Microbial Expert Input and Review for the Third Contaminant Candidate List

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List of Acronyms and Abbreviations

CCL	Contaminant Candidate List
CCL 1	EPA's first contaminant candidate list
CCL 2	EPA's second Contaminant Candidate List
CCL 3	EPA's third Contaminant Candidate List
EPA	United States Environmental Protection Agency
ID_{50}	Infectious Dose 50: The infectious dose of a micoorganism required to produce infection in 50 percent of the exposed population
NAS	National Academies of Sciences
NDWAC	National Drinking Water Advisory Council
NRC	National Research Council
OGWDW	Office of Ground Water and Drinking Water
PCCL	Preliminary CCL
PWS	Public water system
SDWA	Safe Drinking Water Act
US	United States of America
WBDO	Waterborne Disease Outbreaks

1.0 Introduction

As part of the process of establishing a microbial Contaminant Candidate List (CCL), the United States Environmental Protection Agency (EPA) sought expert input on its approach to identifying and prioritizing contaminants. On March 20 and 21, 2007, an expert panel convened in Washington, D.C. at EPA Headquarters to provide input and review of the draft third CCL (CCL 3) microbial prioritization process. A panel of 6 experts was selected based on their experience in the fields of public health, toxicology, and epidemiology; and familiarity with the Safe Drinking Water Act regulations and the CCL regulatory process. This document provides a summary of the proceedings of the two-day workshop, organized and facilitated by Horsley & Witten, Inc. The workshop agenda is included in section 4.0 of this report.

2.0 Background

The Safe Drinking Water Act (SDWA) includes a process that the EPA must follow to identify new contaminants that may require regulation. According to the SDWA, EPA must periodically release a CCL of unregulated contaminants that are known to or anticipated to occur in drinking water at levels that may pose a risk to public health; and therefore, may require regulation. EPA typically conducts an extensive research and data collection effort, and solicits comments from experts and the general public (via the Federal Register), on unregulated contaminants to develop a CCL. These contaminants are then further evaluated by EPA to determine whether they should be regulated. When making this determination, the SDWA specifies three criteria to determine whether a contaminant may require regulation:

- the contaminant may have an adverse effect on the health of persons;
- the contaminant is known to occur or there is a substantial likelihood that the contaminant will occur in public water systems with a frequency and at levels of public health concern; and
- in the sole judgment of the Administrator, regulation of such contaminant presents a meaningful opportunity for health risk reduction for persons served by public water systems.

The first CCL (CCL 1), established in March of 1998, contained 60 contaminants (50 chemical and 10 microbial) that were chosen based on expert opinion. EPA then made their regulatory determinations on the CCL 1 and ultimately decided ***not*** to regulate 9 contaminants, based on their evaluation of "significant risk reduction" as described in the SDWA. The second CCL (CCL 2), established in February 2005, carried forward the remaining 51 contaminants from CCL 1 (9 microbiological contaminants and 42 chemical contaminants). During this time, EPA provided an update on the Agency's work to improve future CCL review processes based, in part, on recommendations from the National Research Council (NRC) and the National Drinking Water Advisory Council (NDWAC).

NDWAC and the National Academies of Science (NAS) proposed a broader, more comprehensive evaluation process than previously utilized by EPA to assist the Agency in identifying contaminants for the CCL. They recommended that EPA develop and use a process

for creating future CCLs. As a result, a broad universe of potential drinking water contaminants were established, assessed, and reduced to a preliminary CCL (PCCL), using simple screening criteria. The screening criteria indicate public health risk and the likelihood of occurrence in drinking water. All of the contaminants on the PCCL would then be assessed in more detail using a classification approach and tools, along with expert judgment, to evaluate the likelihood that specific contaminants could occur in drinking water at levels and at frequencies that pose a public health risk. The outcome of the detailed classification approach results in the draft CCL.

EPA began developing CCL 3 in 2006 using the new procedures described above. During this process, they identified 284 data sources for consideration in the CCL 3 process, including some contaminants from the CCL 2. Each universe (microbial and chemical) was narrowed down to a PCCL using simple screening criteria, based on a contaminant's potential to occur in water systems and to cause adverse human health effects.

The universe for the microbial CCL 3 includes a survey of human pathogens published by Taylor *et. al.*, and pathogens nominated through the public nominations process. Screening criteria were used to indicate the potential for waterborne transmission and identify microorganisms to move to the PCCL.

All of the contaminants on the microbial PCCL are assessed using attributes (e.g., waterborne disease outbreaks, occurrence, health effects) to characterize the potential for the microbial pathogen to occur in PWS, cause waterborne disease outbreaks and adverse health effects. The outcome of the detailed approach resulted in the draft microbial CCL 3 list.

3.0 Project Summary

The goal of this project was to obtain expert input on the approach EPA is using to establish the microbial CCL 3. Specifically, the focus of this review was to provide comment on the draft list of microorganisms, the screening process, and scoring protocols used to establish the lists. Horsley & Witten, Inc. was contracted by EPA to coordinate the expert review of the CCL 3 for microbial contaminants. A pool of potential experts recommended by their peers from national drinking water organizations such as the American Public Health Association, Association of State Drinking Water Administrators, National Science Foundation, and universities with strong public health and medical programs were evaluated.

Horsley & Witten selected 6 experts to participate in the microbial review. Experts were selected based on their experience in the fields of public health, toxicology, and epidemiology; their familiarity with the SDWA regulations and the CCL regulatory process; as well as their level of interest. Horsley &Witten organized and facilitated a two-day microbial workshop that was held in Washington, D.C. at EPA Headquarters (March 20-21), where the experts served on a panel to discuss their findings regarding the draft CCL 3 microbial process. The workshop agenda is included in this report under the workshop section.

