studies and case control cancer-risk studies. This information, compiled into a data base, will assist in determining the need for future studies and identifying areas for future studies. The data will be used to evaluate pregnancy outcomes. Although these seem to be important studies, the description of this project is not clear. Especially unclear is the anticipated products. The reference to evaluation of pregnancy outcome in relation to identifying cancer studies is confusing as there is no description of collecting specific data relating to pregnancy outcomes after identifying the studies. The Agency must follow all on-going cancer studies.

RAD 8, 9, and 10 seem to be related. The agency should show how these projects complement each other. RAD 8 will characterize interactions for mixtures of DBPs (completion date 1997). This project will develop procedures and conduct studies to evaluate interaction data from a number of studies and define the types of interaction. Like RAD 5 to 7, this project sets the stage for proposals listed in the HED section. However, implementation of RAD 5 to 7 does not require that this project be carried out. Some components of this project appear to be add-ons; their utility and even practicability are questionable. How, for example, will PBPK models be used to predict response to mixtures? How will sensitivity analysis be used to identify those parameters that have the greatest influence on response, unless the model includes the interactions in question? If this is the case, are the models to be developed for specific mixtures, prototypical mixtures, or generic mixtures? Nonetheless, the basic intent, to examine interaction data for DBPs closely, is sound. One project (RAD 9, Threshold studies for D/DBPs, completion date 1997) builds a dose-response plane for data from a mixture of D/DBPs under the assumption of additivity. The use of dose-response planes to evaluate interactions is an interesting proposal. RAD 10 (Use of QSAR model to estimate risk for single compounds/classes of compounds with a mixture, completion date, 1996) is developing a model that combines the chemical and physical properties of compounds to define their reactivity and toxicity. QSAR models have good potential for future use in estimating the risk of single and multiple exposures. However, that potential is not likely to be realized within the time frame of this research plan.

In addition, this is more a basic, longer-range research plan than one with direct relevance to immediate needs and goals.

A comparative risk analysis (RAD 11, completion date, 1998) proposes to develop a model to measure and compare the known and potential health risks that might result from exposure to multiple stressors from the same drinking water source. It is to address multiple outcomes, their impacts and costs. This would be useful, when validated, for regulatory decision making. Whether it will yield useful results in time for any of the projected rule making actions is uncertain.

5.2.4 Risk Management Research

Appendix A of the Research Plan briefly describes three categories of risk management research projects being conducted by EPA to address disinfection byproducts. The first category focuses on the effectiveness of different treatment processes in reducing DBP precursors (e.g., enhanced softening for precursor and pathogen removal-RMD 1; control of precursor, pathogen and pesticide removal-RMD 2a; effect of pH on ozonation and enhanced coagulation-RMD 2b; removal of DBP precursors by granular activated carbon [GAC] and membranes-RMD 4a & b; membrane scale-up and fouling-RMD 5). Only one project is included in agency research on the effectiveness of using different disinfectants in limiting DBP formation (ozonation byproduct formation and control-RMD 6). The final category focuses on small system technologies for precursor and DBP control and it contains only one project (membranes/ advanced oxidation and other technology combinations-RMD 7).

Many of the issues discussed in the overview (see Section 5.1) are directed to risk management research. A critical component of the research plan is a decision on which of the three risk management options the Agency and the industry will endorse for control of disinfection byproducts. These are removal before disinfection, removal after disinfection, or changing the disinfection process to minimize formation of related byproducts. Removal before and changing the disinfection process appear to be the most promising. As part of this procedure, RMD 1, enhanced softening for precursor (TOC) and pathogen removal is a project that deserves high priority. If this process is as successful as indicated, both microbial and DBPs may be lowered sufficiently to overcome many of the problems that now occupy a significant number of research projects. High pH will also have a significant impact on virus populations. However, many of the other projects in the Risk Management section including RMD 2, RMD 3, RMD 4, RMD 6 and RMD 7 are also considered of high priority. Further, the Committee suggests that it would be desirable for EPA to develop a white paper on the need for residuals in the distribution system. Appendix A of this report reflects both EPA and Committee priorities for these projects.

Many of the American Water Works Association Research Foundation (AWWARF) projects listed in Appendix C of the Plan are focused primarily on risk management research. Most of these projects have very brief descriptions that make it difficult for the committee to

ascertain the objectives, approach, and methodology of the research. Therefore, a commentary on each of them would be quite superficial. There are, in fact, over eighty-five such research projects listed for AWWARF and five for the National Water Research Institute (NWRI) listed in Appendix C. However, a number of these projects dealing with analytical methods for viruses and protozoa, natural organic matter, chemical contaminants, disinfection byproducts, and methods for control of byproducts made by treatment with ozone, chloramines, and chlorine dioxide that are very high priority projects. A series of projects on DBP control such as granular activated carbon, coagulation, oxidation and biological filtration, membrane technology, and ultraviolet methods also deserve high priority. It is hoped that as these research projects are completed and reported, that the DWC will have the opportunity to be appraised of the results and conclusions achieved.

