Defining the Microbial Universe

1.0 Introduction

This issue paper seeks consensus by the National Drinking Water Advisory Committee (NDWAC) Candidate Contaminant List Classification Process (CCLCP) Work Group on the scope and composition of the microbial universe. It is based upon the issue paper, Dimensioning the Microbial Universe, V.1, February 25, 2003, and subsequent activity group documents intended to stimulate discussion on building a unified Candidate Contaminant List (CCL) universe for chemicals and microbes. (This discussion also presumes that development of potential VFAR applications goes on in a parallel track.)

The National Research Council (NRC) recommended general guidelines for defining the microbial universe of potential drinking water contaminants as those microorganisms that are known or have the potential to occur in drinking water, and those microorganisms that are known or have the potential to cause human disease from exposure to drinking water by ingestion, inhalation, or dermal contact. These guidelines recognize that knowledge of microbial occurrence and health effects is incomplete, and they provide latitude for inclusion of new and emerging pathogens as they are recognized.

The term "CCL Universe" implies a subset of contaminants present or having the potential to be present from an infinite universe. Because of the huge number of contaminants to be considered, the CCLCP work group described a data source compilation approach to building an inclusionary CCL universe by following the basic NRC principles and selectively combining data elements from data sources into a newly constructed CCL universe. Construction of a CCL universe is envisioned to entail selective compilation of existing data sources into an inclusive and unified data set of known contaminant parameters, from many well characterized sources of data and information for contaminants recommended by NRC. While several comprehensive sources of data and information have been developed for chemical occurrence and health effects, no equivalent data sources exist for microbes. Thus, the approach for selection of microbial contaminants for the CCL universe may of necessity incorporate alternative principles-based criteria. While a chemical CCL universe may be built from *data* extracted from existing data sources, the microbial CCL universe may be defined, based upon NRC guidelines, by using *information* from a variety of qualitative sources, including surrogate monitoring, modeling, primary literature review, and expert judgment.

The kind of information used to define the microbial CCL universe is the same kind of qualitative information that was used to construct the first CCL (CCL 1998), based primarily upon expert judgment. On CCL 1998, microbial contaminants were selected by using the criteria of (1) public health significance, (2) known waterborne transmission, (3) demonstrated occurrence in source water, (4) efficacy of current water treatment technologies, and (5) adequacy of analytical methods for detecting organisms. These criteria remain primary considerations in subjective selection processes based upon expert judgment, supported by information available in published literature.

This discussion draft reviews the deliberations of the NDWAC CCLCP activity groups in defining the CCL universe, and suggests how microbes may be incorporated into the CCL universe according to the principle-based iterative approach developed by these activity groups, giving full consideration to the differences between chemicals and microbes, and recognizing the paucity of equivalent data.

This draft incorporates the terminology developed by the activity groups. The term

'*demonstrated*' implies availability of measured values that constitute quantitative *data*. The term '*potential*' implies availability of *information* of a qualitative nature, based upon derived values, estimates, modeling, and judgment.

2.0 Rationale for Constructing the Chemical CCL Universe

The NRC envisioned the CCL universe of drinking water contaminants as inclusionary with respect to contaminants that are not robustly characterized. It consists of:

1. Contaminants with demonstrated or potential occurrence in water
2. Contaminants with demonstrated or potential adverse health effects

Thus, the CCL universe may be defined as the four sets (circles) of the Venn diagram:

1. Contaminants demonstrated to occur in drinking water
2. Contaminants demonstrated to cause adverse health effects
3. Contaminants with potential to occur in drinking water
4. Contaminants with potential to cause adverse health effects

The infinite universe is composed of all contaminants lying outside the four sets of the Venn diagram, a concept consistent with NRC recommendations.

The CCL universe is defined as the starting point for the screening process leading to the Preliminary CCL (PCCL); therefore, the CCL universe contains all contaminants fitting the description of subsets I-IV of the Venn diagram.

I. Demonstrated health effects and demonstrated water occurrence
II. Potential health effects and demonstrated water occurrence
III. Demonstrated health effects and potential water occurrence
IV. Potential health effects and potential occurrence.

Insofar as possible, chemical and microbial contaminants are to be treated according to the same unifying principles.

2.1 NDWAC Activity Group Principles for Construction and Screening of the Chemical CCL Universe

The NDWAC CCLCP activity groups concur with the recommendations of the NRC with respect to the construction of the CCL universe. The two basic principles for construction of the CCL universe are: (1) the CCL universe should include those contaminants that have demonstrated or potential occurrence in drinking water, and (2) the CCL universe should include those contaminants that have demonstrated or potential adverse health effects. These inclusionary principles apply to selection of data sets of chemicals to be used to construct a new CCL universe. The proposed process involves identification of data and information sources, and merging or recombining them into a CCL universe data set. Existing surveillance systems and a nomination process would insure that new and emerging contaminants were added to the CCL universe as they were recognized. It recognizes that EPA has other authorities to provide expedited consideration of contaminants deemed an imminent risk. These principles and related processes are described in more detail in other background papers.