Experts received an organized packet of information prior to the workshops, which included the workshop agenda and all CCL 3 associated materials including documentation of the compilation of the CCL Universe, screening process, scoring process, and contaminant dossiers. Experts

answered all questions posed by EPA and engaged in productive discussions regarding contaminants and whether the draft CCL lists developed by EPA were acceptable, based on the screening and scoring process. A detailed summary of the workshop is included in this document.

4.0 Microbial Workshop

Exhibit 1: Meeting Agenda for Tuesday, March 20 - Wednesday, March 21, 2007

DAY 1		
Time	**Topic**	**Speaker**
8:30 – 8:50 AM	Introductions Welcome	Facilitator: Richard Delaney, Horsley Witten Group, Inc. Pamela Barr, Standards and Risk Management Division Director EPA Office of Ground Water and Drinking Water (OGWDW)
8:50 – 9:10 AM	Meeting Objectives/Ground Rules, Logistics	Richard Delaney
9:10 – 9:40 AM	Overview of the CCL 3 Process – Historical Perspective	Tom Carpenter, EPA OGWDW
9:40 – 10:00 AM	Presentation of Charge	Crystal Rodgers, EPA OGWDW
10:00 – 10:15 AM	Questions/Answers	Experts/EPA Facilitated by Rich Delaney
10:15 – 10:30 AM: BREAK		
10:30 AM – 12:00	Screening Question 1: Are the narratives describing the screening criteria clear, adequate and transparent?	Experts
12:00 – 1:00 PM: LUNCH		
1:00 – 2:30 PM	Screening Question 2: Do the fact sheets adequately represent the available and updated information for each contaminant?	Experts
2:30 – 2:45 PM: BREAK		
2:45 – 3:30 PM	Screening Question 3: Are the attributes and the respective scoring protocols reasonable and transparent?	Experts
3:30 – 4:30 PM	Screening Question 3.1: Do the scoring protocols adequately address the microbes and available data necessary to characterize each attribute?	Experts
4:30 – 5:00 PM	Wrap-up	Richard Delaney
DAY 2		
Time	**Topic**	**Speaker**
8:30 – 9:00 AM	Recap of Day 1	Crystal Rodgers, EPA OGWDW
9:00 – 10:30 AM	Screening Question 3.2: Is the approach for using the highest score between the waterborne disease and the occurrence attributes reasonable?	Experts

10:30 – 11:30 AM	Screening Question 3.3: Is the approach for deriving the overall health effects from the scores of the general population and sensitive subpopulation reasonable?	Experts
11:30 – 12:30 PM: LUNCH		
12:30 – 1:45 PM	Screening Question 3.4: Is the idea of summing attribute scores to get the total score for each microorganism reasonable?	Experts
1:45 – 2:00 PM: BREAK		
2:00 – 2:45 PM	General Question: Does the Draft CCL 3 microbe list represent those pathogens that have the highest potential to occur in public water systems and cause adverse human health effects? Are there pathogens on the Draft CCL 3 list that should not be listed and, conversely, are there pathogens that should be listed?	Experts
2:45 – 3:15 PM	Screening Question 4: Is the ranked CCL produced by the scoring protocol process reasonable?	Experts
3:15 – 4:00 PM	Expert Panel recap of Charge Questions and recommendations	Experts
4:00 – 4:30 PM	Wrap-up	Richard Delaney

4.1 Day 1

Introduction – Rich Delaney, Executive Vice President, Horsley Witten Group, Inc. (Facilitator):

Expert Panel:

Mark Borchardt, Ph.D., Research Scientist, Marshfield Clinic Research Foundation
Patrick Murray, Chief Microbiologist, National Institutes of Health
Kellogg Schwab, PhD, Associate Professor, John Hopkins University, Bloomberg School of Public Health
David Welch, PhD, Clinical Microbiologist, Medical Microbiology Consulting
Jon Mark Hirshon, MD, University of Maryland School of Medicine
Rebecca Hoffman, Wisconsin State Laboratory of Hygiene, University of Wisconsin, Madison

Welcome - Pamela Barr, Director, EPA Standards and Risk Management Division

Ms. Barr discussed the background of the microbial CCL 3. The contaminants on the list are known or anticipated to occur in drinking water and are most likely to cause public health concerns. EPA agreed with the NAS recommendation on how the review process should be transparent. The Agency also agreed with the NDWAC's recommendations on how to streamline the review process through the completion of the following steps; 1) maintain a universe of microbes, 2) screen this list to only include waterborne contaminants and, 3) further

evaluate these waterborne pathogens for their potential to cause adverse health effects. Ms. Barr explained that the reviewers' goal for this workshop is to review draft list, assumptions, and list of recommendations to see if they agree with EPA's conclusions regarding the contaminants.

Ms. Barr reminded the group that the list and the other workbook materials they received are internal agency deliberative documents and asked the reviewers not to quote, cite or distribute the information. She explained that EPA is looking for individual expertise, not information from viewpoint of reviewer's organizations. EPA had received technical information so far, and the next step is to prepare recommendations and information from the workshop for internal Agency review. Ms. Barr stated that the draft list will be published in the Federal Register in February 2008 and the final list will be completed in August of 2009.

