National Drinking Water Advisory Council (NDWAC) Contaminant Candidate List (CCL) Classification Process Work Group

September 18-19, 2002
Washington, DC

Meeting Summary

- Final -

Table of Contents

Welcome and Introductions

The first meeting of the NDWAC CCL Classification Process Work Group was held on September 18-19, 2002. The meeting objectives were

- discuss purpose of the CCL Classification Process Work Group;
- gain an understanding of the neural network and VFAR approaches recommended by the National Research Council (NRC);
- identify questions and issues the work group needs to address and tasks to be conducted to prepare for subsequent meetings;
- identify technical expertise needed on the technical subgroups;
- review CCL Classification Process Work Group ground rules;
- determine meeting schedule for remainder of 2002.

Ephraim King, U. S. Environmental Protection Agency (EPA), welcomed everyone to the meeting. He commented that the general purpose of the work group is to review the NRC recommendations and provide advice to EPA, through the NDWAC, on the CCL classification method. He referred members to the NDWAC ground rules for all work groups (see attachment A). Mr. King expressed excitement for beginning the work group process, noting that developing an approach for the CCL may be the most significant change in twenty-five years in how drinking water risks are identified and addressed. He commented that because the second CCL (CCL2) must be published in February 2003, EPA will develop the CCL2 using the past model used for the first CCL in 1997. Mr. King thanked the NRC presenters and EPA staff for their work preparing for the meeting.

Facilitator Abby Arnold, RESOLVE, introduced herself and asked the work group members and other meeting participants to introduce themselves (see attachment B). She reviewed the materials that were distributed for the meeting and then reviewed the agenda (see attachment C).

Overview of Purpose of Work Group

Ann Codrington, EPA, outlined the statutory requirements for the CCL, the process used to develop the first CCL, EPA steps toward CCL2, the NRC recommendations for future CCLs, and the scope and timeframe of the work group (see attachment D). Ms. Codrington explained that EPA's agenda for standard setting is set forth by the Safe Drinking Water Act (SDWA) as amended in 1996. Key requirements of the SDWA include publishing a CCL every five years and making regulatory determinations on the contaminants listed on the CCL. Ms. Codrington commented that EPA is using lessons learned from the first CCL as it moves to developing the next CCLs. She explained that EPA asked the National Research Council (NRC) of the National Academy of Sciences to provide advice on classifying and prioritizing drinking water contaminants. The charge presented to the work group is to discuss, evaluate, and provide advice on implementing the NRC recommendations.

In response to a question EPA explained that the regulatory determination process is specified by statute, but information gathered or systems developed for the CCL process potentially could be helpful for regulatory determination. EPA staff also explained that EPA has not decided on the neural network classification approach for the CCL and would be open to having the work group explore other classification tools.

EPA later clarified that the CCL2 is not the focus of the work group. EPA would like the work group to examine a more comprehensive approach than could be accommodated by February 2003. To the extent possible, the work group's comments will be factored into the CCL2 after February 2003. He asked that the work group develop a report at a level of detail one step greater than the NRC report.

Overview of *Classifying Drinking Water Contaminants*

Deborah Swackhamer, NRC Committee on Drinking Water Contaminants, University of Minnesota, presented an overview of the work and recommendations of the NRC committee (see attachment E). She explained that the committee's work included two phases and produced three reports: *Setting Priorities for Drinking Water Contaminants* (1999), *Identifying Future Drinking Water Contaminants* (1999), and *Classifying Drinking Water Contaminants* (2001). She outlined the two-step approach recommended by the committee in the 2001 report. Step one would narrow the "universe" of all possible contaminants down to a preliminary CCL (PCCL), and step two would narrow the PCCL down to the CCL.

Some members commented that "potential" adverse health effects as a factor in developing the PCCL would need to be clarified since most any substance has potential effects under the broadest definition. One member suggested that a measure of the probability of potential effects could be used to screen contaminants from the universe to the PCCL. Dr. Swackhamer responded that such a measure might work as a screening factor if it could be calculated quickly. She stressed that screening from the universe of contaminants to the PCCL should be quick and coarse to accommodate thousands of contaminants, which is why the committee chose a binning approach based on potential and demonstrated occurrence in drinking water and potential and demonstrated adverse health effects.