6. CONCLUSIONS AND RECOMMENDATIONS

The Committee recognizes the complexity of this research plan with its multifactorial approach to both microbial and DBP research and acknowledges the considerable progress made by ORD and the Office of Water in comparison to previous versions of the plan. In general, the questions proposed in the research plan are appropriate. However, the plan lacks the identification of a critical path of project progression that would identify the rate limiting components. Such a critical path helps prioritize or plan the research projects so that those of greatest research uncertainty and resource requirements are accorded appropriate and primary attention and placed in a realistic time frame for overall research progress. This would allow sequencing of data acquisition that satisfies requirements for interdependency of project data.

The Committee notes that two of the rules, the long-term ESWTR and the GWDR have not yet been proposed and a third rule, the Stage 2 DBP rule has only been proposed in part. This raises a degree of uncertainty in defining the precise research needs to support the final development of these rules.

The Committee recommends that in iterations of this plan, or in other ORD research plans, that projects be more fully described. This will enable the reviewers to determine what actually is projected in the research and to better appreciate the budgeted costs. This is also applicable to research projects performed by other ogranizations (e.g., AWWARF and NWRI).

A significant number of research projects identified in the plan (e.g., those of the American Water Works Association Research Foundation--AWWARF) have been completed or projected to be completed in the years from 1994 to 1996. It is difficult to ascertain what effect the results of these projects have had, or will have, on the research plan. Full coordination of the drinking water research program by the agency Drinking Water Research Coordination Team was a stated goal of the Agency. The final plan should identify and incorporate the results of this research; which have presumably provided direction to the program. Further, the Committee encourages the Agency to interact with the broadest possible group of organizations doing research in this area.

The research plan has many specific questions on microbial research projects. These are addressed in the microbial section. The following are a few of the more general or overarching recommendations.

a) The Committee recommends that the research goals statement put a greater emphasis on identifying and quantifying the key pathogens and the health risks they pose in drinking water if prioritization of contaminants for regulation is to be risk based. This approach must carry through to the identification and quantitation of the key pathogens and their health risks.

b) The Committee believes that focusing on a single worst case pathogen or arbitrarily creating a large group is a scientifically inappropriate and unacceptable approach. Therefore, the committee recommends that greater emphasis be placed on a risk based approach to the identification and risk based analysis of all microbial pathogens in drinking water.

c) The Committee believes that it is important for EPA to develop a mechanism to identify emerging waterborne pathogens and carry out fast-track research on them as necessary. Further, the Agency needs to be proactive in this area and should establish a program that anticipates these types of emerging pathogenic microorganisms.

d) There is a need for a microbial epidemiological study in ground water systems that should include efforts to identify the pathogens responsible for the measured health effects.

e) The Committee is concerned that the ICR will provide no occurrence information on Norwalk virus. Also, the information on Cryptosporidium will not be sufficient for a detailed risk assessment because the methods used in the ICR do not differentiate between infectious and non-infectious oocysts. Thus the Committee believes that there is a serious disconnect between the priority pathogens of the health effects research (i.e., Norwalk virus and Cryptosporidium) and the priorities of the occurrence research.

f) There is concern that the level of funding and effort in the area of microbial risk assessment is inadequate for the task.

g) The research needs in the area of risk management include: Effectiveness of treatment processes for *Cryptosporidium*; treatment technologies appropriate for small systems; and identification and characterization of factors influencing microbial growth in distribution systems and strategies for its control. Research needs on factors influencing microbial growth in distribution systems and strategies for control should be expanded to include microbial intrusion as well.

Specific comments in the DBP portion of the research plan are also addressed in a separate section. The following are a few of the more general or overarching recommendations on that section.

a) The evaluation and reanalysis of the epidemiologic studies should inform research activities in the areas of health effects and risk assessment. If the reevaluation of existing epidemiologic data and completion of any feasibility or larger epidemiologic research can be completed within a time frame relevant to the rule making process, it should be assigned the highest priority from among this group of proposed projects.

b) The committee endorses a high priority rating for those methodological projects that subsequently are applied to obtain quality exposure data and knowledge of human health effects. Projects that address obtaining population-based

exposure data should be developed and added to the research plan to provide one of the necessary cornerstones for performing risk assessments.

c) The Committee believes that additional research is needed on the reliability of multiple barriers (multiple barriers of treatment can include: watershed protection and pathogen monitoring, multiple chemical inactivation steps, and filtration and/or sedimentation in addition to chemical inactivation).

d) The Committee considers it necessary to decide at the earliest time whether to remove precursor material before disinfection, change the disinfection process or remove DBPs after they are formed. The enhanced softening process run at high pH may provide the means to significantly lower TOC and kill microbes including viruses at the same time. Several projects either underway or completed (AWWARF) should guide this decision (e.g., 608, 814)

e) Membrane research projects and those using ultraviolet or high intensity broad band radiation disinfection should also have high priority. These are a necessary component of deciding on ground water disinfection methods.

f) The Committee urges EPA to develop a definitive paper on protecting the distribution system (why, how, etc.).