Rich Delaney discussed how Horsley &Witten staff will play a listening role and will record points of agreement and "parking lot" items in order to help reviewers move forward. Meeting notes will be issued to reviewers for their comments approximately 2 weeks from the date of the meeting.

History and Process Information - Tom Carpenter, EPA Standards and Risk Management Division

The history of the process was reviewed describing the steps from the CCL 1 to the CCL 2, and then to the CCL 3. NRC and NDWAC identified challenges within the CCL process and these were addressed in this new process for the CCL 3. This process begins with a previously published survey of microbial pathogens identified in the Taylor *et al.* report (2001) used as the CCL universe. Subsequently, this universe of human pathogens is screened to derive a PCCL. The CCL is then selected from the PCCL microbes using attributes to characterize health effects and occurrence. The regulatory decisions that EPA will make regarding the contaminants to include on the CCL 3 will relate to the likelihood for occurrence of the contaminants in a Public Water System (PWS) at a particular frequency, and what adverse heath concerns they cause.

Balancing Occurrence and Health Effects:

1. The slide presentation shows the progression of the CCL 1 to CCL 3.
2. Literature review 1400 (species).
3. Nominations (what did we miss?).
4. Plausibility that waterborne disease can occur (overall screening criteria – see screening document in workbook regarding the 12 screening criteria).
5. Results of screening (see table in screening document) - these are the ones EPA wants to look at now, these are what they feel are the most virulent contaminants.

Attributes to Scoring the PCCL:

1. Treatment process consideration – Long Term Surface Water treatment rule – drinking water treatment NOT considered because there are too many variables (e.g., chlorination, filtration, political decisions, etc.), also because the goal is public health protection – basic assumption.
2. Occurrence - direct detection of microbes using cultural, immunochemical, or molecular detection of pathogens in water.
3. Health effects – including sensitive populations: chronic disease population, pregnant mothers, elderly, children), and gastrointestinal disease.
4. Waterborne Disease Outbreaks - documentation of occurrence of pathogens in drinking water by public health officials through adverse health effects in a population and are direct evidence of exposure.

The goal was to put contaminants on a level playing field. EPA tried to balance Waterborne Disease Outbreaks (WBDO) and occurrence. The highest score (between WBDO and occurrence) is selected in order to elevate pathogens that have been detected in US drinking water or source water above those that have caused WBDOs in other countries but not in the US or pathogens that have not caused WBDOs in any country but have been epidemiologically associated with water-related disease.

Overview of Charge and Questions – Crystal Rodgers, EPA Standards and Risk Management Division

EPA's expectation is that reviewers will provide substantive comments on the draft CCL 3 and on the scoring and screening processes. EPA hopes that reviewers will work towards answering the following question: does the CCL 3 represent pathogens that have the most potential to occur in PWS and cause adverse health effects.

Expert Discussion: Regarding PWS & occurrence – how do distribution systems fit into occurrence? For example, typically, distribution systems run for miles after treatment, which adds another layer of complexity.

EPA Response: SDWA regulations define PWS as supplying 25 or more people or having 15 or more service systems. They do not include private wells or smaller systems. The components of the PWS do not stop at end of treatment; therefore, the distribution system is included. PWS also includes premise plumbing, meaning the service line to buildings (water is considered public until this point). However, the definition of premise plumbing depends on the water system's jurisdiction.

An important overall question for reviewers to consider is: Are there contaminants that reviewers think should NOT be on list, taking scoring and screening protocols into consideration, would you have come up with same list? Please see the 12 screening criteria (section 3 of screening document). Please note that criteria 1-8 have had numerous discussions, so they are not likely to be changed.

There should be 30 fact sheets, each one for the contaminants that made it to PCCL. This is forum to discuss issues regarding the literature.

This process is partially to determine if reviewers would come up with similar scoring. EPA called upon 10 microbiologists with different specialties to score the PCCL and choose/rank the draft CCL 3. EPA has not looked at statistical variation of scores.

The following identifies issues and clarification that experts noted during the presentations:

- There are no substantive changes from the CCL 1 to CCL 2; however, there have been substantial changes from the CCL 2 to the CCL 3. It seems that EPA has shifted gears (i.e., gone back on some of their determinations) because treatment is no longer accounted for. Perhaps some organisms are included that should not be.
- Perhaps there is an issue regarding the measure of reproducibility for scoring (i.e., could similar scores be reproduced with other experts or is there too much flexibility in scoring and professional judgment?). The group recommends that another group scoring should occur to determine scoring variability.
- The reason why 7.0 was selected by EPA as the cut-off point for pathogens that made it to the draft CCL 3 should be explored. For example, will rescoring make a difference if more or less "weight" is placed on occurrence? What does the group feel is the rational break point of scoring? Experts agreed that they should not ignore the lower scored pathogens even though occurrence is not prevalent.

Discussion of Questions (In the order in which they were approached):

Question #1: Are the narratives describing the screening criteria clear, adequate and transparent?

The experts began their discussion by going through each screening criterion to determine whether the criteria were clear and transparent. A number of key questions and points of clarification were raised by the experts, as follows:

1. Screening Criterion 1: Were all anaerobes excluded from the PCCL through this screening criterion?
    - Expert recommendation: the parenthetical is misleading in document, and therefore, the reasons why these are excluded should be made clearer. For future iterations of the CCL there should be allowances for exceptions (e.g., if documentation of a WBDO becomes available).
2. Screening Criterion 2: Wording of criterion 2 is confusing. The meanings of "obligate intracellular or fastidious pathogens" should be clarified.
3. Screening Criteria 3 & 4: The following preamble should be added to both criteria: "These are examples of those excluded because they did not cause a waterborne disease outbreak", for clarity sake.