In response to questions, Dr. Swackhamer and other NRC committee members made the following additional comments:

- The committee considered multimedia exposure.
- The committee had extensive discussions on data quality and how to address data gaps and uncertainty. The committee concluded that the CCL process should not just rely on existing datasets but should actively address data gaps and uncertainty.
- The committee implicitly avoided grouping contaminants. The general thinking was that grouping would be a consideration later in the process when regulating contaminants. The committee, however, did not recommend that contaminants not be grouped for the CCL classification process; it may make sense to keep certain contaminants together.
- The NRC made a conscious decision not to consider treatment in the classification approach.

Additional comments from individual work group members included the following:

- Where possible, EPA should take advantage of nationwide health tracking being done by other agencies.
- Data collected for the Endocrine Disrupter Screening and Testing Advisory Committee (EDSTAC) would be a good starting point for the universe of contaminants.
- Determining the balance of risks and benefits should involve consideration of secondary impact and risk, such as worker safety at treatment plants.
- An important reason for transparency is to allow a broad group of people to understand the

process and join the discussion on weighing risks and benefits.

Underlying Public Participation and Communication Considerations

Rebecca Parkin, NRC Committee on Drinking Water Contaminants, George Washington University, explained that the committee felt it was important to consider non-technical as well as technical issues to make the process credible (see attachment F). She stressed that the non-technical issues provided a framework for the committee's discussions. Dr. Parkin reviewed the specific issues considered by the committee, including sound science, the task of classification, risk perception, protection of vulnerable subpopulations, transparency, and public participation. Key issues the committee identified included the following:

- The decision tool must be justified to the satisfaction of stakeholders.
- The underlying rationale for the approach chosen must be clearly presented.
- The relationships between EPA's judgments and the tool's results must be stated.
- Decisions that may be controversial must be anticipated and addressed early.

The committee's recommendations on these issues were as follows: 1) use a broad definition of vulnerable subpopulations to ensure protection of the public's health; 2) treat transparency as fundamental to the design and development of the entire process; and 3) involve the public substantively, early and throughout the process.

Ms. Arnold commented that the challenge to the work group is to be innovative in regard to public involvement and communication. A work group member suggested looking at other EPA programs for ideas of successful models. A NRC committee member noted that some European models are discussed in the committee's report. A work group member commented that the National Environmental Justice Advisory Council has worked with the states to form "hearing sections" to provide opportunities for two-way communication with the public.

Presentation and Discussion of Recommended Neural Network Approach

Catherine Peters, NRC Committee on Drinking Water Contaminants, Princeton University, presented the approach recommended by the committee for narrowing the PCCL to the CCL (see attachment G). She explained that the methods the committee considered for developing a classification algorithm were rule-based algorithm and prototype classification. The committee recommend a prototype classification approach such as a neural network method. A classification prototype approach would use contaminant data and past regulatory decisions to "train" or calibrate a model to predict whether new contaminants on the PCCL should be placed on the CCL. The approach is based on the construction of a training dataset—data on the features or attributes of a chosen set of contaminants. The model uses the training dataset to determine what features or attributes indicate that a contaminant warrants consideration for the CCL list.

Dr. Peters described the framework the committee presented for how a prototype classification approach could be used, in conjunction with expert judgment, to develop the CCL. She also described how the committee demonstrated the prototype classification approach by 1) constructing a training dataset, 2) fitting a neural network model to it, 3) examining the errors, and 4) testing the model with contaminant data. She stressed that the exercise was done with limited time and resources and was meant only to serve as an example of the kind of analysis

EPA could do and the kind of information that could be provided by a prototype classification approach.

A work group member commented that a statistical approach is appropriate but suggested that other models in addition to neural networks should be considered. Dr. Peters clarified that the committee's recommendation was not that EPA should use a neural network model but that EPA should use some kind of model that lets the data define the algorithm. The member also suggested it would be good to formally incorporate expert judgment into the process at the step from the PCCL to the CCL as well as the step from the universe of contaminants to the PCCL.