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APPENDIX A

EPA RESEARCH PLAN SHOWING RESEARCH PROJECTS AND PRIORITIES ARRANGED BY RULE, AND RISK ASSESSMENT-RISK MANAGEMENT PARADIGM COMPONENTS

The following is the key to spreadsheet column headings in Appendix A.

1) **Date:** Expected completion date

2) **EPA Priority:** H=High, M=Medium, L=Low
   Italicized project name and asterisk in priority column indicates that the project is either underway or planned for start in FY'96.

3) **SAB Priority:** 1 to 10; 1=Highest and 10=Lowest

4) **Funds** (Resource Estimate):
   1=<$0.5m
   2=$0.5 - 1.0m
   3=$1.0 - 1.5m
   4=$1.5 - 2.0m
   5=$>2.0m

5) **Page #:** Page number in Appendix A of the Research Plan where project information can be found.

APPENDIX A. EPA DISINFECTION RESEARCH PLAN ARRANGED ACCORDING TO THE RISK ASSESSMENT/MANAGEMENT PARADIGM

RA/RM PARADIGM CATEGORY / APPLICABLE RULE	ESWTR		DBP		GWDR	Microbes	DBPs	date	EPA	SAB	funds	page #
	Interim	L-Term	Stage 1	Stage 2					priority	priority		
RISK MANAGEMENT RESEARCH												
EPA Supported												
1. Removal												
RM M 1 - Filtration studies for controlling pathogens	X					X		ongoing	H*	1	1	
RM M 2 - Filtration removal of protozoa and indicators	X					X		97	H*	1	1	
RM M 3 - Optimize conventional treatment for removal of oocysts	X					X		98	H*	2	2	
RM M 4 - Filtration damage viability studies	X					X		98	H*	1	2	
RM M 5 - Evaluate disinfection and optimization in full-scale treatment plants		X				X		2000	H*	2	3	
RM M 6 - Biological treatment for control of oocysts	X					X		98	H*	1	4	
RM M 7 - Filtration techniques other than conventional treatment	X					X		99	M*	5	1	
RM M 8 - Control of Norwalk virus by chlorine and ozone	X					X		98	H	1	1	
R M M 9 - UV disinfection efficiencies for Norwalk viruses					X			97	H	2	1	
RM M 10 - Inactivation of Giardia & Crypto by sequential disinfectants	X					X		98	H	1	2	
RM M 11 - *Cryptosporidium removal using bag filters*		X				X		98	H*	3	1	
RM M 12 - Cost effectiveness of prefiltration for ultrafiltration unit		X				X		98	H*	3	1	
RM M 13 - Development/test innovative technologies for small systems		X				X		97	H*	3	1	
2. Distribution Systems												
RM M 14 - Bacteria interference with detection of coliforms and E coli		X				X		99	M	10	1	
RM M 16 - Enhancement to the EPANET distribution system water quality model		X				X	X	98	H*	1	1	
RM M 17 - Prelim studies of biofilm formation rates in pilot scale distribution systems		X				X		98	M*	5	1	
RM M 18 - Opportunistic pathogens in biofilms		X				X		TBD	M	1	2	
RM M 19 - Impact of nutrient removal on growth potential for bacteria		X				X		98	M*	2	2	
RM M 20 - Impact of alternative treatment of biofilm growth		X				X		2000	M	5	1	
RM M 21 - Water quality factors in distribution systems		X				X	X	97	M*	6	1	
RM M 22 - Water quality impacts of dead ends		X				X	X	97	M*	3	1	
RM M 23 - Mixing in storage facilities		X				X		97	M*		1	
R.M M 26 - Bacterial growth in distribution systems		X				X		97	H	3	1	
R.M M 27 - Integrated approaches for controlling pathogens		X				X		2000	M	7	1	
3 Effectiveness of treatment processes												
RM D 1 - Enhanced softening for precursor and pathogen removal		X						98	H*	1	2	
RM D 2 - Effects of ozonation & biofiltration for control of precursor, pathogen & for pesticide removal		X										
a - Control precursor, pathogen and pesticide removal						X		98	H*	2	2	