4. Screening Criterion 5: No discussion, no changes recommended.
5. Screening Criterion 6: Under this criterion, *Legionella* would be excluded. A preamble clarifying this criteria is also needed, similar to the one noted above.
6. Screening Criterion 7: It is a little unclear whether EPA is including source water under this screening criterion. A "fuzzy line" occurs if a contaminant occurs in recreational source water - according to EPA; it appears that they would not consider this, unless compelling data suggests inhalation on ingestion. This point should be made clearer in the criterion description.
7. Screening Criterion 8: No discussion, no changes recommended.
8. Screening Criterion 9): The group discussed this criterion at length, specifically contaminants that could have met this criterion, but were excluded from the PCCL. For example, *Acanthamoeba* was on the CCL 1 but was screened from the CCL 3. In addition, it is plausible that water is a source for *Pseudomonas* because their cells grow well in water and may amplify in distribution systems; however it is not included in the PCCL. Furthermore, Legionella is included on the PCCL – a contaminant that almost mirrors *Pseudomonas* in transfer.
    - Expert Recommendation: Additional research on *Pseudomonas* is needed to agree with EPA's conclusion. It seems that there is a systematic bias based on occurrence scoring - weighting positive results, but excluding negative results. Negative results should also be evaluated for PCCL. The group understands excluding a pathogen if it was looked for, but not if it was excluded because it was never looked for. This criterion needs to be reviewed more carefully to account for this issue. In addition, a preamble should be added to this criterion discussing this uncertainty.
9. Screening Criterion 10: A preamble, similar to what was requested for Screening Criterion 9, is required.
10. Screening Criterion 11: In general, EPA should better identify which pathogens were included in PCCL, and why, in the CCL documentation.
11. Screening Criteria 12: Taxonomy clarification is needed.

Question #1 - Experts Summary Answer: No. The exclusion of some pathogens from the PCCL should be made much clearer. Documentation for drinking water disease should have a higher weight. In addition, two outbreaks involving 1-2 individuals received the same weight as 100 outbreaks involving thousands of individuals. Experts concluded that some assessment of impact of exposure on the general population needs to be factored into the risk analysis. EPA should clarify who conducted the screening process (e.g., a flowchart could better illustrate this). Preambles are needed for criteria, as described above. Further information regarding whether there is a waterborne disease outbreak is needed for a number of contaminants on the PCCL.

Question #3: Are the attributes and the respective scoring protocols reasonable and transparent?

The discussion began with further clarification of the question by EPA. It was stated that EPA would like to know if there are contaminants that they should not invest research resources in, but could still be included on the list (i.e., could there be a different weighting system)?

First, an overview of EPA's scoring formula for WBDO or Occurrence + Health Effects, as follows:

Score Equivalency	
WBDO	Occurrence
5	None
4	None
3	3
2	2
1	1

The protocol took the highest score of each category. Occurrence was determined by EPA to mean any occurrence of the pathogen in the US WBDO was interpreted as multiple outbreaks in a US PWS.

Experts began their discussion regarding perceived variances in occurrence and WBDO classification. For example, there is great variability in US climate and conditions of each PWS. In addition, it seems that the number of times (frequency – e.g., 2 deaths vs. 20,000 people sick) a pathogen occurred in a PWS was not taken into account. Experts should apply their technical expertise in reviewing each fact sheet for PCCL contaminants. Human prevalence disease data is not included in scoring, just because we don't know if they are waterborne.

An overview of the health effects scoring process was provided by EPA, as follows:

- Surrogates for potency and severity were used ("ID_{50}" model).
- An illness to mortality evaluation was completed by EPA to evaluate sensitive subpopulations (1-7, respectively).
- Within each subpopulation the normal incidence was selected, not extreme cases. (However, prevalence data was not always available because not all cases have been reported to the medical field or by the medical field.)

Expert Discussion: There does not appear to be any weighting of the general population disease burden, so perhaps the scoring is biased? Rare vs. frequent illness events should be included for the general population. There also seems to be a glaring omission of some pathogens on the draft CCL 3; therefore, it is unclear whether there was enough information on some pathogens to score them properly. There are available studies, but most lump water with food based ingestion.

Question #3 - Experts Summary Answer: Experts felt that scoring is too subjective and that the overall score only allows for ranking as long as part of ranking is subjective. They recommend that the variability and range of scoring process be clarified. Experts have concerns that the scoring system - mainly health effects - may not be a reasonable representation of the population burden, based on available knowledge. The lack of population burden does indeed show up in some studies about rare organisms that cause rare disease. The general population disease burden (frequency) should be taken into account.

Sub-Question #3.2: Is the approach for using the highest score between the waterborne disease and the occurrence attributes reasonable?

Experts began their discussion by reviewing the assignment of scores to contaminants on the PCCL. Experts felt that the water source path definition is too broad, specifically statements found on Attachment 1 of the PCCL Scoring Protocols document. In addition, "fresh water used for recreation", should be clarified because another interpretation can lead one to include other pathogens on PCCL.

Sub-Question #3.2 - Experts Answer: It appears that the approach for using the highest score between WBDO and occurrence attributes is an acceptable methodology; however, criteria for associated definitions must be clarified for these attributes to be properly utilized. In addition, experts conclude that WBDO and occurrence scoring appears like "double counting" and; therefore, should not be scored separately, rather using the qualifier "either/or".

Sub-Question #3.3: Is the approach for deriving the overall health effects from the scores of the general population and sensitive subpopulation reasonable?