A member expressed concern about using currently regulated contaminants as the training set. He noted that many contaminants have been regulated because Congress required them to be regulated. Dr. Peters reminded the group that the CCL classification process is not to determine the level at which a contaminant should be regulated but rather to determine whether a contaminant should be considered for regulation. Another member noted that choosing the training set and then assigning and weighting attributes in the training set are the critical steps in the approach.

Observing that the proposed prototype classification approach essentially replicates past decisions, a member questioned whether this approach would, in the end, be an improvement from the approach used in the past. Another member observed that while he saw merit in the proposed approach, other methods, such as structured discourse, can also lead to coherent, rational decisions. Dr. Peters responded that the committee began with the idea that the process needed to include more contaminants—on the order of thousands at the PCCL level—and then decided that the past method of using expert judgment would not be able to handle that many contaminants. Dr. Parkin added that prototype classification is intended as a tool to be used, along with expert judgment, within the larger public process.

In the second presentation, Nancy Kim, NRC Committee on Drinking Water Contaminants, New York State Department of Health, described the method the committee used to score contaminant attributes for the algorithm for the committee's demonstration of the prototype classification approach (see attachment H). The committee chose five attributes: two related to health (severity and potency) and three related to occurrence and exposure (prevalence, magnitude, and persistence-mobility). Dr. Kim noted that to the extent possible, the scoring systems for the attributes were designed to allow both chemical and microbial contaminants to be scored with the same system. After explaining how each attribute was scored, Dr. Kim shared several lessons learned from the exercise: 1) denominator data should be included in databases (number of detects, number of analyses); 2) calculating median concentrations using non-detects was not the right approach; 3) because the data systems with information on potency are more mature and better developed than those for occurrence, data quality and comprehensiveness are probably better for potency; and 4) naturally occurring chemicals and essential nutrients may need different scoring than xenobiotics.

A member noted that potency was scored based on low observed adverse effect level (LOAEL), no observed adverse effect level (NOAEL), or reference dose (RfD), depending on which value was available for a given contaminant. He asked Dr. Kim whether the scores, therefore, should be standardized somehow. Upon reflection following the meeting, Dr. Kim responded that the scores should not have to be standardized because although LOAELs, NOAELs and RFDs were

ranked separately by scoring chemicals within the range from the highest to the lowest value in each group, they are correlated to some extent already. For example, LOAELs and NOAELs for many chemicals differ probably by a factor of 2 to 5, and NOAELs and RfDs for many chemicals probably differ by a factor of 100. As such, using the different values for scoring probably does not matter too much for most chemicals since this is roughly an order-of-magnitude scoring.

In response to another question, Dr. Kim explained that consideration of sensitive subpopulations factored into the scoring of severity in that scores were based on the most sensitive health effects. A member noted, however, that existing databases do not cover many of the populations identified as more sensitive.

Asked how scoring could be done for contaminants on which there are no data, Dr. Kim suggested that structure-activity relationships (SARs) or quantitative structure-activity relationships (QSARs) may have to be used. She said that the question to address then would be how to compare scores based on SARs or QSARs with scores based on LOAELs, RfDs, or other experimental values. She noted that for the demonstration, all of the contaminants were scored, even if data were absent, and commented that the work group will have to decide how to move forward without data on all contaminants.

The work group discussion moved from scoring attributes to the universe of contaminants and screening criteria for narrowing the universe to the PCCL. A member commented that rather than starting with the universe and applying a filter, perhaps the approach should begin by determining which contaminants are causing public health problems and addressing them. Another member responded that the public health community has stressed the importance of a forward-looking model that does not wait for a problem to develop to identify contaminants to regulate.

Presentation and Discussion of Recommended VFAR Approach

Jeffrey Griffiths, NRC Committee on Drinking Water Contaminants, Tufts University School of Medicine, and Joan Rose, NRC Committee on Drinking Water Contaminants, University of South Florida, introduced the virulence-factor activity relationship (VFAR) approach. (A VFAR is defined as the link between the biological characteristics of an organism and its ability to cause harm.)