APPENDIX A EPA DISINFECTION RESEARCH PLAN ARRANGED ACCORDING TO THE RISK ASSESSMENT/MANAGEMENT PARADIGM

RA/RM PARADIGM CATEGORY / APPLICABLE RULE	ESWTR		DBP		GWDR	Microbes	DBPs	date	EPA	SAB	funds	page #
	Interim	L-Term	Stage 1	Stage 2					priority	priority		
b - Effect of pH on ozonation and enhanced coagulation						X		97	H*	3	1	
R M 3 - Analyze ICR data from GAC, membrane bench and pilot studies				X				99	H	3	2	
RM D 4 - Removal of DBP precursors by GAC and membranes												
a - Evaluation of membrane reliability				X			X	98	M*	5	1	
b - Evaluation of GAC				X			X	98	M*	5	1	
RM D 5 - Membrane scale-up and fouling				X			X	98	M*	3	1	
RM D 6 - Ozone by-product formation and control				X			X	98	H*	2	1	
RM D 7 - Membranes/advanced oxidation/other technonology combinations				X			X	98	H*	2	1	
RM M 15 - Kinetic Models for chlorine decay in distribution systems				X			X	95	H*	2	1	
RM M 16 - Enhancement to the EPANET distribution system water quality model				X				99	H*	1	1	
RM M 24 - Alternative kinetic models for decay and DBP formation				X			X	97	H	3	1	
RM M 25 - Real-time monitoring systems				X				98*	H	4	1	
RA M 1 - Devel compre micro risk assess paradigm for water					X	X		96	H*	1		
RA M 2 - Application of categorical regression model for quantitating pathogenic risks					X	X		98	H*	1	1	
RA M 3 - Threshold modeling of pathogens					X	X		98	M	6	1	
AWWARF Supported (unless otherwise specified)												
525 - Demo scale eval of PEROXONE evaluation for disinfection, DBPs	X		X			X	X	1996			----	5
181 - Biological particle surrogates for filtration performance eval	X					X		1997			----	15
908 - National assess of particle removal by filtration	X						X	1996			----	15
835 - Practical guide to on-line particle counting	X						X	1995			----	15
423 - Joint project on treatment process selection particle removal optimization	X						X	1996			----	16
266 - Quantitative particle count method devt standardization, sample stability	X						X	1998			----	15
Filtration performance workshop								1995			----	16
817 - Membrane filtration techniques for microbe removal	X					X		1996			----	17
264 - Integrated multi-objective membrane systems for microbes/DBP precursors	X					X	X	1999			----	17
703 - Optimization of filtration for cyst removal	X					X		1996			----	17
155 - Enhanced/optimized coagulation for removal of microbial contaminants	X					X		1997			----	17
731 - *Ozone disinfection of Giardia and Crypto*	X					X		1994			----	19
608 - Lime softening processes for Giardia and viruses	X					X		1994			----	19

APPENDIX A. EPA DISINFECTION RESEARCH PLAN ARRANGED ACCORDING TO THE RISK ASSESSMENT/MANAGEMENT PARADIGM

RA/RM PARADIGM CATEGORY / APPLICABLE RULE	ESWTR		DBP		GWDR	Microbes	DBPs	date	EPA	SAB	funds	page #
	Interim	L-Term	Stage 1	Stage 2					priority	priority		
906 - Effect of various disinfection methods on inactivation of Crypto	X					X		1996			----	19
273 - Synergistic effects of multiple disinfectants	X						X	1998			----	19
??? - Utility Giardia and Crypto inactivation study - Southern Nevada Water Authority	X					X		1997?				20
282 - Innovative electrotechnologies for Crypto inactivation	X					X		1998			----	20
702 - Devl and validation of rational design methods of disinfection	X						X	1995			----	18
636 - Evaluation of roughing filter design variables	X							1994			----	16
429 - Male-specific coliphages as indicators of viruses & treatment effectiveness	X					X		1995			----	15
254 - Managing & operating finished water storage facilities	X							1998			----	24
271 - Improving clearwell design for DBP and CT compliance	X					X	X	1998			----	9
180 - UV inactivation of viruses in natural waters					X	X		1997			----	21
817 - Membrane filtration techniques for microbial removal					X	X		1996			----	17
809 - By-products of UV treatment of groundwater					X		X	1995			----	9
NWRI Supported												
Norwalk inactivation study					X						----	
Deposition mechanisms and long-time scale factors influencing virus transport in porous media					X			1995				21
Virus fate and transport under saturated flow conditions					X			1995				22
Field experiment and modeling of vira transport in groundwater					X			1996				22
Transport and fate of viruses in the vicinity of pumping wells					X			1996				22
AWWARF Supported (unless otherwise specified)												
630 - Full scale ozone contactor evaluation	X						X	1995			----	20
632 - Modeling dissolved ozone in contactors	X						X	1996			----	20
Norwalk inactivation study (NWRI)						X					----	
263 - Colonization of biologically active filter media with pathogens	X	X				X		1998			----	18
291 - Particle Image Velocimetry	X						X	1998			----	16
936 - Pathogens in model distribution system biofilms		X				X		1996			----	22
704 - Factors limiting microbial growth in distribution systems		X				X		1996			----	23
Interactions between pipe materials, corrosion inhibitors,biofilm NWRI											----	23
260 - Water quality monitoring of distribution syst. storage facilities		X				X	X	1998			----	25
254- Managing and operating finished water storage facilities		X						1998				24
262 - Booster disinfection for pathogen and DBP control		X					X	1998			----	25
815 - Characterization and modeling of chlorine decay		X					X	1996			----	25
270 - Occurrence and control of Mycobacterium avium complex		X				X		1998			----	22
154 - Biological stability of drinking water in treatment plants and distribution systems		X				X		1997			----	24