The panel began their discussion regarding the general assignment of health effects scores. All experts agreed that the scoring is confusing. They did not fully understand how the rating was determined. Experts noted that certain viruses are not being tested, and are therefore excluded from the PCCL and draft CCL 3. Many pathogens on the PCCL list are those w/ available information.

The group discussed whether some organisms could be lumped into a representative category. (e.g., how total coliform represents a group of human-based bacteriologic organisms). Experts discussed how the health effects ratings seem inconsistent (e.g., Human enterovirus received a rating of 6 as well as *Escherichia coli,* which is regulated and controlled by treatment*).*

Experts concluded that these types of variations are not visible in the document, but they should be. There needs to be a definition spelled out regarding rating variables, e.g., most severe versus most common.

Experts continued their discussion regarding the definition of "meaningful opportunity". There seems to be quite a bit of flexibility on EPA's part in determining what this means. Does this lend to consistent scoring? The discussion then turned back toward the variability in the human effects scoring. Experts concluded that documented outbreak is so variable; therefore, it could be better to weigh score based on occurrence (i.e., yes/no), severity, and waterborne disease. The experts concluded that there is a "systematic bias" to the WBDO scoring protocol. Experts

recommended that EPA recognize and discuss the "systematic bias" to allow the public to better evaluate the protocol.

Sub-Question #3.3 - Experts Summary Answer: There is a general lack of transparency and consistency in the health effects scoring. In particular, there is a lack of transparency and consistency for the general population & subpopulations. Experts identified the following specific issues:

1) ***The methodology applied to the general population and subpopulations appears to be inconsistent, particularly regarding burden of disease.***

2) ***There needs to be a more definitive balance between health effects & WBDO. Solutions can be offered with further review.***

Sub-Question #3.4: Is the idea of summing attribute scores to get total score for each microorganism reasonable?

Sub-Question #3.4 - Experts Summary Answer: Experts agreed that the attribute scoring resulted in a ranked list that was reasonable, but not necessarily appropriate.

Day 1 Summary Discussion:

The reviewers concluded Day 1 with a summary of their recommendations regarding scoring, ranking, and issues that need to be further discussed, as follows:

- Prioritization/ranking appears to be a good approach, but it needs to be more clearly defined.
- A systematic bias towards occurrence and WBDO scoring is prevalent. Experts should review this in more detail to determine a best answer to the general question on Day 2.
- The population burden or disease frequency is missing from the scoring system.
- Qualification of the regulation of potential pathogens versus unknown or newly identified pathogens should be addressed. Experts share an overall concern that EPA is not proactive about new pathogens because the information is not as available. Including only pathogens that have been fully researched will dilute the effort.
- Methods and limitations section should be included in PCCL Scoring and Screening documentation.

Expert Summary of Questions 1, 3.1-4: Experts expressed that the CCL process included an impressive research effort on EPA's part. However, there are some gaps in the data that experts would like further clarification on from EPA. In particular, experts would like a response from EPA regarding the likelihood or frequency of pathogen occurrence to make would make scoring more accurate.

Rich Delaney: Tomorrow will begin with scoring clarification and then dive into fact sheets. Experts have requested the following supplemental information from EPA:

1. Goal of CCL (summary).
2. CCL 1, 2 & 3 status information.
3. Overview of nominated CCL 3 contaminants.
4. Logic for scoring process (i.e. issues related to scoring inconsistency).
5. Text and journals regarding health effects data for reference.

4.2 Day 2

Day 2 of the workshop began with a follow-up on the expert's questions above, and an overview of supplemental information provided to reviewers today by Eric Bergman. EPA began with a detailed clarification of the CCL 3 goals, as requested:

- Purpose of the CCL: EPA must identify non-regulated contaminants that are known or anticipated to occur in public drinking water, cause adverse health effects, and may require regulation.
- Research priorities are secondary.
- It is acknowledged that there is a line between how much information is available about contaminants, and being able to list them. Contaminants should have data sufficient to make a regulatory determination.

EPA continued to discuss the issue reviewers raised regarding the quantification of the number of pathogens to be included on the CCL 3. EPA clarified that they haven't quantified the number of CCL 3 contaminants that can be researched/regulated; therefore, reviewers should refocus on whether EPA has the ***right*** contaminants on the list versus the broad number of contaminants included. However, the disadvantage of a large CCL 3 list is that it would be difficult for EPA to effectively research and make regulatory recommendations on each contaminant due to resource constraints.

Regulatory determination process includes the following steps:

1. Demonstrate adverse health effects;
2. Identify likelihood for the contaminant to occur in PWS at a level and frequency to cause health effects and;
3. Determine whether there is a meaningful opportunity for changing this (e.g. treatment or changing exposure).

The challenge is having scientific certainty regarding risk assessment to compare health effects and occurrence, as well as WBDO data. This will drive the regulatory determination. EPA acknowledges reviewers concerns regarding pathogens that are on the PCCL that already have

regulation associated with them. However, EPA will evaluate whether existing treatment/limits should be changed or if new treatment/regulations should be developed for these contaminants.

EPA provided the following information, per expert's request:

1. Handout describing the status of the CCL 1, 2 & 3.
2. Handout describing the nomination process.
3. Regarding scoring variability; scores were brought forward from the internal EPA review, as shown on the 3 example scoring worksheets that EPA provided the group. Individual experts scored each on their own and then a group came together to discuss scores. Citations of data were required, especially for any alteration in original scores after group discussions. All reviewers received the same data sheets.