Dr. Griffiths made the first presentation (see attachment I). He explained that developing a database of potential and emerging pathogens is limited by the traditional approach to detecting pathogens, which requires identification and culturing of a pathogen. In contrast, the VFAR approach identifies potential and emerging pathogens through inferences based on organisms' genomic and proteomic components and known links between those components and health effects. The VFAR approach asks whether an organism resembles a known harmful organism in regard to key characteristics such as surface proteins, toxins, attachment factors, metabolic factors, or invasion factors. Dr. Griffiths commented that there has been a phenomenal growth in knowledge in the fields of genomics and, to a lesser degree, proteomics in recent years, which strengthens the feasibility of the VFAR approach.

In response to questions, Dr. Griffiths and Dr. Rose made the following points:

- Studies have been done on the extent of correlation between characteristics and virulence. Generally, the less similar the genetics of the organisms, the less inference can be drawn. The robustness of the method is high.
- The NRC committee felt that VFARs should be developed for use in EPA's drinking water program. They may be useful in the step of moving from the universe of contaminants to the PCCL as well as in the step from the PCCL to the CCL.
- The databases and relationships are not yet sufficiently developed for all of the important attributes. For example, there is not a lot of data to correlate genes to potency.
- Microbes on the CCL generally end up in the category of "more research needed." Molecular approaches can help move this bottleneck forward.
- EPA can use the GenBank database to help characterize organisms. The question then is how to detect the organisms, though our detection ability is good and improving. Occurrence information is more likely to come from knowing that a microbe exists in urine, feces, or water than from VFARs.
- Information such as clinical and outbreak data and hospitalization rates can be used to account for sensitive subpopulations for the health effects attributes. Potency will be the same among sensitive individuals and the general population, but the severity or outcome may be different.
- Ecological data are also important, though currently they are not being collected into a database.

Comments from individual work group members included the following:
- An additional attribute for treatment should be considered for the step from the PCCL to the CCL.
- Water systems collect occurrence data on some microbes and could easily supply that data to EPA.

Dr. Rose began her presentation by outlining several conclusions about developing the VFAR approach: 1) data mining and data management will be the backbone of the program; 2) more than just virulence genes will be needed; 3) microarray technology will provide one of the tools needed to gain the necessary information; and 4) there has been a tremendous explosion of the science recently (see attachment J). Using *Escherichia coli* as an example, Dr. Rose illustrated the kinds of knowledge and data that exist or are being developed currently. She explained that typically it is not one gene sequence that is of interest but a whole series of gene sequences. Microarray technology enables researchers to check for similarities among series of sequences. The degree of homology gives some indication of whether inferences may be drawn, though Dr. Rose cautioned that even with a high degree of homology, incorrect inferences could be made. Again using *E. coli* as an example, Dr. Rose said that the current step to move VFARs forward is largely a matter of data mining: review the literature on *E. coli* to select representative genes, download the gene sequences, and apply microarray technology. She offered examples of the databases and software available to assist in these tasks and noted that comparative genetics has begun to play a similar role in the study of foodborne pathogens. In closing, Dr. Rose commented that VFARs have the potential to be used currently.

A member observed that a lot of information is available from genomics and proteomics, but how it should be used in determining virulence, potency, or other attributes is not yet clear. Dr. Rose agreed, commenting that one remaining question is how to weight genomic information to obtain reliable predictions. She said that the first step is to determine what data are available and

how to query the data for known pathogens. She commented that the initial genes chosen will be critical: they must be genes for which there is sufficient information in the database for a potentially successful test.

Asked whether data are available to consider chronic exposure rather than acute, Dr. Rose said that some information is available to take chronic health outcomes into account.

A member commented that it seems that microarrays could be used to screen from the universe of contaminants to the PCCL, but a threshold of homology would need to be established. Another member responded that there must be at least seventy percent homology for microarrays to be technically feasible. He noted that there are differences in working with nucleotide sequences, which have four bases, versus protein sequences, which have twenty amino acids. He commented that proteomics is perhaps eight years away from being developed to the point of being useful for VFARs, while genomics is closer. The timing may be such that genomics can be employed in developing the third CCL and proteomics will be viable for developing the future CCLs.