APPENDIX A. EPA DISINFECTION RESEARCH PLAN ARRANGED ACCORDING TO THE RISK ASSESSMENT/MANAGEMENT PARADIGM

RA/RM PARADIGM CATEGORY / APPLICABLE RULE	ESWTR		DBP		GWDR	Microbes	DBPs	date	EPA	SAB	funds	page #
	Interim	L-Term	Stage 1	Stage 2					priority	priority		
917 - Microbial effects of biological filtration		X				X		1996			----	18
183 - Factors affecting microbial growth in distribution systems		X				X		1997			----	22
??? - On-line monitoring of pathogen ecology in distribution system		X				X		1997				23
534- Fatty acid profiling for identification of environmental bacteria in distribution system		X				X		1995				22
293 - Role of pipe-water interface inDBP formation & disinfection		X					X	1997			----	24
294 - Travel times & water quality in deadends		X						1997			----	25
729 - Biofilm reactor BOC measurement		X				X		1996			----	24
157 - Distribution system water quality post corrosion control		X					X	1997			----	25
834 - Balancing multiple water quality objectives		X				X	X	1996			----	27
504 - Ozone & biological treatment for DBP control and biological stability			X			X	X	1994			----	7
159 - Methods for characterizing natural occurring matter			X				X	1997			----	3
709 - Impacts of ozonation on formation of chlorinated DBPs			X				X	1996			----	4
830 - Bromide-Ozone interactions in water treatment			X				X	1996			----	4
156 - Strategies to control bromide and bromate ion			X				X	1997			----	4
937 - Chloramine decomposition kinetics and degradation products			X				X	1996			----	5
803 - Factors affecting DBP formation during chloramination			X				X	1996			----	5
710 - Nitrification occurrence and control in chloraminated water systems			X				X	1995			----	6
611 - Sources, occurrence, & control of ClO2 byproduct residuals in drinking water			X				X	1994			----	6
816 - Removal of DBP precursors by GAC adsorption			X				X	1996			----	6
814 - Removal of DBP precursors by optimal coagulation & and precip softening				X			X	1996			----	6
631 - Removal of natural organic matter in biofilters				X			X	1995			----	7
252 - Optimizing filtration in biological filters				X		X		1998			----	7
531 - Evaluation of humic substance removal using ferric chloride				X			X	1995			----	6
601 - Ultrafiltration membrane pretreatment & nanofiltration of surface water				X			X	1994			----	8
712 - Design of biological processes for organics control				X		X		1996			----	8
934 - Optimizing Ozonation for turb & Organics removal				X			X	1996			----	7
??? - Adsorption & Filtration using iron-oxide-coated olivine				X			X	1996			----	
163 - Development of improved method for haloacetic acids			X				X	1996			----	3
417 - Development of fiber optic chemical sensors for monitoring organics			X				X	1996			----	3
159 - Improved methods for isolation and characterization of NOM			X				X	1997			----	3
533 - Effect of carbonate/bicarbonate alkalinity on advanced oxidation processes			X				X	1996			----	4
504 - Ozone/biological treatment for DBPs and microbes			X				X	1994			----	7
709 - Impacts of ozonation on formation of chlorinated DBPs			X				X	1996			----	4
830 - Bromide-ozone interactions in water treatment			X				X	1996			----	4