Discussion on New Materials Presented by EPA During Day 2:

Expert Question: The genera *Mycobacterium* are grouped. What is EPA's rationale for scoring this way?

EPA: *Mycobacterium avium* was selected as a representative organism because it has significant occurrence and transmission; therefore, treatment of this pathogen would control all species – rapid or slow growing.

Expert Response: This grouping is acceptable if rapid growers do not cause more significant disease than the representative organism, under EPA's scoring scheme. However, the experts expressed caution about this potential grouping issue. Experts collectively suggested that a better description of the scoring process is necessary. Also, scoring variability should be presented in the CCL 3 documentation, possibly graphically. In the future, an independent group of clinicians is recommended to best score the pathogens on health effects to potentially eliminate some scoring variability.

Expert Question: Although good scoring examples were presented, there are other manifestations of disease associated with these pathogens. Furthermore, most common manifestations would score differently than other possible or extreme manifestations. How does this get factored in?

EPA Response: This statement is true. However, the scoring process included a mechanism to avoid variability. Specifically, EPA reviewers were instructed to refer to the data facts sheets and score on the common disease presentation with each subpopulation. Variations occurred when staff brought in additional, data or background information.

Expert Summary Comments: EPA has scored subjectively. Severity, potency, and frequency were "rolled" into health effects scoring because there was limited data on these criteria. However, the information is available. Perhaps for future CCLs there should be separate scoring process for other manifestations of disease, other than the most common manifestations. In

addition, there should be a different process for chronic diseases. The following limitations to the scoring and screening approach should be well documented in the CCL 3 literature:

1. Bias towards pathogens that cause acute WBDO. For example, *Helicobacter pylori* takes a long time to grow; and therefore, does not cause an immediate WBDO. It may take weeks to months to recognize disease caused by *Helicobacter pylori*, so it is unlikely that a WBDO would ever be recognized.
2. Difficulties in evaluating the quality of information on which scoring is based (e.g., what journal should be cited).
3. Subjectivity in converting scientific data (non quantitative) to a numerical score.
4. Difficulties in quantifying uncertainty in scoring, particularly reproducibility (i.e., limited resources to do statistical analysis and missing information).

Experts clarified that they would try to reproduce the scoring using the data given to them and scoring process provided by EPA. Therefore, other (or extreme) manifestations of disease other than primary will be ignored, ***except*** when there are pathogens with severe outcomes that have a higher percentage of occurrence – these should be ranked higher. The following table reflects the experts' illustration of how the health effects score was normalized to the occurrence score. It shows minor shifts in the health effects scoring (i.e., 5 vs. 4 for a subpopulation) would have minimal impact in the overall scoring process. However, some scoring changes would have an effect on pathogens clustered around a cutoff developed by EPA. Experts also used this scoring table to assist them in their rescoring of the PCCL (described in later sections).

Exhibit 2: PCCL Rescoring Data

Health Effects Score	Normalized Adjustment Ratio (Maximum WBDO or Occurrence over the Maximum Health Effects Score)	Adjusted Score
14	5/14	5.0
13	5/14	4.6
12	5/14	4.3
11	5/14	3.9
10	5/14	3.6
9	5/14	3.2
8	5/14	2.9
7	5/14	2.5
6	5/14	2.1
5	5/14	1.8
4	5/14	1.4
3	5/14	1.1
2	5/14	0.7

Question #2: Do the fact sheets adequately represent the available and updated information for each contaminant?

Expert General Issues/Comments:

- ***Mycobacterium avium*:** Most infections are minor aside from elderly and those with chronic disease, so reviewers questioned why *Mycobacterium avium* received a score of 5 in the general population. Experts noted that HIV patients could have more complications in overall population, but the scoring does not account for this disease burden. Experts concluded that the scores will be re-evaluated.

- **S*almonella enterica*:** Experts stated that this is a marker organism in terms of testing, so it represents all *Salmonella* organisms. Experts recommended that EPA change the child and elderly health effects scores from 3 to 4 due to disease-related complications in these subpopulations. Experts noted that there is no distinction in occurrence (waterborne) or frequency because of limited data. Experts concluded that their scoring recommendations be verified.

- **Hepatitis E virus:** Experts noted that it is often difficult to determine transferability from one species to another (e.g., from swine to human) of this pathogen. However, it is important to look for future transferability data and consider this data when evaluating the CCL. Outside the US, Hepatitis E has high serial presence and significant mortality in acute cases. There is epidemiological evidence of exposure and high mortality rate; however, it is difficult to determine what is common versus extreme exposure issues. Experts discussed the lack of US epidemiological data and whether it is appropriate to default to extreme or common disease manifestation in this case. The unknown factor is of persons exposed - how many become infected? Experts concluded that they are unable to properly evaluate the health effects data without information regarding disease frequency.

- ***Cyclospora cayetanensis*:** Experts recommended that EPA change the fact sheet to reflect one US outbreak detection in water.

- ***Naegleria fowleri*:** Experts noted that there has been only 1 outbreak in drinking water; others were in recreational surface water. This information should be corrected on the fact sheet. Experts also commented that the health effects data are unclear. They suggested that EPA consider developing a health advisory, if the Agency decides not to regulate this pathogen.

- ***Exophiala jeanselmei*:** Experts noted that common manifestation of illness is minimal – sub clinical (soft tissue infection); however, the pathogen can cause severe disease (uncommon). Experts raised the question whether it is truly waterborne. Cadmus explained that fungi were found in PWS distribution (probably from construction – soil contamination). Experts recommended that EPA re-evaluate the screening of all fungi for future CCLs, and possibly eliminating fungi, since they are not believed to be waterborne (soil based). However, they concluded that they do recommend changing current CCL 3 criterion # 9.

