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U.S. ENVIRONMENTAL PROTECTION AGENCY HEALTH EFFECTS RESEARCH ON DRINKING WATER CONTAMINANTS

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INTRODUCTION

The Safe Drinking Water Act of 1974 (SDWA), as amended in 1986, provides a mandate to the U.S. Environmental Protection Agency (EPA) to ensure the safety of the nation's drinking water. The SDWA requires that most public water supplies use filtration and/or disinfection to prevent waterborne infectious disease. Chemical and microbial contaminants on the Drinking Water Priority List are regulated in phases every three years. For each contaminant that is regulated, the EPA must establish Maximum Contaminant Level Goals (MCLGs) and Maximum Contaminant Levels (MCLs). MCLGs are non-enforceable health-based standards that represent water treatment goals. MCLs are enforceable standards based on health concerns plus a consideration of risk management factors such as the technological feasibility of controls, the availability of analytical techniques, and the economic impact of the regulation. For chemicals that may enter drinking water by accident, risk assessment-based health advisories (HAs) are developed. HAs are concentrations of a contaminant that are not expected to cause adverse noncancer health effects after exposures varying from one day to a lifetime.

The development of these requirements depends in part upon the ability of EPA to comprehensively assess the risks associated with exposure to chemical and microbial contaminants for the various water treatment options. The EPA Office of Research and Development (ORD) conducts research that forms the scientific basis for this comparative assessment, and provides data and methods that are used by the EPA Office of Water in the development of regulations required by the SDWA. This research is conducted within the context of the various components of the National Academy of Sciences risk assessment paradigm[1]: hazard identification, dose-response assessment, exposure assessment, and risk characterization.

Several ORD laboratories and offices are involved in drinking water research and assessment activities. These include the Health Effects Research Laboratory (HERL) in Research Triangle Park, North Carolina, and the Environmental Monitoring Systems Laboratory, the Environmental Criteria and Assessment Office, and the Risk Reduction Engineering Laboratory in Cincinnati, Ohio. This paper briefly discusses drinking water health research

needs, and then focuses on the health effects research program at HERL. It should be pointed out that several health-related research projects, such as the study of waterborne pathogens and the development of risk assessment methods, involve multi-laboratory/office collaboration within EPA.

HEALTH RESEARCH NEEDS

Health effects concerns for drinking water generally fall within the following areas:

1) The chemical and microbiological quality of source waters. Chemical contaminants of concern in source waters include substances such as arsenic, pesticides in agricultural areas, and solvents from underground injection of wastes. Source water microbial contaminants include pathogens such as Cryptosporidium, Giardia, and waterborne enteric viruses (e.g., Norwalk virus).

2) The safety of the disinfection process. Disinfection of drinking water with chlorine has been the conventional treatment of choice for protecting the public against waterborne microbial disease. Public health concern over the safety of the disinfection process is based on the recognition that chlorination and alternative disinfectant treatments produce a wide variety of by-products, many of which have been shown under experimental conditions to cause cancer and other toxic effects. Drinking water requirements must therefore minimize the risk associated with exposure to the most toxic chemical contaminants, while protecting against microbial contamination.

3) The impact of nondisinfectant chemical additives. These include clarifying agents such as alum that are used to remove suspended particulate matter in source water, and other substances that are added to adjust such characteristics as pH and water hardness.

4) The safety of distribution system contaminants. Toxic chemicals such as copper, lead, and other metals may leach into the drinking water as it passes through the distribution system. Microbial concerns relate to the growth/ regrowth of pathogens in the distribution system.

The list of health research needs for drinking water contaminants is extensive, particularly for certain microbes and chemicals found in source waters and for the chemical by-products of disinfection. The toxic effects of many chemical contaminants are unknown or poorly characterized. This is particularly true for the by-products of ozonation. Beyond the need for basic toxicological data, an improved understanding of the chemical, physical and biological processes involved in toxic responses is critical to evaluating the human risk associated with exposure to these contaminants. Studies are needed to evaluate the toxicity of the complex mixture of contaminants to which human populations are exposed. For microbes, there is considerable uncertainty with regard to the infectious dose for high priority waterborne pathogens, the

influence of host factors (e.g., immune status) on infectivity and pathogenicity in humans, and the occurrence of endemic microbial disease in populations consuming water that meets existing treatment standards.