The activity groups propose to use subsets I-IV of the Venn diagram to selectively screen contaminants in the CCL universe for inclusion in the PCCL based upon occurrence and adverse health effects. The term 'gate' is assigned to subsets I-IV to indicate the selective screening and admittance process used in construction of the PCCL. Thus, Gate I admits those contaminates with demonstrated health effects and demonstrated occurrence in water, etc. To provide a mechanism for incorporating new and emerging contaminants, Gate V is proposed as a stakeholder or expert nomination process to expeditiously add contaminants to the PCCL as new *data* or *information* become(s) available.

NDWAC suggests limiting the CCL universe to demonstrated or potential contaminants of ambient or finished water. While not explicitly stated, the implication is that ambient water refers to freshwater, and thus excludes marine waters. This assumption is supported by the list of waters considered by the methods group, e.g. tap water, distribution water, finished water, source water (both ground water and surface water), and watersheds. The microbe activity group recognizes that marine waters are used extensively for recreation, and they will be used increasingly in desalinization processes, therefore, marine microbes deserve consideration in construction of the CCL universe.

3.0 Considerations for Construction of the Microbial CCL Universe

Chemicals and microorganisms behave in markedly different ways in the environment and within the human host. Chemicals exert their toxicological effects regardless of host defenses, while microbes may or may not exert their pathological effects following exposure via ingestion, inhalation, or dermal contact, depending upon many agent and host dependent variables. Some robustly characterized human and animal pathogens cannot survive outside their hosts, and therefore would not be candidates for waterborne transmission. Some robustly characterized saprophytic microorganisms have never been known to infect humans, despite their presence in water at logarithmic concentrations. Thus, inclusion of all microbes with the *potential* to occur in water or all microbes with the *potential* to cause disease without regard for their biological properties places robustly characterized microbes that are biologically incapable of surviving ambient conditions or incapable of causing human disease in the CCL universe. The differences in chemical and biological properties of demonstrated and potential water contaminants suggest that modification of NDWAC's suggested principles for chemicals may be applicable for constructing the microbial CCL universe.

For microbes, we live in the world of the *potential*. We have *information*, albeit incomplete, but we have little or no *data*. Paradoxically for microbes, the only *demonstrated* occurrence *data* result from indicator (surrogate) studies, that are defined as *information* according to operational definitions. Following NDWAC's gate concept, no microbes might meet/enter most of the gates related to the lack of *data* for occurrence and health effects. Health effects for microbes are typically measured as presence (or absence) of disease or presence (or absence) of an immune response following infection. For microbes we have almost no *data* and little *information*. Much epidemiological and clinical 'data' are in fact qualitative. Animal 'data' for microbes are not equivalent to toxicological *data* for chemicals since infectious processes are markedly different between hosts. In acknowledgment of the difficulty of defining chemical and microbial contaminants according to the same definitions, the activity group first introduces microbes at gate III, and recognizes that three types of *data/information* may be considered, i.e. qualitative, semi-quantitative, and quantitative. The relationship of microbes to the other gates has not yet been addressed.

The chemical universe may be *built* according to a data source compilation approach by selectively combining *data* elements of existing data sets into a new CCL universe data set. Because microbial equivalent data are not available, the microbial CCL universe is being *defined* based upon available

information. Both approaches use a data source compilation process to overcome uncertainty introduced through limitations of knowledge and experience. The microbial universe is infinitely large and dynamically expanding as a result of physical, chemical and genetic effects on living populations of microorganisms. Much of the microbial universe is neither known or measurable, i.e. neither *information* nor *data* exist. As new and emerging microbes are recognized and characterized through surveillance activities or genomic investigations, they may be incorporated into the CCL universe and/or added directly to the PCCL by stakeholder or expert nomination.

The NDWAC describes developing a universe from data sources. Since few data sources exist for microbes, their selection relies upon information obtained from surveillance systems, monitoring activities, case reports, research reports, and published literature. The microbe (VFAR) activity group has expressed reservations about incorporating microbes into the CCL universe without regard for the biological diversity and population dynamics of microorganisms. Thus, the microbial CCL universe is envisioned to consist of all organisms that are known, or have potential, to cause human disease **and** occur, or have the potential to occur, in water. This definition may seem to violate inclusionary principles, however, inclusionary principles are intended to capture contaminants that are not robustly characterized. They do not preclude selective omission of robustly characterized microbes that are known NOT to cause water-related human disease or organisms that are known NOT to occur (survive) in water. Indeed, the activity groups exclude ergonomic hazards from health effects data sets during construction of the chemical CCL universe and marine waters by implication. This precedent is consistent with the recommendation to selectively exclude obligate anaerobes, arthropod borne pathogens, and other microbes from the microbial CCL universe based upon robustly characterized biological properties. The operative process for determining the legitimacy of exclusions is relevant to the CCLCP and U.S. EPA regulatory mandates.