Question #2 Expert Summary Answer: Experts decided that they can not properly answer this question because there was not enough time for the group to thoroughly evaluate data references. However, it appears that the draft fact sheets may not adequately represent the available and updated information for each contaminant; a number of data omissions were pointed out.

Sub-question #3.1: Do the scoring protocols adequately address the microbes and available data necessary to characterize each attribute?

The experts commented that they needed to thoroughly review the fact sheets and evaluate each pathogen using the scoring protocols provided by EPA to accurately answer this question. They also detected errors in the translation of the information on the fact sheet to an actual score and recommended that EPA conduct a quality assurance check to ensure that translation of factual data to numeric values.

Based on their judgment, the experts re-scored the draft PCCL. The draft PCCL was ranked by total score, in descending order (see table on page 20). Experts disagreed on the order in which the pathogens exist on this list. For example, some commented that magnitude of disease is still not properly reflected in this draft PCCL. Others commented that some pathogens were still not scored high enough and others are ranked too high on the PCCL.

Experts also discussed whether they should accept imperfections in the scoring methodology or should they recommend specific changes. Experts raised the question whether it would be possible to develop a weighting rule for health effects based on population burden. EPA staff noted that frequency of disease is an evaluation that is reviewed, and further evaluated frequency during the regulatory determination.

Sub-question # 3.1 – Expert Summary Answer: Experts agreed that the current revised scoring does not reflect the organisms that they are most concerned about. The group also agreed that frequency and population disease burden is missing in the scoring criteria. This information would help to properly reflect the public aspect of the public health risks. It is important to factor in the public burden of disease and frequency to make it reasonable in terms of true public health risk. Experts concluded that the current scoring system was not acceptable, particularly since the overall scores were the factors that determined which organisms would be selected for intervention. They felt that the scoring should be revised; however they did not receive an answer from EPA whether this would be possible. They recommended that the public burden of disease needs to be included in the scoring method.

Question #4: Is the ranked CCL produced by the scoring protocol process reasonable?

Question #4 – Expert Summary Answer: Inconsistencies have been pointed out in above discussions and should be included in the CCL documentation – if this occurs, they would agree that the scoring protocol process is reasonable. Experts would recommend their revised PCCL list is if it is quality assured/quality controlled by outside experts (clinicians).

Expert Microbial PCCL List:

Experts evaluated and rescored each microbe on the EPA PCCL. This table reflects the rank ordered list based on expert review. The comments note why scores were changed.

Exhibit 3: Rank Ordered Microbe List Based On Expert Review

Pathogen	WBDO	Occurrence	Health Effects					Normalized Health Effects Sum	Total Score	Comments
			General	Child	Elderly	Pregnant Women	Chronic Disease			
Naegleria fowleri	4	3	7	7	7	7	7	5.0	9.0	No score changes, yet only 1 WBDO - drinking water (others rec.) - data must be changed on fact sheets.
Legionella pneumophila	5	3	4	3	6	4	6	3.6	8.6	Significant possibility of pneumonia in chronic & elderly - raised scores.
Escherichia coli (pathogenic)	5	3	3	6	6	3	3	3.2	8.2	Pathogenic #0157. Marker org. Hemmoralogic colitis - only major disease assoc.
Shigella sonnei	5	3	3	6	4	3	3	3.2	8.2	Same complications as Salmonella in children.
Giardia duodenalis	5	3	3	5	3	3	3	2.9	7.9	Did not re-score or evaluate b/c already regulated.
Human enterovirus	5	2	2	6	4	2	2	2.9	7.9	A collection of viruses that vary in severity & occurrence. Question of severity vs. commonality - changed scores to reflect.
Salmonella enterica	5	3	3	4	4	3	3	2.5	7.5	Marker org. - rep. all Salmonella orgs. Raised child score -

Pathogen	WBDO	Occurrence	Health Effects					Normalized Health Effects Sum	Total Score	Comments
			General	Child	Elderly	Pregnant Women	Chronic Disease			
										complications.
Campylobacter jejuni	5	3	3	6	4	3	3	3.2	8.2	Gastroenteritis is self-limiting (except in children).
Cryptosporidium parvum	5	3	3	3	3	3	4	2.5	7.5	
Hepatitis A virus	5	3	3	3	4	3	3	2.5	7.5	
Vibrio cholerae	5	1	3	4	4	4	4	2.5	7.5	Doc. Occurrences were not waterborne. Hospitalization not always nec. - lowered scores.
Rotavirus	4	2	3	6	3	3	3	3.2	7.2	Only 1 documented case (lower occ score), 50-80 child deaths per year (R. Glass) - raise scores to reflect.
Arcobacter butzleri	5	3	3	3	3	3	3	2.1	7.1	Outbreaks in Idaho & Ohio. Taxonomy grouping questionable. Lesser score b/c complications are uncommon, no hospitalization.
Entamoeba histolytica	5	1	3	3	3	3	3	2.1	7.1	More adult cases than children, do not always require hospitalization - lowered child score.
Human adenovirus	5	2	2	4	4	2	2	2.1	7.1	
Human calicivirus	5	3	2	4	4	2	3	2.1	7.1	Documented deaths & hospitalization & resistant to chlorine - raised chronic score.