EPA DRINKING WATER HEALTH RESEARCH

Priorities for selecting health effects research projects on drinking water contaminants are based on a consideration of several criteria: the potential regulatory and public health impact of a research issue; the ability to lead to a major scientific improvement in a drinking water risk assessment; the likelihood of significant progress within a 3-5 year time frame; and the ability to extend results to other drinking water scientific issues. Resources for drinking water health research at EPA have gradually declined since the mid-1980's. Due to resource constraints, research in a number of high priority areas is either nonexistent or inadequate.

The primary emphasis of the program is on key disinfection by-products and source water contaminants. An integrated research program has been developed at EPA in three major areas: toxicology, pharmacokinetics, and human studies. A brief description of the research in each of these areas is found below.

Toxicology

Cancer. The drinking water regulatory program requires quantitative estimates of cancer risk (e.g., for the development of MCLs) for carcinogens of concern. The rodent cancer bioassay program at HERL addresses this need by providing data on cancer potency as well as mechanisms of action for key disinfection by-products. The long-term research goal is the development of biologically-based models to improve the scientific basis for risk assessment.

The list of chemicals selected for study reflects the regulatory priorities of the Office of Water. Chemicals for which studies are either ongoing or planned include bromodichloromethane, di- and trichloroacetic acid, chloral hydrate, bromate, and the brominated acetic acids. By-products of ozonation have been given the highest priority due to the anticipated increase in use of this disinfection practice and the critical need for toxicologic information on these substances. An additional feature of the chronic bioassay program is that it provides opportunities for collaborative research across disciplines at HERL. Animals exposed to the various disinfection by-products are being used for parallel studies in pharmacokinetics, neurotoxicology, reproductive toxicology, immunotoxicology, and genetic toxicology.

Genotoxicity. This research involves the application of short-term *in vitro* tests for genotoxicity (e.g., mutagenicity assays in Salmonella), in combination with chemical fractionation, to study the complex mixtures of by-products in water subjected to different treatment processes. Studies are also underway to

characterize the genotoxicity of complex mixtures of by-products at the molecular level. The overall goal is to identify toxic species within mixtures so that control technologies can be developed to reduce or eliminate them from potable water.

Reproductive and Developmental Toxicity. Studies are underway to evaluate the developmental and reproductive toxicity of high priority disinfection by-products. The long-term goal of this research is to evaluate the sensitivity of reproductive measures to assess the risk of key disinfection by-products. Acute and subchronic tests in rodents are underway to evaluate the male reproductive toxicity of the brominated acetic acids. Reproductive endpoints are also being evaluated in animals exposed to dichloroacetic acid and chloral hydrate in the cancer bioassay program.

Neurotoxicity. Research is being conducted to evaluate the potential neurotoxic effects of selected disinfection by-products. Current studies involve qualitative and quantitative assessments of the neurotoxicity of dichloroacetic acid. A battery of tests is being developed for rapid hazard identification of developmental neurotoxicants found in drinking water. In addition, a short-term test is being developed to assess the potential neurotoxicity of chemicals in drinking water.

Research on aluminum, a widely used clarifying agent in water treatment processes, is being conducted to address concerns that this metal may be associated with neurodegenerative disorders in highly susceptible populations such as the elderly. The toxicity of aluminum to the nervous system is well-established; however, whether neurotoxicity may arise from the levels and routes of exposure that occur in the environment is a controversial and inadequately studied issue. The goal of this research is to provide a qualitative and quantitative assessment of the risks associated with exposure to aluminum in drinking water, using a homologous model of learning and memory in humans and animals.