Microbial contaminants defined by the NRC include organisms that occur naturally in water, organisms that are shed in human or animal feces or urine and may contaminate source water, organisms that may proliferate in water distribution systems, and biological toxins. Restricting the microbial CCL universe to organisms in these categories removes saprophytic organisms found in water and soil from consideration, thereby reducing the scope of the CCL universe to those organisms that are associated with waterborne transmission (demonstrated or potential occurrence) with demonstrated or potential ability to cause human disease. This definition removes from consideration those organisms that are exclusively transmitted by means other than water ingestion, inhalation or dermal contact, and those organisms that cannot survive in the aqueous environment. Categories of microbial contaminants proposed for inclusion in the CCL universe are shown in Exhibit 1.

Exhibit 1. Recommended Categories for the Microbial CCL Universe

Class	Category
Microbial Occurrence	Naturally occurring organisms in water
	Organisms associated with human or animal feces that may contaminate water
	Organisms associated with human or animal urine that may contaminate water
	Organisms associated with water distribution systems and domestic plumbing systems

Class	Category
Microbial Health Effects	Organisms that have caused waterborne outbreaks
	Organisms that have caused water-related opportunistic infections

This process could result in a CCL universe containing several thousand microorganisms, most of which lack the biological properties to infect humans or survive in the ambient environment. The reference materials necessary to compile the lists of organisms that occur in water and the organisms that occur in human or animal feces and urine that may contaminate ambient water have not yet been identified. An extensive search of primary literature would be required to compile the information necessary to construct a microbial CCL universe according to this proposal.

3.1 NDWAC Microbe (VFAR) Activity Group Proposal for Constructing the Microbial Universe

The microbe (VFAR) activity group proposes to construct a list of organisms known to occur in water and known to cause human disease following ingestion, inhalation or dermal contact with water. Appendix A from Taylor et al. (2001) informs the basic list of organisms causing human disease. No equivalent list of organisms known to occur in water has been compiled, and it would be necessary to construct a list of these organisms from published sources. Advances in genomics and proteomics offer the possibility that molecular techniques (such as the VFAR approach) may one day provide objective screening capability for selection of microbes for the CCL universe.

For chemicals, judgment is based primarily upon *data*. For microbes, judgment is based primarily upon *information*. Since expert judgment will of necessity be a major part of the microbial CCL universe selection process, microbe (VFAR) activity group members have posed the questions, "Is it logical to include organisms in the CCL universe that will *a priori* be excluded from the PCCL by the gate screening process?", and "Is it reasonable to merge the microbial CCL universe and the PCCL into a single list of contaminants?" These questions need to be addressed by the CCLCP work group before the microbe (VFAR) activity group can formulate final recommendations for constructing the microbial CCL universe.

The microbe activity group proposes to consolidate the CCL universe and the PCCL into a single list of microbes. The process would begin with the list of 1,415 recognized human pathogens (Taylor et al 2001), and from that list those microbes that are known to be associated with source water, recreational water, or treated drinking water would be selected for inclusion in the PCCL.

The proposed steps for constructing the microbial PCCL follow:

1. Edit the list of known human pathogens (Taylor et al 2001) to add missing pathogens and to eliminate those whose biological properties are incompatible with water transmission by ingestion, inhalation or dermal contact.
2. Compile a list of microbes that occur in water, and that are known or have the potential to cause adverse health effects in humans, and reconcile this list with the edited list of known human pathogens.
3. Monitor CDC/WHO surveillance data and information for new and emerging pathogens associated with water.
4. Establish a mechanism for adding microbes to the CCL universe based upon genomic or proteomic information suggestive of emerging pathogenicity and biological properties that

may facilitate waterborne transmission.

5. Establish a nomination process for expeditious addition of pathogens to the CCL universe based upon new data or information provided by stakeholders or experts.

The resulting microbial PCCL is estimated to number fewer than 400 microbes. Microorganisms having the potential to cause human disease, but not yet demonstrated to do so could be added to the CCL universe by identification of genomic or proteomic elements suggestive of virulence as the technology develops. Microbes suddenly emerging as the cause of waterborne outbreaks or recognized as causing significant water associated morbidity could be added to the PCCL as a result of public health surveillance processes already in place, and by an expert or stakeholder nomination process. Microbes on the PCCL would be screened for inclusion on the CCL by attribute scoring, by a means to be determined, but based on the same attributes as chemicals. This process results in a realistic, if not ideal CCL universe (and PCCL). NRC acknowledged that practical limitations would constrain the development process, and the alternative proposal attempts to be consistent with NRC recommendations and NDWAC work group principles.

4.0 Reference

Discussion Draft for NDWAC CCL Workgroup. Dimensioning the Microbial Universe. February 25, 2003.

Taylor, Latham and Woolhouse. 2001. Risk factors for human disease emergence (Appendix A). Phil. Trans. R. Soc. Lond. B 256:983-989.