April 3, 1996

EPA-SAB-DWC-ADV-96-002

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

Subject: Advisory by the Science Advisory Board's (SAB) Drinking Water Committee (DWC) concerning the Health Significance of HPC Bacteria Eluted from POU/POE (Point of Use/Point of Entry) Drinking Water Treatment Devices.

Dear Ms. Browner:

On August 16-18, 1995, the Drinking Water Committee met to review, among other items, EPA's proposed project on the Health Significance of HPC (heterotrophic plate count) Bacteria Eluted from POU/POE (point of use/point of entry) Drinking Water Treatment Devices. At this point in the Agency's planning process, the Committee was asked to conduct an Advisory. An SAB Advisory is a peer review of an Agency work-in-progress. Typically, the Agency asks for an Advisory when it is in the midst of an extensive, complex project that would benefit from an objective, independent scrutiny of its work to date. The goal of the Advisory is to provide suggestions for mid-course corrections and/or new thrusts that will refine the trajectory of the project. The output of the Advisory is similar to that of a Review; i.e., a written report to the Administrator. Generally, an Advisory would be followed by an SAB Review of the completed Agency project at some point in the future. The Board would take steps to insure that the final Review Panel had a significant presence of new participants so as to insure an independent assessment of the Agency's work.

This letter transmits to you a summary of the Committee's comments and reactions to the Project and to the specific questions raised in the charge to the Committee. These questions are as follows: a) Is existing epidemiological evidence sufficient to conclude that amplification of HPC concentrations by POU/POE devices, used on centrally treated water, does not pose a threat of adverse health effects to the normal population? b) If existing evidence is not sufficient, could the proposed research (especially the normal controls), potentially provide enough information to conclude there is no threat to the normal population? If not, what other research is needed? c) Is

there a need for additional research to assess the potential threat posed to immuno-compromised persons by elevated HPC concentrations eluted from POU/POE devices (relative to other HPC exposures)? d) If so, what is the most appropriate type of research: animal studies, epidemiological studies, or a combination? e) If animal studies are appropriate, is the ORD research proposal a scientifically sound and adequate proposal for determining the potential threat to immuno compromised persons? If not, how should it be modified?

1. Brief Responses to the Charge:

a) Is existing epidemiological evidence sufficient to conclude that amplification of HPC concentrations by POU/POE devices, used on centrally treated water, does not pose a threat of adverse health effects to a typical population?

No. This is addressed in the text below.

b) If existing evidence is not sufficient, could the proposed research (especially the normal controls), potentially provide enough information to conclude there is no threat to a typical population? If not, what other research is needed?

No - Other research needs are addressed in the text below.

c) Is there a need for additional research to assess the potential threat posed to immuno compromised persons by elevated HPC concentrations eluted from POU/POE devices (relative to other HPC exposures)?

The answer depends on what part of the immuno compromised population. For the severely immuno compromised, the answer is no. These people should not be drinking POU water; they should be drinking boiled water. For other susceptibles in the population, the answer is yes (see details below).

d) If so, what is the most appropriate type of research: animal studies, epidemiological studies, or a combination?

Both animal and epidemiological studies can be justified. There should be a well-defined research program and a commitment of needed resources for each type of study.

e) If animal studies are appropriate, is the ORD research proposal a scientifically sound and adequate proposal for determining the potential threat to immuno compromised persons? If not, how should it be modified?

No - This project is not adequate. Suggestions for adequacy are addressed below.

2. Review of the Proposed Project

2.1 General Rationale and Approach of the Study

This research proposal raises the general issue of the overall health significance of microbial contaminants in drinking water as well as the specific issue of those contaminants that may proliferate in POU and POE devices. The Drinking Water Committee agrees there is a need for greater understanding of the significance and human health effects of microbes that proliferate in drinking water distribution systems, consumer plumbing, as well as POU and POE devices. The HPC is an important method used to assess the prevalence of the majority of these organisms, but research efforts should not be limited to organisms that the current HPC methods assay successfully.

Other organisms that the HPC method is not designed to detect, such as certain fungi and non-culturable heterotrophs, may also be significant. The Committee agrees that it is important to identify the risks associated with the use of POU and POE devices because members of the public place great reliance on their performance, but they do not possess the resources to evaluate their performance beyond impacts or aesthetic quality.

The EPA drinking water research program should have a research plan designed to characterize microbiota and their ecology in drinking water distribution systems, in consumer plumbing and at the consumer's tap and to identify their human health effects. It should also have a research plan to address the risks associated with POU and POE devices. Research projects in this area should not go forward until plans are prepared that identify and encompass all of these components. We think that careful consideration needs to be given to approaches and designs that could be used to address the problem overall.

Animal studies as described in this proposal are only one such approach. Epidemiological studies are another approach that should be considered. All three need to be evaluated in terms of their scientific feasibility, goals and objectives, experimental design, costs and time period for completion.

2.2 Target human populations

The target human population of health effects concern has not been clearly identified and consistently defined in the formulation and description of this study. Both normal, healthy individuals and immuno compromised populations are mentioned. It is

essential that the goals and objectives of the study be specified for the particular target human populations. The most seriously immunocompromised human populations (such as persons with AIDS and those undergoing immunosuppressive therapy) are not the appropriate target population for studies on the human health effects of the microbial population of POUs. Such seriously compromised individuals should be advised to boil their drinking water, as recommended by the recent advisory from the Centers for Disease Control and Prevention. This may be a policy issue for EPA to consider. The Committee recommends the EPA address the public health risks of HPC bacteria to the more sensitive members of the typical human population (infants, elderly, etc.).