Pathogen	WBDO	Occurrence	Health Effects					Normalized Health Effects Sum	Total Score	Comments
			General	Child	Elderly	Pregnant Women	Chronic Disease			
Plesiomonas	5	3	2	3	3	2	3	1.8	6.8	Not on orig. PCCL, but EPA added b/c of new data.
Cyclospora cayetanensis	4	3	3	4	4	3	3	2.5	6.5	US occurrence - changed score.
Mycobacterium avium	4	3	3	3	4	3	3	2.5	6.5	Most infections are minor (except elderly & those w/ chronic disease).
Hepatitis E virus	2	2	5[1]	3	3	7	3	4.3	6.3	Can't eval. General health effects w/out manifestation data (extreme or common) or frequent (exposure to disease), except in pregnant women.
Fusarium solani	1	3	4	4	4	4	4	2.9	5.9	Exposure is very frequent but common manifestation asymptomatic.
Toxoplasma gondii	2	1	2	2	2	7	2	3.2	5.2	Causes fetal illness so raised pregnancy score. Asymptomatic disease in general pop, so score lowered.
Exophiala jeanselmei	1	3	3	3	3	3	3	2.1	5.1	Common manifestation of illness is minimal, sub-clinical (soft tissue infestation mainly). Severe disease possible but unlikely - scores reflect.

Pathogen	WBDO	Occurrence	Health Effects					Normalized Health Effects Sum	Total Score	Comments
			General	Child	Elderly	Pregnant Women	Chronic Disease			
Helicobacter pylori	1	3	3	3	3	3	3	2.1	5.1	Lesser score - too weighted re: malignancy concern (less than 10% to gastroenteritis). Common manifestation literature avail.
Yersinia enterocolitica	1	2	3	4	3	3	3	2.5	4.5	EPA cited outbreaks in water so occ. Will remain as 2. Appendicitis possibility in children only - adjusted scores accordingly.
Human astrovirus	2	2	2	2	2	2	2	1.4	3.4	No data of hospitalization.
Aspergillus fumigatus	1	3	3	3	3	3	3	2.1	5.1	No changes in scores.
Aeromonas hydrophila	1	3	2	3	3	2	2	1.8	4.8	Outbreaks in Bangladesh & Nigeria.
Human coronavirus	1	1	2	2	2	2	2	1.4	2.4	Only 1 case, overseas - sewage inhalation (not drinking water).
Microsporidia	1	2	2	2	2	2	2	1.4	3.4	Detection is not up to par, adverse health effects less likely in sub-pops - lowered scores.
Blastocystis hominis	1	1	2	2	2	2	2	1.4	2.4	
Isospora belli	1	1	2	2	2	2	2	1.4	2.4	No score changes.

1. Subsequent to the workshop, reviewers provided varying comments regarding the general scoring for Hepatitis E Virus. One expert requested that the score of 5 is lowered to a 2 due to the minimal probability of subclinical infection. Another expert requested that the general score be changed to a 3 rather than a 2 because the incidence data for subclinical infections is not well-defined. The score was not lowered due to the lack of group consensus.

General Charge Question: Does the Draft CCL 3 microbe list represent those pathogens that have the highest potential to occur in public water systems and cause adverse human health effects? Are there pathogens on the Draft CCL 3 list that should not be listed and, conversely, are there pathogens that should be listed?

The experts went through each of the contaminants on their newly developed PCCL list and voted on what ***should*** and ***should not*** be included on the draft CCL. It is important to note that pathogens carried forward from the expert's PCCL list are not necessarily based on score or rank. The panel felt that any "cutoff" value would be arbitrary. Selection of a population of organisms for control would have to consider additional factors than simply an overall score. This is illustrated in this exercise.

Experts voted on each on the pathogens based on their potential to cause adverse human health risks and their prevalence in water. In addition, not all experts were prepared to render a definitive vote on all pathogens. The ranking below reflects the general consensus only of those who voted.

Exhibit 4: Rank Reflecting General Consensus of Experts that Voted

Expert CCL		**Number of Expert Panel***		
Pathogen	Total Score	For Inclusion	Against Inclusion	Abstained
Legionella pneumophila	8.6	6	0	0
Escherichia coli	8.2	5	0	1
Shigella sonnei	8.2	4	0	2
Human enterovirus	7.9	6	0	0
Campylobacter jejuni	7.5	4	0	2
Salmonella enterica	7.9	4	0	2
Hepatitis A virus	7.5	6	0	0
Rotavirus	7.2	3	3	0
Human adenovirus	7.1	6	0	0
Human caliciviruses	7.1	6	0	0
Mycobacterium avium	6.5	4	2	0

*All other organisms received one or no votes for inclusion.

However, this exercise was done only to gauge the experts' reaction to some changes to the CCL based on their new scoring. What was ultimately decided is that overall, EPA's approach was reasonable. Experts agreed with EPA's ranking, but they identified some concerns. For example, although *Naegleria fowleri* received a high score, it may not be appropriate to include it on the CCL due to its rarity in the environment. Experts also discussed the issue of organisms that are controlled with treatment such as *Salmonella enterica, Shigella sonnei, Yersinia enterocolitica* and *Vibrio cholerae,* and their standing on the CCL; however, there was no consensus on this issue. In addition, experts discussed the issue of emerging contaminants such as *Helicobacter pylori* that require additional research, yet may be discovered to have great

health effects consequences; and therefore, should be elevated on the CCL. Furthermore, it was discussed that the current protocol may not account for chronic diseases and may focus on acute disease manifestation and data, such as the case with *Helicobacter pylori*.