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RA/RM PARADIGM CATEGORY / APPLICABLE RULE	ESWTR		DBP		GWDR	Microbes	DBPs	date	EPA	SAB	funds	page #
	Interim	L-Term	Stage 1	Stage 2					priority	priority		
832 - Reaction of ozone and hydroxyl radicals with amino acids			X				X	1995			----	5
156 - Strategies to control bromide and bromate ion			X				X	1997			----	4
937 - Chloramine decomposition kinetics & degradation products			X				X	1996			----	5
803 - Factors affecting DBP formation during chloramination			X				X	1996			----	5
710 - Nitrification occurrence and control in chloraminated water systems			X				X	1995			----	6
816 - Removal of DBP precursors by GAC adsorption			X				X	1996			----	6
814 - Removal by optimized coagulation and softening			X				X	1996			----	6
631 - Removal of NOM in biofilters			X			X	X	1995			----	7
252 - Optimizing filtration in biological filters			X			X		1998			----	7
531 - Humic acid removal using ferric chloride			X				X	1995			----	6
904 - Biofouling in membrane processes			X			X		1997			----	8
826 - Membrane technology for drinking water - Joint Report			X				X	1997			----	9
601 - Ultrafiltration membrane pretreatment and nanofiltration			X				X	1994			----	8
833 - Minimizing chlorate ion formation in drinking water when hypochlorite used			X				X	1995			----	9
289 - Advanced oxidation and biodegradation processes			X			X	X	1998			----	7
170 - Reverse osmosis and nanofiltration for organics removal			X				X	1997			----	8
RISK ASSESSMENT RESEARCH												
EPA Supported												
RA M 1 - Devel comprehensive microbio risk assess paradigm for water	X	X				X		96	H*		----	
RA M 2 - Application of categorical regression model for quantitating pathogenic risks		X				X		98	H*		1	
RA M 3 - Threshold modeling of pathogens		X				X		98	M		1	
RA D 1 - Cancer risk assessments				X			X	97	H*	3	1	
RA D 2 - Cancer combination study for bromates				X			X	97	H*	1	1	
RA D 3 - Noncancer risk assessments				X			X	98	H*	1	2	
RA D 4 - Risk characterization				X			X	98	H*	2	1	
RA D 5- Evaluate newer epidemiologic studies				X			X	97	H*	1	1	
RA D 6- Assessment of previously conducted studies				X			X	97	H*	2	----	
RA D 7 - Identify on-going cancer studies				X			X	96	H*	2	----	
RA D 8 - Characterization of interactions for mixtures of DBPs				X			X	97	M*	5	2	
RA D 9 -Threshold studies for D/DBPs				X			X	97	H*	2	2	
RA D 10 - Use of QSAR model to est risk for single cmpnds/classes of compounds within a mixture				X			X	96	H*	3	----	
R.A D 11 - Comparative Risk Analysis				X		X	X	98	H*	1	3	

RA/RM PARADIGM CATEGORY / APPLICABLE RULE	ESWTR		DBP		GWDR	Microbes	DBPs	date	EPA	SAB	funds	page #
	Interim	L-Term	Stage 1	Stage 2					priority	priority		
801 - Microbial risk assessment for drinking water	X					X		1996			----	14
HEALTH EFFECTS RESEARCH												
EPA Supported												
HE M 1 - Infectious dose of Cryptosporidium	X					X		96	H*		----	
HE M 5 - Infectious dose of Norwalk virus	X				X	X		98	H*		2	
HE M 6 - Infectious dose of other priority pathogens (to be determined)		X			X	X		TBD	M		3	
HE M 7 - Characterization of endemic disease (with AWWARF)	X	X				X		2000	H*		3	
HE M 8 - Immunological assay for assessing exposure in epi studies (with AWWARF)	X	X				X		99	H*		2	
HE M 9 Investigations of waterborne disease outbreaks	X	X			X	X		ongoing	H*		1	
HE M 10 - Surveillance tool for waterborne disease outbreaks	X	X			X	X		97	H*		----	
HE D 1 - Improving estimates of residential DBP exposure in epidemiology studies				X			X	96	H*	3	----	
HE D 2-Improving measures of biologic effect Field evaluation of biomarkers				X			X	2000	H	6	2	
HE D 3-Improving methods for managing health and exposure data				X			X	98	H*	4	1	
HE D 4 - Feasibility studies Cancer				X			X	97	H	1	2	
HE D 5 - Feasibility studies Reproductive effect				X			X	97	H*	1	1	
HE D 6 - Full scale studies, Cancer and reproductive effects				X			X			1		
- Cancer								TBD	feasible H		5	
- Reproductive effects								TBD	feasible H		5	
HE D 7 - Cancer dose-response studies				X			X	2000	H*	5	2	
HE D 8 - Reproductive/developmental effects screening studies				X			X	99	H*	3	2	
HE D 9 - Neurotoxicity studies				X			X	98	M*	8	1	
HE D 10 - *Immunotoxicity studies*				X			X	98	M		1	
HE D 11 - Development of biological based dose-response (BBDR) model for priority DBPs				X			X	2000	H*	7	2	
HE D 12 - Develop physiological based pharmacokinetic (PBPK) model for priority DBPs				X			X	2000	H*	7	2	
HE D 13 - *Mechanistic research on reproductive toxicity/developmental effects*				X			X	2000	H*	3	3	
HE D 14 a - Mixtures workshop				X			X	1996	H*	1	1	
HE D 14b - Mixtures feasibility study				X			X	97	H	2	1	
HE D 15 - Toxicologic evaluation of drinking water mixtures				X			X	TBD	feasible H		2	
HE D 16 - Mutagenicity screening studies of drinking water mixtures				X			X	2000	H	8	1	
HE D 17 - Studies of DBP interactions				X			X	99	M	3	1	