2.3 Choice of Animal Model and Animal Exposure Methods

The animal models and exposure methods should be relevant to the target members of the human population and their route of exposure to microbes in drinking water. It is not clear to the Committee that the proposed experimental animal model, route of exposure and other methods for the animal studies are relevant to the appropriate target human population and its exposures via drinking water. It would be more appropriate to use newborn and elderly animals and animals that have been immunocompromised or otherwise physiologically challenged in ways that reflect the sensitive but typical members of the human population.

The intraperitoneal injection of bacterial concentrates from water is not the appropriate experimental route of exposure to evaluate effects of opportunistic pathogens in drinking water. While the likelihood of demonstrating adverse effects might be greater upon intraperitoneal injection, the objective is to determine whether these organisms are pathogenic when exposure occurs via the normal oral route. To model exposure from ingestion of drinking water, it would be more appropriate and relevant for the route of exposure to be by oral ingestion, particularly via drinking water.

2.4 Choice of Opportunistic Bacterial Pathogen Models and Animal Treatments

The study proposes to use the methods of Lye and Dufour to determine three virulence properties, hemolysis, cytotoxicity and protease activity of the slow growing HPC population. Frank and opportunistic bacterial pathogens may have a variety of different mechanisms of pathogenesis and virulence, including various endo- and exotoxins, proteases, invasins, adhesins (pili, fimbriae), effacement agents, hemolysins, siderophores, capsules, flagella, and lysogenic bacteriophages (prophages). Therefore, it is more appropriate to identify and then target the virulence and pathogenesis mechanisms of the opportunistic pathogens likely to be present in the microbial population and likely to have health effects on typical susceptible individuals in the human population. The choices of model opportunistic pathogens

used to establish the experimental models and methods of this proposed study are based on two food borne opportunistic pathogens rather than waterborne pathogens. Therefore, they do not represent the opportunistic pathogens in the HPC waterborne microbial population and their mechanisms of pathogenesis and virulence. Furthermore, the basis for the choice of one of them, *Listeria monocytogenes*, targets the AIDS population, which the Committee believes is inappropriate.

The design of such a study should give more consideration to existing quantitative data on microbiota in POUs, their virulence properties, and their human health effects in typical human populations. Payment and colleagues have reported on health effects in a normal human population from HPC bacteria in membrane POU units. These studies provide more appropriate information and are a more relevant model for designing new research approaches to human health effects from HPC bacteria in POUs. Furthermore, Payment and colleagues have modified some of the HPC bacteria virulence methods of Lye and Dufour in ways that may make them more clinically relevant to the virulence characteristics of the HPC bacteria that have human health effects. It is not clear that the slow growing HPC bacteria that grow on R2A are adequately representative of the HPC opportunistic pathogens that would proliferate in POUs and pose a risk to human health.

Cyclophosphamide treatment for PMN (polymorphonuclear) leucocytes suppression and carrageenan treatment for macrophage suppression are not the most appropriate or relevant models of physiological compromise or challenge for the human populations and HPC bacteria of interest. These two treatments are specified on the basis of mechanisms for health effects from opportunistic pathogens exemplified by *Listeria monocytogenes* and *Vibrio vulnificus*, neither of which are considered to be significant pathogens by the drinking water route.

2.5 Choice and Characteristics of POU for HPC Production

The rationale for POU devices using GAC (granular activated carbon) treatment is not provided. While GAC POUs are an important option, membranes (RO, UF, etc), filter-adsorbers, particulate filters, resins and other POU devices are also common. For example, the situation in Suffolk, VA. (Appendix A of the proposed study) was one in which membranes were used for treatment. EPA's studies should, as a minimum, examine each of the most common POU and POE technologies. It is also true that different sequences of processes in POE and POU devices will have an important impact in both the number of species and population density of microorganisms present. For example, oxidative processes preceding adsorption and/or filtration processes are likely to increase the density of heterotrophs. RO membrane processes preceding adsorption or UV processes following adsorption are likely to reduce microorganism density altogether.

2.6 Operation of POU - Sources and Frequencies of Samples

The basis for monthly sampling of both initial and product water for six months is not provided. This sampling frequency and time period should relate to the operational life of the POU. Typical and "worst-case" (beyond normal lifespan) operating conditions should be identified. The first 200 ml of water from the units should not be discarded as many users will drink it.

The organisms of most interest are those that proliferate in the POU and are likely to appear in the product water. Parallel sampling and analysis of the microbiota in the influent are not of less interest because they may not appear at significant levels in the product water of the POU. Some of the microbial species in the influent water may not be able to compete with other species that do proliferate. If the POU selects for certain microbes, the composition of the initial water is important only as the source of organisms to be concentrated and amplified by the POU. The continuous testing and isolation of influent populations are unnecessary. It is better to focus on what gets selected and amplified by the POU itself.

2.7 Choice of and Basis for Selection of Water Supplies

The choice and basis for selection of water supplies for these proposed health effects studies are specified only in terms of representation from certain geographies and from both ground and surface waters. The Committee recommends that more specific criteria be used to select water sources for these studies. In addition to the criteria already proposed, site selection should also consider the likely presence of specific opportunistic pathogens and other characteristics of the water that may influence microbial proliferation (assimilable organic carbon (AOC), biodegradable organic carbon (BDOC), temperature, other nutrients, etc.).

The characteristics of the distribution system, such as type of pipe material, position of the household in the distribution system, and presence or absence of disinfectant residue, should also be considered.

Thank you for the opportunity to provide our input at an early stage in the development of this project. We look forward to providing further advice and assistance as the project is developed.

Sincerely,

Dr. Genevieve M. Matanoski, Chair
Executive Committee

Dr. Verne Ray, Chair
Drinking Water Committee

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Mrs. Mary L. Winston, Staff Secretary, Science Advisory Board (1400-F), U.S. EPA, 401 M Street, SW, Washington, DC 20460 (202) 260-6552 - FAX (202) 260-7118

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