Dr. Griffiths reminded the group that what the NRC committee concluded was that VFAR merits further consideration, and what the committee recommended was that EPA conduct feasibility projects to determine the usefulness of VFAR. EPA staff noted that the work group's charge includes pilot projects and EPA's request is that the work group help determine whether and how current knowledge on VFARs could be used in the CCL process. Dr. Rose commented that the first step is development of VFAR as a tool and the second step is to determine how it could be used in the process. A member commented that though VFAR may not yet be perfected it seems to be the best tool on the horizon. He added that the public will want to know that it is a sound tool for the applications for which it is recommended. Another member commented that there will be knowledge gaps for chemical contaminants as well. He said given that information will never be perfect, the task is to decide whether we have an approach that can be used with other tools to get reasonable answers, keeping in mind that these are tools for developing the CCL, not for making regulatory determinations. EPA staff noted that VFAR is an umbrella term for several tools, some of which may now be feasible for certain applications while development of others continues. Dr. Griffiths added that having a transparent, defendable method is key.

Operational Protocols

The four work group members who also serve on the NDWAC helped to clarify the relationships between the NDWAC and EPA and the NDWAC and the work group. The NDWAC views itself as an advisory group; it does not make decisions for EPA. The NDWAC's usual approach for issues that require in-depth thought (such as the CCL classification process) is to establish a work group with the appropriate, focused expertise and stakeholder representation. The role of NDWAC members who serve on the work group is to clarify the NDWAC's request of the work group and to represent the work group's discussions and recommendations back to the NDWAC. In establishing work groups, individuals and organizations nominate candidates, but once appointed, work group members serve as individuals (i.e., members sign on to final work group products or recommendations as individuals, not as organizations).

The work group discussed and revised its operational protocols (see attachment K). Section 1 of the protocols, the group's mission, was revised as follows:

The purpose of the National Drinking Water Advisory Committee (NDWAC) Work Group on Contaminant Candidate List (CCL) Classification Process is to provide advice to the NDWAC as it develops recommendations for the U.S. Environmental Protection Agency (EPA) on the classification process and its application to contaminants to develop its list of candidate contaminants. The work group is charged with:

> Evaluating recommendations made by the National Research Council, including methodologies, activities and analysis, and making recommendations for an expanded approach to the CCL listing process. This may include, but not be limited to, advice on developing and identifying:
>
> i. Overall implementation strategy
> ii. Classification attributes and criteria (and methodology that ought to be used)
> iii. Pilot projects to validate new classification approaches (including neural network and other prototype classification approaches)
> iv. Demonstration studies that explore the feasibility of the VFAR approach
> v. Risk communication issues
> vi. Additional issues not addressed in the NRC Report

The product of the work group will be a set of recommendations, including the methodology to implement the recommendations. Ms. Arnold explained that the group would revisit the protocols at its next meeting and adopt them if all members agree to them.

Questions to Answer

The work group began to identify and list questions it would need to answer to fulfill its charge of advising EPA on developing and implementing a CCL classification process (see attachment E). The work group will revise the list as the process continues, adding, deleting, or modifying questions as necessary.

Public Comment

No members of the public expressed an interest in making comments to the work group at this meeting.

Next Steps

The work group identified four activity areas for small group discussions prior to the next plenary meeting. Each member chose an area in which to be involved. EPA agreed to provide materials to the members of each activity group. Ms. Arnold explained that RESOLVE would contact members for their schedule availability and arrange a conference call for each group.

Activity: Characterize the universe of contaminants
Members: Laura Anderko, Gary Lynch, Rick Becker, Wendy Heiger-Bernays, Nancy Kim, Buck Henderson

Activity: Discuss classification systems including prototype options
Members: Ken Reckhow, Doug Crawford-Brown, Laura Anderko, Alan Elzerman, Michael Dourson

Activity: Review approaches for VFAR
Members: Jeff Griffiths, Colin Stine, Graciela Ramirez-Toro

Activity: Draft guiding principles for the work group
Members: Ed Thomas, Benson Kirkman, Brian Ramaley, Ken Merry, Wendy Heiger-Bernays

Future Meeting Dates

The work group chose dates for meetings in December and February as listed below. Members also agreed to hold two sets of dates in March, one of which will be chosen for a meeting depending on the group's progress.

- December 16-17, 2002
- February 5-6, 2003
- March 5-6 or 27-28, 2003