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RA/RM PARADIGM CATEGORY / APPLICABLE RULE	ESWTR		DBP		GWDR	Microbes	DBPs	date	EPA	SAB	funds	page #
	Interim	L-Term	Stage 1	Stage 2					priority	priority		
AWWARF Supported (unless otherwise specified)												
268 - Fingerprinting techniques for opportunistic pathogens & illness		X			X	X		1998			----	10
432 - Mechanistic basis and relevance of rat kidney tumor formation			X				X	1994			----	1
617 - Carcinogenic mechanisms in rat & mouse hepatocytes			X				X	1996			----	1
701 - Induced hepatic tumors with induction of peroxisomes			X				X	1996			----	1
738 - Dose-response relationship of DCA & TCA-induced proliferation			X				X	1995			----	1
Chlorite/Chlorine Dioxide 2 generation reproductive study - CMA								1996			----	
919 & 168- Prospective Epi Study of waterborne microbial disease (with EPA)	X											
177- Association between Crytosporidium in finished water and crytosporidosis	X											
in population												
EXPOSURE ASSESSMENT												
EPA Supported												
EX M 11 - Intensive eval of micro constituents/treatability in surface source waters		X				X		2000	H*		5	
EX M 12 - Identification of viruses resistent to disinfection		X				X		2000	M		1	
EX M 13a - Distinguish animal versus human sources		X				X		98	M*		1	
EX M 13b - Detecting fecal contamination in its sources		X				X		98	H*		----	
EX,M 14 - Occurrence of Mycobacterium		X				X		98	H*		1	
EX M 15 - Occurrence of heterotrophic bacteria with virulence characteristic		X				X		97	H*		1	
EX M 16 - PCR method for Legionella		X				X		96	L*		1	
EX M 17 - Pathogenicity of heterotrophic bacteria found in drinking water		X				X		98	H*		1	
EX M 18 - Occurrence of opportunistic pathogens in biofilms		X				X		98	M		1	
EX M 19 - Opportunistic pathogens assoc with (POU)/ (POE) filter effluents		X				X		97	M		1	
EX M 20 - Potential pathogenicity of heterotrophic bacteria eluted from point-of -use GAC filters		X				X		99	H		1	
EX M 21- Occurrence of newly emerging pathogens		X				X		2000	M*		1	
EX M 22 - Exposure as a function of populatoin distribution		X				X		99	H		3	
EX D 17 - Exposure as function of population distribution				X			X	2000	M	5	1	
AWWARF Supported (unless otherwise specified)												
162 - UV-VIS spectroscopy for rapid on-line detection of protozoa		X				X		1988			----	11
253 - Viability method for Giardia and Cryptosporidium		X				X		1998			----	11