Pharmacokinetics

Pharmacokinetic research determines the relationship between the applied or environmental exposure level of a chemical agent and the dose of the chemical or its metabolite at a target site in the body. Studies of chemical uptake, distribution and metabolism in rodents are being conducted to facilitate the extrapolation of effects from animals to humans and from high to low dose levels. These studies are being complemented by toxicity studies (hepatotoxicity and renal toxicity in particular) and by chemical reactivity studies that include structure/activity analyses. Research is being conducted on the trihalomethanes and the haloacids, with a primary focus on bromodichloromethane. The goal of this program is to develop physiologically-based pharmacokinetic models, to be used in combination with biologically-based dose-response models, for the most important disinfection by-products of regulatory concern.

Research on arsenic is addressing several key scientific issues that impact the risk assessment for this important source contaminant. The goal of this research is to provide a better understanding of the dose-response relationship for arsenic toxicity, the relationship of metabolism to toxicity, and other important factors that can affect sensitivity (susceptible subgroups). These studies will make significant improvements to the risk assessment for arsenic and will also provide information of general utility in understanding mechanisms of chemical carcinogenicity.

Human Studies

The epidemiologic research program at HERL assesses the possible changes in morbidity and mortality linked to the consumption of treated water. HERL is evaluating the feasibility of conducting epidemiologic studies of populations consuming water that is treated with chloramines or with ozone. Another feasibility study involves an assessment of the risk to communities served by water contaminated with arsenic. A number of infectious disease epidemiology/clinical studies are planned in collaboration with the EPA Environmental Monitoring Systems Laboratory and other groups inside and outside of EPA. Possible activities include an epidemiologic study of endemic waterborne infectious disease, clinical dose-response studies of waterborne pathogens (e.g., Cryptosporidium), and a waterborne disease outbreak and reporting project.

SUMMARY

Three critical and interrelated research needs for drinking water are to identify the chemical and microbial contaminants of greatest public health concern, to relate the toxic effects observed experimentally in animals to potential effects in humans, and to determine the actual risks associated with human exposure to these contaminants in drinking water. Health effects research at EPA to address these needs can be described within the context of the four components of the risk assessment process: hazard identification, dose-response assessment, exposure assessment, and risk characterization.

To determine the chemicals and microbes of greatest public health concern, EPA conducts hazard identification and dose-response research in animals and humans. Such studies help to characterize the toxic endpoints of concern and the exposure levels at which these effects occur. *In vitro* studies and structure/activity analyses are useful screening tools to provide additional information about the potential toxicity of contaminants of concern.

EPA research to facilitate the extrapolation of toxicity data from animals to humans involves pharmacokinetic studies and studies to determine the biological mechanism by which toxic agents cause their effects. This type of research leads to the development of biologically-based dose-response models for use in risk assessment. The use of these models for specific chemical contaminants

represents a significant improvement over the conventional approach that generally relies upon a number of conservative default assumptions.

Finally, characterization of the risks associated with human exposure to contaminants in drinking water involves incorporating the results of the research described above, in combination with environmental exposure data, into chemical and microbial risk models. The many uncertainties in the underlying health effects data base and in the models used for assessing chemical and microbial risks highlight the need for a strong drinking water health research program in the years to come.

REFERENCE

1. National Academy of Sciences, 1983. "Risk Assessment in the Federal Government: Managing the Process", National Academy Press, Washington, D.C.

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16. ABSTRACT

The Environmental Protection Agency's (EPA) Health Effects Research Laboratory (HERL) provides chemical-specific data and scientific methods that are used by the EPA Office of Water in the development of regulations required by the Safe Drinking Water Act. To determine the chemical and microbial contaminants in drinking water that are of greatest public health concern, HERL conducts hazard identification and dose-response research in humans, animals, and in vitro. HERL conducts studies on pharmacokinetics and mechanisms of action to facilitate the extrapolation of toxicity data from animals to humans. Characterization of the risks associated with human exposure to contaminants in drinking water involves a multi-laboratory/office effort to incorporate information on hazard, dose-response, and exposure into chemical and microbial risk models. The many uncertainties in the underlying health effects data base and in the models used for assessing chemical and microbial risks highlight the need for a strong drinking water health research program in the years to come.

17. KEY WORDS AND DOCUMENT ANALYSIS		
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