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RA/RM PARADIGM CATEGORY / APPLICABLE RULE	ESWTR		DBP		GWDR	Microbes	DBPs	date	EPA	SAB	funds	page #
	Interim	L-Term	Stage 1	Stage 2					priority	priority		
612 - Analysis of viruses by gene probe		X				X		1996			----	12
251- Evaluation of sources of pathogens and NOM in watersheds		X				X		1998			----	13
METHODS DEVELOPMENT												
EPA Supported												
1. Microbial Methods												
EX M 1 - Immunological techniques for protozoa		X				X		99	H*		1	
EX M 2 - Gene probes for detection of viable Cryptosporidium oocysts		X				X		2000	H		1	
EX M 3 - *Cultural method for Cryptosporidium in environmental samples*		X				X		98	H*		2	
EX M 4 - PCR methods for Giardia and Cryptosporidium (CRADA)		X				X		95	M*		----	
EX M 5 - Protozoa methods protocol development workshop		X				X		95	H*		----	
EX M 6 - Comparison of methods for Giardia and Cryptosporidium in water		X				X		98	H*		----	
EX M 7 - New protozoa agents		X				X		98	H*		1	
EX M 8 -Application of PCR technologies and gene probes for virus detection in water		X			X	X		96	M*		1	
EX M 9 - Norwalk virus		X			X	X		98	H*		1	
EX M 10a - Methods for emerging viruses		X			X	X		99	H*		1	
EX M 10b - PCR detection of viruses in water		X			X	X		98	H*		----	
EX,M 14 - Occurrence of Mycobacterium					X	X		98	H*		1	
EX M 15 - Occurrence of heterotrophic bacteria with virulence characteristic					X	X		97	H*		1	
EX M 16 - PCR method for Legionella					X	X		96	L*		----	
EX M 17 - Pathogenicity of heterotrophic bacteria found in drinking water					X	X		98	H*		1	
EX M 18 - Occurrence of opportunistic pathogens in biofilms					X	X		98	M		1	
2 *Ground water contamination*												
EX M 23 - Virus survival in the subsurface					X	X		2000	H*		5	
EX M 24a - Virus transport in the subsurface					X	X		2000	H*		3	
EX M 24b - Norwalk virus -like particles for studying natural gw disinfection					X	X		98	H*		----	
EX M 25 - Viral transport and fate models					X	X		2000	M*		2	
EX M 26 - Vulnerability of ground-water to pathogens					X	X		2000	H*		5	
EX M 27 - Delineation of natural protection zones					X	X		2000	M*		2	
1. D/DBP Methods												
EX D 1 - Low level bromate measurement			X				X	99	H*	1	1	
EX D 2 - Improved method for haloacetic acids			X				X	98	H*	3	1	
EX D 3 - Expand quality control for TOC, evaluate new TOC methods			X				X	98	H*	2	1	

RA/RM PARADIGM CATEGORY / APPLICABLE RULE	ESWTR		DBP		GWDR	Microbes	DBPs	date	EPA	SAB	funds	page #
	Interim	L-Term	Stage 1	Stage 2					priority	priority		
EX D 4 - Low level ClO2 measurement			X				X	99	M	5	1	
EX D 5 - Real-time monitoring for disinfectant residuals			X				X	98	L	9	1	
EX D 6 - PE studies for DBPs and disinfectants			X				X	ongoing	H*	4	5	
EX D 7 - Methods for peroxides				X			X	2000	M*	5	1	
EX D 8 - Real-time, in-plant monitoring of DBPs				X			X	2000	L	9	2	
EX D 9 - Improved method for aldehydes				X			X	98	M*	4	1	
EX D 10 - Identify new DBPs from alternate disinfectants				X			X	2000	H*	2	2	
EX D 11 - *Methods for non-volatile DBPs*				X			X	2000	H*	2	2	
EX D 12 - DBP changes in distribution system				X			X	2000	M	5	4	
EX D 13 - DBP interactions with foods and associations with dietary intake				X			X	2000	M	7	4	
EX D 14 - Exposure to DBPs through showering				X			X	2000	M	8	4	
EX D 15 - Markers of DBP exposure				X			X	2000	M	3	4	
EX D 16 - Models of DBP exposure				X			X	2000	H	3	4	
AWWARF Supported (unless otherwise specified)												
162 - Innovative & rapid methods for Giardia & Cryptosporidium	X					X					----	11
259 - Improve the IFA method for Giardia and Cryptosporidium	X					X		1998			----	11
283 - Detection of Giardia & Cryptosporidium by flow cytometry	X					X		1996			----	11
160 - Vital stain for Giardia and Cryptosporidium	X					X		1997			----	13
151- Cyst and oocyst survival in watersheds and factors affecting inactivation	X					X		1997			----	13
251 - Evaluating of sources of pathogens and NOM in watersheds	X					X		1998			----	13
825 - Bromide Survey			X				X					3
830 - Bromide-ozone interactions (incl develop analytical technique for total organic bromide)			X				X	1996				4
832 - Reaction of ozone and hydroxyl radicals with amino acids			X				X	1995			----	5
803 - DBP formation during chloramination (incl. developing analytical techniques for new DBPs)			X				X	1996			----	5
611 - Sources, occurrence, & control of ClO2 byproduct residuals in drinking water			X				X	1994			----	6
916 - Application of PCR techniques for virus detection in groundwaters					X	X		1996			----	12
726 - Survey of enteric viruses in groundwater					X	X					----	12
612 - Analysis of viruses by gene probe					X	X		1996			----	12
262 - Field study of virus and indicator transport in ground water					X	X		1998			----	21?
702 - Development and validation of rational design methods of disinfection					X		X	1995			----	18
429 - Male-specific coliphages as indicators of viruses					X	X		1995			----	15
292 - Rapid PCR-based monitoring of entero virises					X	X		1998			----	12
186 - Survey viruses in ground waters					X	X		1997			----	12

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